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Tamil Nadu Chapter

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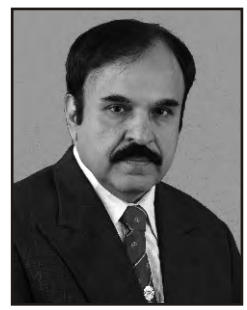

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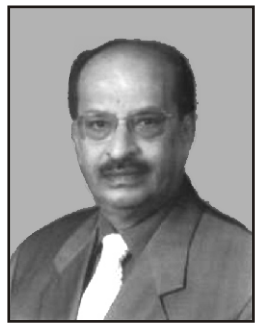
Contents

Chairman's Message



My dear friends,

I with great pleasure wish you all very happy and prosperous New Year. May this 2010 bring in all the fame, wealth and very good health to each one of you, your family and loved ones.

We have 491 members in our fold; I request each and every one of you get 1 new member in to our Tamilnadu chapter of API. TAPICON 2010 will be held on 3rd and 4th of April at Chennai. I once again request all our esteemed members to induct 1 new member into our association. I know you all can do it and you will do it so that in Chennai TAPICON 2010 we will have at least 800 members. This is my humble request. More the numbers more stronger we will be and our association will do well in near and distant future.

With warm regards and best wishes

Yours

Dr. A.R.Vijayakumar, MD.,
Email id: vatcbe@vsnl.net, drvijayakumar@gknmh.org

From the Editor's Desk

Dear Colleague,

I am happy to present to you the first issue of 2010. The quality of articles is going up and this time we have some good original articles, case reports and review articles written by experts from all disciplines of medicine and from all parts of the state.

I hope you will find the articles interesting and useful in your practice.

With warm regards

Dr Vijay Viswanathan MD., Ph.D., FRCP (London)
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ASSOCIATION OF PHYSICIANS OF INDIA
TAMIL NADU CHAPTER

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The Secretary
Association of Physicians of India – Tamil Nadu State Chapter
Chennai.

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Original Article

Myasthenia Gravis – Phenotypic Characters and Course in a South Indian Population

Dr. S.R.Chandra*, Dr. Sinchu Mangett**

ABSTRACT

This study reports the three years experience of Government Medical College, Trivandrum in patients with Myasthenia Gravis. Analysis of phenotypic characters, correlation with age, sex, antibody response, thymic tumours, morbidity, mortality and course are analyzed. The study reveals males were affected than females. Ocular onset is commonest but more than fifty percent turned generalized. Crisis occurred in 22%, which was heralded by drug default or infection in majority of cases. Generalized myasthenia and thymoma-associated patients carry higher risk of crisis. More than one hospital admission was needed in 28% only. No definite correlation between clinical course and antibody status was observed in contrast to the study reported from Karnataka. Good quality of life is achieved in majority of patients though full immunological, electrophysiological remission is not always reached.

Key Words

Myasthenia gravis, AChRAb, Quality of life.

INTRODUCTION

Myasthenia gravis is a well known disease of neuromuscular junction transmission. It was first described by Thomas Willis – 17th century physician in 1672 [1]. Friedrich Jolly called it as pseudoparalysis. Lindsay in 1899 introduced the term Myasthenia gravis. In 1934, Mary Walker of St. Alfege's hospital described the use of anticholinesterase. The autoimmune nature was established in 1973[2]. However, the factors that initiate, sustain or produce remissions is not very clear. In 1984, Gourie devi et al reported a prevalence of 2/100,000 population[3], female to male ratio is 57:43, average age of onset is 28 for females and 42 for males but after 50 years males are more affected[4]. Thymus, anti-acetylcholine receptor antibody (anti-AChRAb) and anti-muscle specific kinase (anti-MUSK) antibody are etiologically implicated[5]. Here we analyze the role of phenotypic characters like generalized, ocular, bulbar, limb onset and the presence of anti-AChRAb, thymoma and other comorbidities in predicting the prognosis and outcome.

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PATIENTS AND METHODS

We analyzed all the patients with Myasthenia Gravis treated in the neuromedicine department of Government Medical College, Trivandrum from the year 2005 January to 2008 January. All patients had fatigable muscle weakness involving ocular, bulbar, neck and or all muscles. All patients were evaluated using Myasthenia Gravis Foundation of America scale (MGFA)[6]. Maximum scale reached by the patient is crisis and intubation[5]. Post intervention scale was used to measure outcome. Patients score in the last outpatient follow-up was compared to the maximum score reached by the patient. Poor outcome was considered under the following situation, death, MGFA scores unaltered or worsening, need for pyridostigmine more than 120 mg per day or prednisolone dose required more than 0.5 mg / kg for maintenance. All patients had positive response to neostigmine and had more than 10% decrement in repetitive nerve

stimulation test conducted in the electroneuromyography laboratory of the government medical college hospital, Trivandrum, Kerala state, South India. The CT mediastinum was done in the radiology department of the same institution. Thyroid profile and anti-AChRAb were also done. Anti-MUSK Ab were not done in any case. Anti-AChRAb was reflected at the end of one year of treatment in 32 patients. 26 patients remained positive. Repetitive nerve stimulation (RNS) was done on three sites - nasalis, trapeziuus and abductor digiti minimi on the right side. Nasalis: R1 was kept at midpoint of nasalis and R2 above eyebrow. Stimulation was given below and anterior to tragus. Trapezius : R1 was kept midway between acromion and C7 spine and R2 at glabellar point and stimulated behind sternocleidomastoid midpoint between clavicle and mastoid. Abductor digiti minimi : R1 kept over middle of hypothenar muscles and R2 at base of 5^{th} digit and stimulated from wrist. Supramaximal stimulation was used at the stimulating site[7]. Slow RNS (3Hz) was performed at rest, 30 seconds postexercise and repeated every minute for 5 minutes. The amplitude of the CMAP was measured from base to peak. Decrement confined to nasalis was labeled ocular and any of the other muscles if involved was considered as generalized. Single fibre EMG was not done in any case. At the end of one year RNS was repeated in all patients. It was performed after discontinuing pyridostigmine for eight hours and 52% patients revealed normalization in all the muscles tested.

DATA ANALYSIS AND STATISTICAL METHODS

Total patients with myasthenia gravis seen were seventy three. However investigations were completed only in fifty cases. Among these 50 patients there were twenty three females and twenty seven males. There age group varied from eleven years to sixty-five years. Mean age was 39 years. In the age group between 11 years to 19 years there were 5 female patients. In the 20 to 29 years age group there were eight patients, three males and five females. In the 30 to 39 years age group there were 10 patients , 6 males and 4 females. In the 40 to 49 years age group thirteen patients, eight males and five females. In the 50 to 59 years age group seven patients, 6 males and one female. In the age group 60 and above, 7 patients 4 males and 3 females. Females seen to dominate before 3^{rd} decade and males dominated after 4^{th} decade. The duration of disease varied from few months to eleven years. Total hospital admission was only once in 36 patients, twice in 9 patients, thrice in three patients, 4 times in one patient, 6 times in one patient in the last 3 years. First presenting symptom was ocular in 40 patients, bulbar in 2 patients and limb onset in 7 patients. However after evaluation 35 patients were generalized of which 5 were limb onset type, one neck flop onset, 2 bulbar onset type and 22 were ocular onset type. AChR Ab (direct ELISA method only) was considered negative if titres were less than 25, positive if more than 40 and equivocal if between 25 and 40. It was negative in nine all of whom were ocular onset. Among the ocular onset type AchRAb was negative in nine, and positive in 31 out of which nine were ocular only and 22 were ocular with generalized. Equivocal in seven cases, none were ocular onset type. Anti-MUSK Ab were not done in any case. Thymic tumour was detected in 5 patients , there were 3 females and 2 males. One female had thymic lipoma and others had thymoma. Thyroid profile done in 18 patients based on clinical suspicion showed T3 of 415,552,536 in 3 cases, One female and 2 males (normal range 70 to 204) T4 levels were 14, 22, 28 ug, two male and one female (normal range 5-12). TSH 0.005, 0.65, 0.014, 0.01 one female and three males (normal range 0.3 to 5.5) suggests hyperthyroidism in 4 patients – 3 males and 1 female. Low T3 was found in none. T4 was low in 2 cases, 2.9 and 4.1 (range 5 to 12) both were females.

Myasthenic crisis occurred in 11 patients during the 3 year period. Three were females and nine were males. Three of these patients had

undergone thymectomy. Drug default was the cause of crisis in four patients. Five patients had pneumonia as a complicating problem. Two patients succumbed and others survived. One patient was on treatment for reactive depression and commited suicide and died. The mean age of the patients was 39.2 +/- 14.76 years. Males mean age was 44.33 +/- 12.55. Mean age for female is 33.17 +/- 15.12, p value 0.006. Male patients are significantly older compared to female patients. Evaluation of relationship between gender and ocular versus non-ocular presentation using chi square test showed no significant association. Mortality is 6% of which 4% is myasthenic crisis related, 2% is due to reactive depression. Myasthenic crisis was seen in 22% of cases. Among those with crisis 45% were due to pneumonia, 36% due to drug default and 9% was unexplained cause. All the patients who had myasthenia crisis belonged to generalized myasthenia. 27% of patients who had crisis were patients with thymoma in post thymectomy phase.

DISCUSSION

This present study consists of fifty patients with myasthenia gravis confirmed by clinical examination, pyridostigmine test, RNS at rest and post exercise and Anti-AChR antibodies titres. The study period is three years. The mean age of patients is 39 years. Male patients were significantly older compared to females. However no significant gender differences exist between ocular versus non ocular group. Limb onset is found in 10% of patients suggesting that careful evaluation of patients presenting with limb girdle syndrome is likely to be rewarding.

Thymoma is found in about 10% of patients and except the one patient with thymic lipoma, the thymoma group appears to be most prone for crisis. Prognosis does not seem to be altered by the seropositivity for AChRAb positivity in contrast to short communication reported from another study from South India [8]. Crisis is often precipitated by infection. Hence protection from infection and once they occur aggressive treatment of infection is very important.

Nearly fifty percent of patients with ocular onset turned generalized later. Quality of life can be maintained by regular follow up, proper adherence to the drug regimen and careful monitoring of adverse effects and comorbidities management. Patients also need counseling as the treatment is prolonged. Even though immunological and electrophysiological remission is not easily attained effective control of the clinical symptoms can be achieved.

Chart 1: General Details of all Patients

No.	Name	Age	Sex	Onset	Initial Symptom	Type	MG crisis	Steroids	Thymoma	Thymectomy	IVIG	Adm	AChRAb	TFT	Sur
1	G	60	M	58	P	G	N	Y	**	N	N	1	–		
2	S	33	F	33	P	O	N	N	Y	Y	N	1	+		
3	SD	57	M	57	L	G	Y	Y	N	N	N	3	–		
4	P	25	F	15	P	G	Y	Y	NA	NA	N	1	+		
5	F	43	F	39	P	O	N	Y	Y	Y	N	2	–		
6	J	62	F	62	P	G	N	Y	N	N	N	2	–		
7	RK	33	M	27	P	O	N	Y	N	Y	N	1	+		
8	V	43	M	43	P	G	Y	Y	Y	Y	N	3	+		
9	T	54	M	54	N	G	N	Y	NA	NA	N	1	–		
10	S	35	F	34	B	G	Y	Y	Y	Y	Y	1	Equivocal		

No.	Name	Age	Sex	Onset	Initial Symptom	Type	MG crisis	Steroids	Thymoma	Thymectomy	IVIG	Adm	AChRAb	TFT	Sur
11	Y	51	M	48	P	G	Y	Y	Y	Y	Y	6	+		
12	N	22	F	22	B	G	N	N	N	N	N	1	–		
13	S	53	M	52	P	G	N	Y	N	N	N	1	–		
14	S	51	F	50	D	G	N	N	NA	NA	N	1	–		
15	S	13	F	13	P	O	N	N	NA	NA	N	1	+		
16	N	31	M	30	P	G	Y	Y	N	Y	Y	1	+		
17	V	38	M	38	D	G	Y	Y	NA	NA	Y	2	–	I,	
18	S	21	M	20	P	G	Y	Y	N	Y	N	3	+		
19	N	45	F	45	P	G	N	N	Y	N	N	2	+		
20	S	40	F	36	P	O	N	Y	NA	NA	N	2	+		
21	UM	65	M	65	P	G	N	Y	NA	NA	N	1	–		
22	V	61	M	50	P	O	N	N	N	N	N	1	–		
23	S	15	F	15	L	G	N	N	NA	NA	N	1	+		
24	M	47	M	47	P	O	N	N	NA	NA	N	1	+		
25	P	48	M	48	L	G	N	Y	Y	Y	N	4	+		
26	K	35	F	35	P	G	N	N	N	N	N	2	+		
27	R	12	F	12	P	G	N	N	NA	NA	N	1	+		
28	S	35	M	34	P	G	N	Y	N	N	N	1	+	I	
29	SK	29	F	29	P	O	N	N	NA	NA	N	1	+	I	
30	S	16	F	16	P	O	N	N	NA	NA	N	1	+		
31	R	25	F	25	P	O	N	Y	Y	Y	N	2	+		
32	R	45	M	45	P	O	N	N	NA	NA	N	1	–		
33	I	32	M	32	D	G	N	Y	NA	NA	N	2	+		
34	VN	55	M	55	D	O	N	Y	N	N	N	1	–		
35	A	11	F	11	P	O	N	N	N	N	N	1	+		
36	KK	31	M	31	P	G	Y	Y	NA	NA	N	2	+	I	
37	SK	49	F	44	P	G	N	Y	NA	NA	N	1	+		D
38	L	41	F	41	D	O	N	N	NA	NA	N	1	+		D
39	FP	37	F	37	D	G	N	N	Y	Y	N	1	+		
40	H	23	F	23	L	G	Y	Y	NA	NA	Y	1	+		
41	N	40	M	38	P	O	N	N	NA	NA	N	1	–		
42	J	63	F	60	P	G	N	Y	NA	NA	N	1	–		
43	RK	58	M	43	L	G	Y	Y	Y	Y	Y	1	+		
44	I	38	F	37	P	G	N	N	NA	NA	N	1	+		
45	M	48	M	47	P	O	N	N	NA	NA	N	1	–		
46	S	60	M	60	D	G	N	N	N	N	N	1	–		
47	R	40	M	35	P	O	N	Y	N	N	N	1	+		
48	O	21	M	21	D	O	N	N	NA	NA	N	1	+		
49	S	43	M	43	P	O	N	Y	N	N	N	1	–		
50	A	27	M	27	D	O	N	Y	N	N	N	1	+		

CHART 2 Patients with Myasthenic Crisis 11 Patients

Name	Age	Gender	Duration	Crisis	factor	AchRAb	Thymectomy	Steroids	IVIG	PLEX	Survival
S	57	M	1	57	Default	–	–	+	–	–	+
P	25	F	10	25	Pneumonia						
					+	–	+	–	–	+	
V	43	M	1	?	Default	+	+	+	+	–	+
S	34	F	1	35	Pneumonia	Borderline	+	+	+	–	+
Y	48	M	3	51	Pneumonia	+	+	+	+	–	Died
V	38	M	1	38	?unexplained	–	Nil	+	+	–	+
S	21	M	1	21	Pneumonia	+	+	+	+	+	Died
N	30	M	1	31	Default	+	–	+	–	+	+
KK	31	M	1	31	Default	+	–	+	–	+	+
H	23	F	1	23	Pneumonia	+	–	+	+	–	+
RK	43	M	1	43	default	+	Y	+	–	+	+

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Review Article

Treating a diabetic foot ulcer A Challenge?

Dr.P.Vijayarathinam

Introduction

Diabetic foot problems are the commonest cause of hospital admission with a diabetes-related problem. Management of the diabetic foot requires knowledge and practical skills in a number of different key areas, which are diverse and interesting in their own right. As Diabetic foot problems quickly reach a point of no return, it is vital to diagnose them early and provide rapid and intensive treatment. Every year about 40,000 leg amputations are carried for non traumatic conditions in India. Majority of them are diabetic foot ulcers. Is Amputation is the answer? For diabetic foot ulcer. amputation is not the answer. It is the beginning of the end. Of all the amputees, 50 % will loose their other leg or their life in 3-5 years. God has created doctors to save the limb. Not to amputate. Deformed limb is better than absence of limb. Foot Ulcers are independently linked to mortality in diabetic patients. The mortality rate for diabetic patient with a history of foot ulcers was 49.0%, much higher than the 35.2% and 10.5% rates seen in the diabetics without a foot ulcer history and the non-diabetics, respectively. Apart from mortality the morbidity in diabetic foot problem is enormous as it not only causes economic burden on the patient but also the psychological problem like depression. In spite of our best effort of preventive diabetology, foot ulcer remains a challenging complication of diabetes today and increasing day by day. Delayed or inadequate treatment or lack of attention to foot problems results in loss of limb in diabetic foot ulcer. Since Indian diabetic foot ulcers are 95% neuropathic, superimposed by infection we can prevent 99% of lower limb amputation. It is our duty to identify the diabetic foot ulcer early and start the treatment immediately. Time delay will end in catastrophic with amputation of the lower leg. Clinician should start the treatment as soon as he finds the foot ulcer. If not refer the patient to the concerned surgeon immediately insisting the patient that any delay will end up in amputation.

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Normal foot

Normally we have seen many of the Indian people walking bare foot day in and day out. But they don't cause any foot problems because of intricate mechanism of the foot. The human foot is a complex structure composed of 26 bones and 33 joints. It has more than 100 muscles, tendons and ligaments and a net work of blood vessels and nerves, skin and soft tissues. It is also soft but rigid. It is elastic and flexible and serves the purpose of shock absorber and propulsion engine. It took nearly 4 million years of evolution to perfect the human foot. Human foot is an engineering and architectural marvel. It cannot be compared to any structure. All these structures work together to provide the body the support, balance and mobility. A structural flaw or malfunction as it occurs in diabetes or leprosy will result in the development of foot problems like hammer toe, in growing nail, charcot's arthropathy and pathophysiological alterations like autonomic neuropathy and peripheral neuropathy which causes the development of fissures, corn, Callus, dry skin etc. which predisposes the development of foot ulcer and super added infection. Today the number of leg amputations are on the rise. Even for minor ulcer of toe infection amputations are carried out. Reason being poor knowledge of diabetic foot

problems among the public and poor knowledge of diabetic foot management among the clinicians, be it a general practitioner, physician or a surgeon. Proper repeated, patient education about the foot problems to the diabetic persons and proper knowledge about the diabetic foot ulcers to the clinicians will reduce the incidence of lower limb amputations.

Pathophysiology of diabetic foot:

A normal individual responds to infection by increasing the blood supply to the site, as blood supply has to be increased 12-15 times to maintain the viability of the skin. If this increased demand cannot be met, the skin breaks down and tissue necrosis results. Necrosed tissue is a good nidus for organisms to thrive. Arches of the foot helps in the equal distribution of body weight. In diabetes this equal distribution is affected resulting in new pressure points. This is the starting point of foot ulcer in diabetes. Majority of the diabetic foot ulcers are in the region of 1st metatorso phalangeal joint. Foot Pressure abnormalities precede the appearance of neuropathy. High foot pressures predict ulcers. Plantar callus is associated with high pressure and predicts ulcer formation

Why diabetic foot ulcers take long time to heal?

1. Poor blood supply to the distal area
2. Another factor that contributes to development of ulcerations of the foot is the presence of an autonomic neuropathy in many of these patients. They are unable to vasodilate small vessels in response to injury; therefore, a diminished number of WBCs reach the site of injury.

   The diminished number of WBCs can lead to infection and ulceration.
3. Hyperglycemia. Infection increases the counter regulatory hormones, decrease the insulin secretion, and increase the insulin resistance. All these factors worsens the hyperglycemia leading to ketoacidosis. All these worsens the situation and the infection spreads and worsens.
4. Hyperglycemia decreases the immunity of the individual. Diabetes is a secondary immunodeficiency disease. Cells have diminished cell function, inadequate phagocytosis, poor chemotaxis, and diminished microbial killing.
5. Development of oedema further reduces the blood supply, oxygen, nutrients and antibiotic supply. Venous return decreases and stasis occurs. The surrounding medium acts as a good culture media for the organism to grow.
6. The pathophysiology of diabetes significantly alters the wound healing process, leading to an increased risk for foot ulceration.
7. Moist wound heal. Dry wound do not.
8. Offloading the wound augment healing.

Evaluation of the diabetic foot ulcer.

1. Simple X-ray of the affected foot to rule out osteomyelitis.
2. If necessary CAT scan or MRI scan.
3. Culture and sensitivity of the infected wound. Sample should be obtained from deeper areas to get correct culture.
4. Doppler study to assess the blood supply to the distal foot.
5. Blood sugar estimation
6. Urine ketone examination to find out ketosis. Since it is a complication of diabetes, many times pt will be positive for urine ketones.

Treatment of diabetic foot ulcer.

Since the diabetic foot is the sequel of interaction of multitude of factors, intervention must be directed towards correction of all causative factors.

1) Establish the ulcer's etiology; 2) Measure its size; 3) Establish its depth and determine the involvement of deep structures. 4) Examine it for purulent exudates, necrosis, sinus tracts and odour. 5) Assess the surrounding tissue for signs of oedema, cellulitis, abscess and

fluctuation. 6) Exclude systemic infection; and 7) Perform a vascular evaluation.

On seeing the patient with diabetic ulcer if necessary wash the wound with running water. Washing mechanically removes the foreign bodies, reduces the number of micro organism and removes all the dirts which the patient had applied before arriving which is delaying the healing process. Washing the wound with running water is the simple form of cleaning the wound without any expenses.

The nature of treatment fall in

1. Debridement of necrotic tissue i.e. skin, subcutaneous tissue, bones & tendons

(a) More debridement is desirable to less debridement.

(b) Wound that are adequately debrided heal quickly.

2. Opening all the cavities to evacuate the pus and for proper drainage.

3. Incision of abscess and deroofing the abscess cavity.

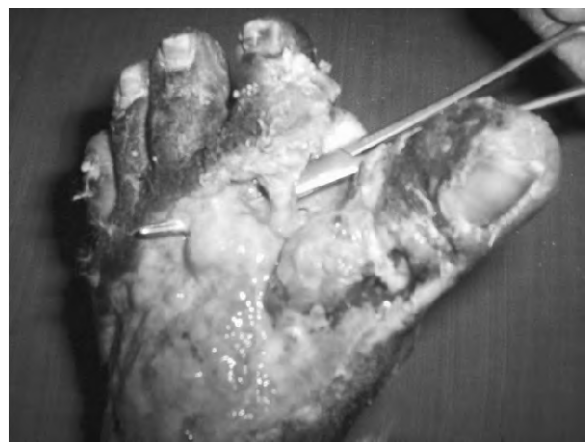
4. Decompression of the oedematous areas to enhance and improve the blood, oxygen, nutrients and antibiotic supply and also for adequate venous return.

Débridement

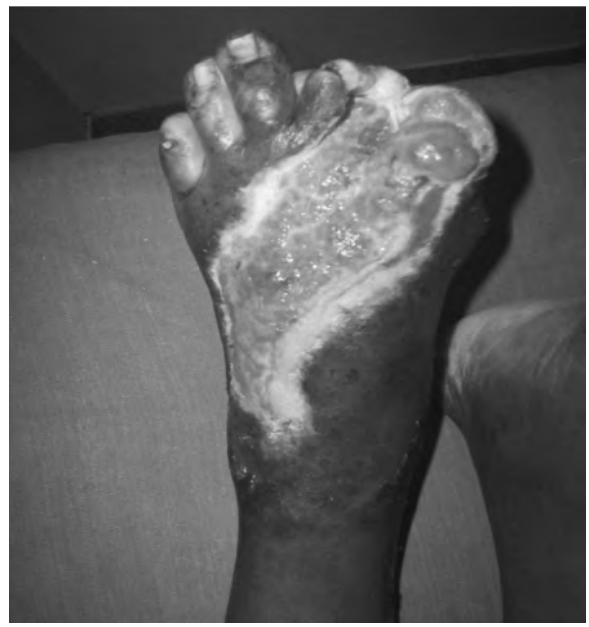
The removal of necrotic and dead tissue as well as foreign and infected material from the wound — is a crucial part of this process. Although autolytic, enzymatic, or chemical debridement may be used, sharp débridement is more commonly used and has been the most thoroughly studied and found to be useful than other forms of treatment

Sharp débridement involves the removal of callus and may be carried out with the use of a scalpel and forceps. Surgical debridement should be done until good healthy granulation tissue develops; it not only cleans the wound of necrotic and infected tissues but also changes the chronic wound into an acute one. Acute wounds have been shown to behave differently from chronic ones. Patients with foot infections should be explored and abscesses drained completely at an early stage. All necrotic tissue must be widely debrided.

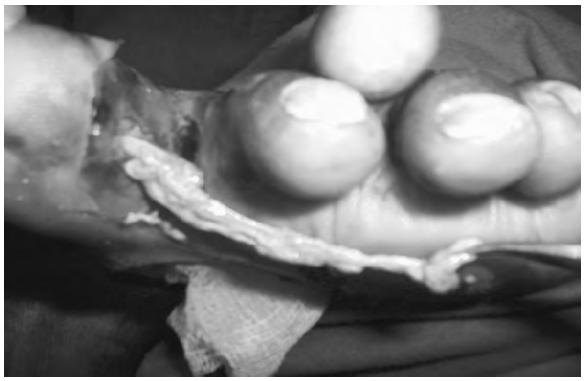
Sharp debridement is contraindicated in the presence of severe occlusion. If the patient has a dry intact eschar, do not debride, but if it is wet and loose, the loose tissue should be removed gently without causing damage to viable tissue. Diabetic patients may also present with lower-extremity ulcers of venous, vasculitic, or other etiologies. The underlying pathophysiology needs to be addressed even when it is not related to diabetes. Misdiagnosis may result in a higher incidence of morbidity and mortality.



Unhealthy granulation tissue



Healthy granulation 45 days after repeated debridement



Remove all the necrotic tissues.

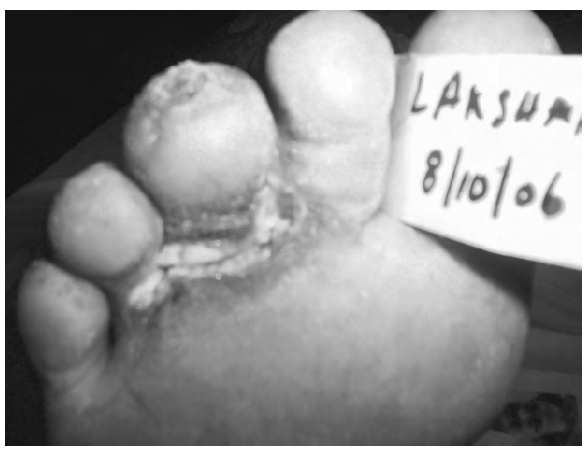
How to manage a simple ulcer:

Examine the foot of every diabetic patient because of it is of paramount importance. Since most of the diabetic foot problems are painless and the patients are unaware of it because of insensitive foot.

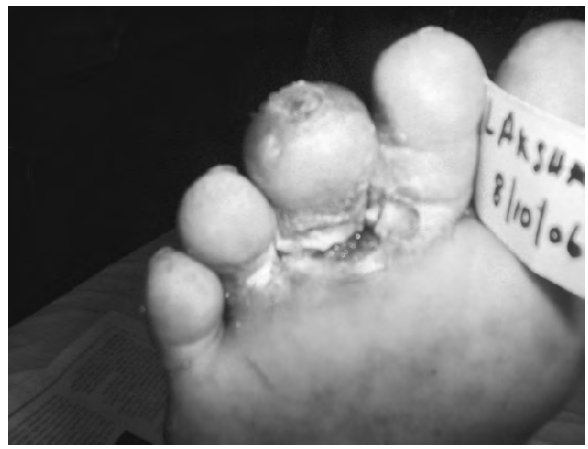
The presenting ulcer may be simple but non- healing for months together. The small ulcer which appears to be a small and superficial may be only the tip of the iceberg. It may be a penetration deep into the deeper tissues.

If it is contaminated, ask the patient to wash the ulcer and its surroundings in running water. After cleaning the wound apply a saline gauze, pad and apply a tight bandage.

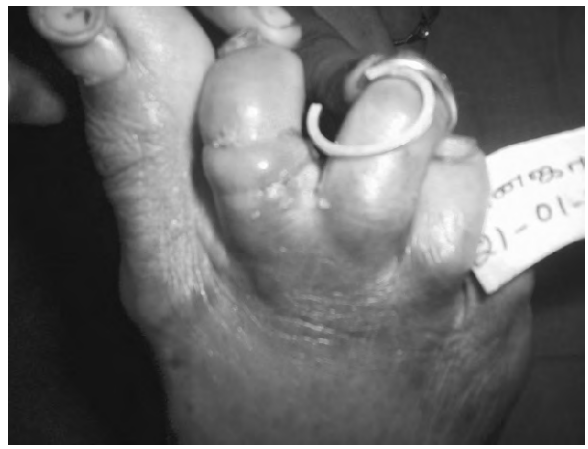
Scooping: Scooping out all the purulent material from the ulcer bed. By just scooping the dead tissue and pus the wound gets cleaned



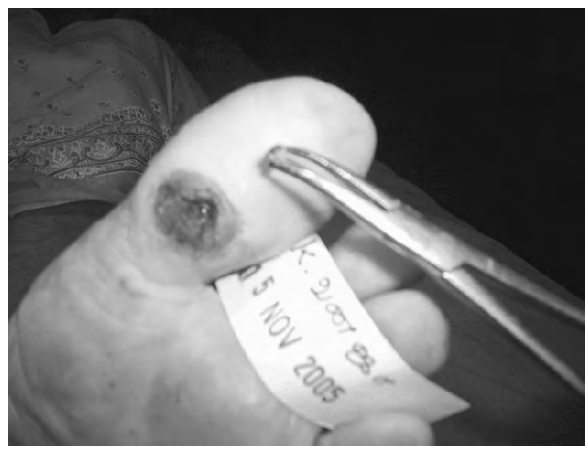
Infected wound



Necrotic tissue debrided. Clean wound



Toe ring constiction Oedema & Infection

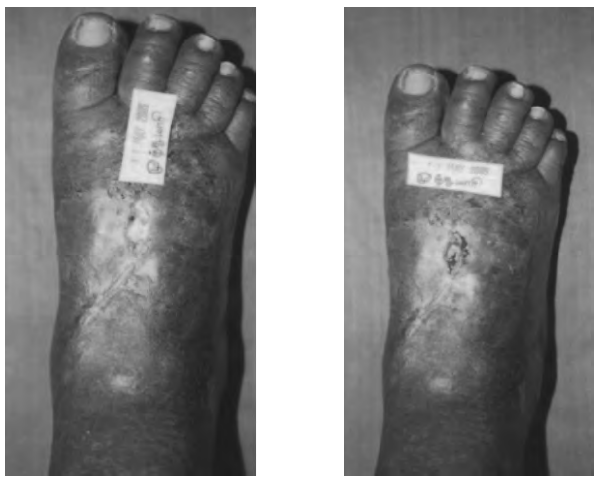


Stone inside the callus

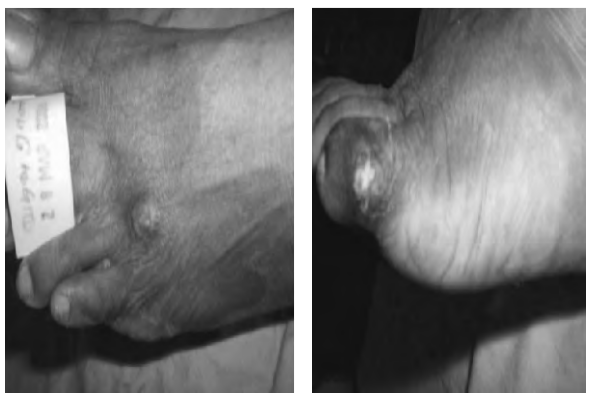
Scraping:

Sometime the ulcer may be superficial, no oedema. Make the chronic non healing ulcer into an active bleeding ulcer by scraping with the back of the blade handle. By scraping the ulcer bed, the blood supply to the affected part is

improved and healing process is initiated resulting in good healthy granulation tissue. The ulcer heals very quickly with good glycemic control.



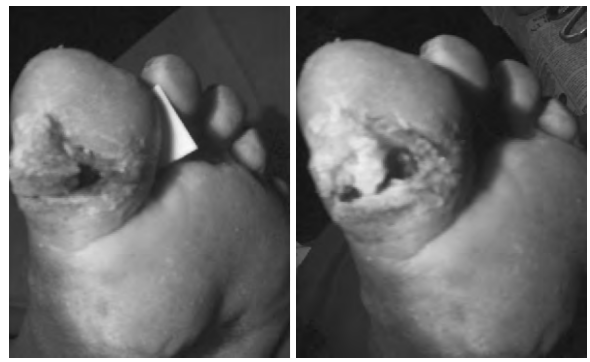
6months old chronic ulcer. Scraping done Healed in a week with good glycemic control



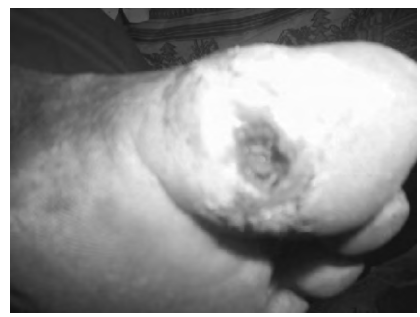
Looks like a healed ulcer. But active ulcer. C/o fever & adenitis

Callus

If the person present with callus, cut away all the callus tissue and clean the ulcer. Underneath the callus it harbors the foreign bodies like small stone, sand, hair etc. These foreign bodies will irritate the underlying healthy tissue and erode and lead to deeper ulcer involving the muscle, deep tissue and even bone. So, callus has to be excised for early healing of a foot ulcer

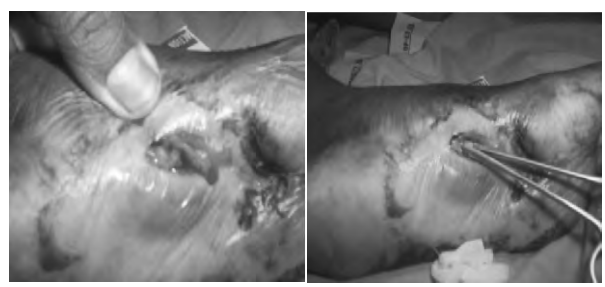


Callus **Being removed**

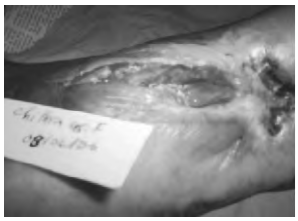


7days after

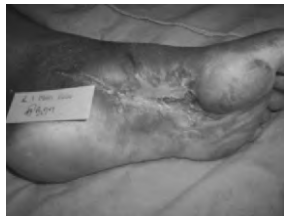
Discharging sinus: If a diabetic foot ulcer present with discharging sinus i.e. serous or purulent discharge, probe the wound with the help of a probe i.e. sterile artery forceps and assess the depth of the wound and where it goes (to find any important structure like nerve of vessel) Explore the wound to find any dead tissue like tendon or any bone, and remove all the necrotic material, cut and remove as long as you can till there is dead tissue. Once the dead tissue hidden in the discharging wound is removed the ulcer will heal automatically with suitable antibiotics and good glycemic control.



1.Six months old chronic ulcer 2. Ulcer cavity probed



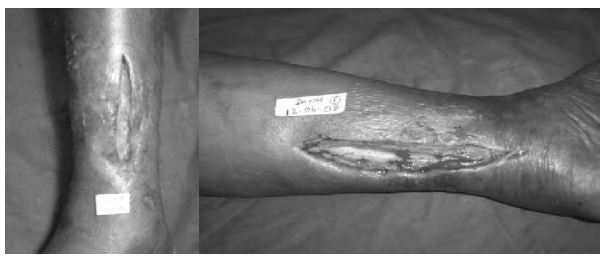
3.Ulcer cavity explored. Necrotic tendon seen & excised



4. Ulcer healed.

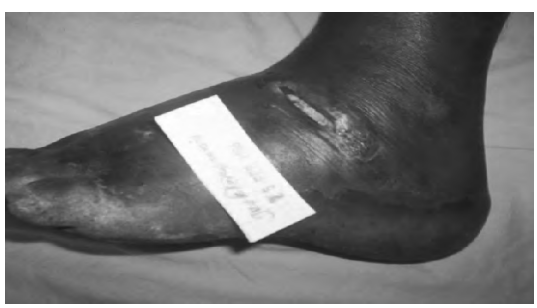
Abscess

Abscess should be drained adequately with generous incision. Incision should extend the length and breath of the abscess. Don't put small incision. The drainage will not be adequate with very small incision. It will not heal easily. If the incision is generous then the drainage will be adequate and should be deroofed. The wound will heal very quickly.



Cellulitis—Generous decompression

Abscess deroofed



Abscess—Generous Incision

The dressing should be changed daily or twice daily if there is more collection in the pad. Once the healing process has started, by the appearance of pink red granulation tissue dressing can be changed once in two days. Throughout the course of the treatment blood sugar should be kept less than 150 mg/dl. Regular short acting insulin is the insulin of choice administered 6^{th} hourly. Blood sugar estimation should be done 6^{th} hourly before giving insulin injection and dosage titrated according to the blood sugar value. At the start of the treatment urine should be analyzed for ketone bodies. Wound swab taken from the deeper structure should be sent for pus culture and sensitivity. Accordingly antibiotics should be administered once the culture result is known. Diabetic foot ulcer is an emergency. It should be dealt immediately. Otherwise we may have to lose the limb.

My own experience. Total no. of diabetic foot ulcer… 284, Toe disarticulation…10, Ischemic Gangrene … 08, Amputation... 03, Mortality…02, Absconded…..04, In my experience the duration of the ulcer ranges from 10 days to 18 months. 99 % of the ulcers healed well in quick time. The treatment ranges from scrapping of the wound, decompression, and generous debridement. At the end if necessary skin grafting was done. With good glycemic control, off loading of the foot with adequate regular debridement of all dead tissues should be done. Debridement of decompression should be done as early as possible as the patient is admitted. If it is delayed we will end up amputation. Pus should be sent for culture and sensitivity. Accordingly antibiotics should be administered. In severe infection parenteral antibiotics is advised. Blood sugar should be kept under control i.e. less than 150mg/dl. Regular human insulin (short acting) is the insulin of choice. Without debridement the wound will not heal and the blood sugar will not fall. Once we start debridement the infection gets controlled with antibiotics and the blood sugar also begins to fall. Antibiotics are recommended for foot ulcers that

have clinical signs of infection, such as redness, cellulitis, pus, lymphangitis or abscesses, and also when osteomyelitis is suspected. As many wounds are usually polymicrobial, prolonged uses of broad-spectrum antibiotics have traditionally been used. The specific antibiotics used should depend on known local sensitivities, but regional approaches can be taken where local sensitivities are known to be similar, with adjustments depending on the results of specific cultures. It is now advised that shorter courses, such as one to two weeks for soft-tissue infections, narrow-spectrum antibiotics should be used. Recommended antibiotics change with increasing severity of the infection, and longer courses (e.g. 6 weeks or longer) of antibiotics with the addition of agents such as rifampicin are advised in the presence of osteomyelitis. For patients who do have osteomyelitis, around 80% can be treated successfully with medical therapy and debridement alone, without the need for surgery.

Dressings

It is not what you put on the wound that is important. It is what you remove from the diabetic wound. Betadine solution, hydrogen peroxide are toxic to the tissues and slow the wound healing. So it is not routinely used now. It is better avoided. Normal saline dressing is the ideal dressing solution. It mimics physiological body fluid. No organism will grow in sterile normal saline. It is bio friendly and ulcer friendly.

Topical antimicrobials have neither been proven to eradicate an infection nor to be effective in the treatment of an infection. The primary line of therapy for infection is the use of oral or systemic antibiotics.

As the ulcer starts healing…..

1. Relief of pain
2. Relieved from uneasy weighty leg
3. Fever subsides & feels better
4. Edema decreases
5. Toxic secretion comes down
6. Foul smell vanishes
7. Arrest the spread of infection
8. Appetite improves
9. Blood sugar comes under control
10. Insulin requirement comes down
11. Healed areas skin peels off
12. Smiles at young nurse

Future India

If each one treats an ulcer/ year (Neuro-infective) Thousands of limbs saved in Indian Type 2 Diabetes. Patients' health is Nation's wealth. By saving the limb crores of rupees are saved. Man working days are restored. For the doctor, professional satisfaction. With good glycemic control incidence of neuro infective foot ulcer will come down drastically. By improving the lifespan of diabetics incidence of ischemic limb will increase. Changing the scenario is in our hands. We will take the challenge. Reminding you of Dr.B.C.Roy's words

Cultivate a heart that never hardens, a touch that never hurts, and a temper that never tires. Whatever the therapeutic discipline, sympathy was the essence of being a good doctor…….,B.C.Roy.

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Review Article

Toxicology clinics-bench to bed side Antimuscarnic therapy in organophosphate poisoning

Dr.S.Senthil Kumaran*, Dr.N.Balamurgan, Dr.V.Karthikeyan*****

Unintentional and intentional organophosphate (OP) poisonings continue to be a significant cause of morbidity and mortality in our country. Basic pharmacology and animal work suggests that early antagonism of pesticide toxicity should be associated with better outcomes. The principles of therapy in OPC poisoning include resuscitation of patient (patent airway, effective breathing and adequate circulation), high flow oxygen, a muscarinic antagonist and fluids. The role of oximes is dubious. Therefore, atropine is the mainstay of therapy. Atropine blocks muscarinic receptors limiting neuro-effector transmission by excessive acetylcholine. In this issue we have tried to answer some important FAQs on antimuscarnic therapy with available evidences.

Does the patient need atropine?

The important features of OPC poisoning are miosis, bronchospasm /bronchorrhoea, bradycardia, hypotension and excessive sweating. The presence of these cholinergic signs suggests that the patient has taken an OP compound and requires atropine.

If none of the signs are present, patient does not require atropine but careful observation is required to look for the development of cholinergic signs. This is because signs may be delayed due to a pro-poison (thion) OP getting converted to an active oxon form, and being released into the blood later or if the patient has presented soon after the ingestion.

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Is there any contraindication for atropine?

No absolute contraindication for atropine in OPC poisoning.

How much atropine he needs?

The aim of atropine therapy is to reverse the cholinergic features and improve cardiac and respiratory function as quickly as possible. Severely poisoned patients may require hundreds of milligrams of atropine.

How to give atropine?

An initial bolus of intravenous atropine, 1–2 mg (into a fast-flowing infusion) should be given. Atropine takes only a few minutes to act and blood levels peaks within three minutes after an intravenous administration. Waiting just five minutes for a response before deciding whether to give another dose is probably sufficient.

Therefore, if a consistent improvement in the cholinergic features does not occur within 3-5 minutes after the initial loading dose, the recommendation is to double the dose, and continue to double the dose until atropinisation is achieved. Do not simply repeat the initial dose of atropine.

This regimen requires no more than 20 minutes to administer 25 mg of atropine.

Can I give large initial bolus doses of atropine of 50 mg or so?

No, this is dangerous and may result in cardiac failure due to greatly increased peripheral resistance, and tachycardia which results in the diminished diastolic filling time.

Is he atropinised?

There should be a uniform improvement in most of the cholinergic signs, not improvements in just one. However, the most

important parameters are air entry on chest auscultation, heart rate, and blood pressure.

What are the target end-points for atropine therapy?

- Clear chest on auscultation with no wheeze
- Dry axillae
- Heart rate >80 beats/min
- Systolic blood pressure >80 mmHg
- Pupils no longer pinpoint

There is no need to aim for a heart rate of 120–140 beats/min. Such high heart rates will cause particularly severe complications in older patients with pre-existing cardiac disease – myocardial infarctions may result.

How to maintain adequate atropinisation?

Once atropinised (with clear lungs, adequate heart rate [more than 80 beats/min] and blood pressure [more than 80 mmHg systolic with good urine output], dry skin, and pupils no longer pinpoint) an infusion of atropine is started to maintain blood atropine concentration in the therapeutic range, reducing fluctuation compared with repeated bolus doses.

How to start atropine infusion?

In the infusion, try to give 10 – 15% of the total amount of atropine required to load the patient and it has to be given every hour as an intravenous infusion. The maintenance dose should be titrated against symptoms. The infusion rate should be sufficient and there should not be any signs of atropine toxicity.

How long atropine to be given?

The atropine infusion need to be continued for 48hours and tapered over 3-4 day

What are signs of atropine toxicity?

Excess atropine causes agitation, confusion, urinary retention, hyperthermia, bowel ileus and tachycardia.

What to do if patient develops atropine toxicity?

Stop the atropine infusion. Check again after 30 min to see whether the features of toxicity have settled. If not, continue to review every 30 min or so. When they settle, restart at 60–70% of the previous rate. The patient should then be seen frequently to ensure that the new infusion rate has reduced the signs of atropine toxicity without permitting the reappearance of cholinergic signs.

Is there any alternative to atropine?

Yes, it's ***Glycopyrrolate.***

This is a quarternary ammonium antimuscarinic agent with peripheral effects similar to those of atropine. It is a longer acting drug which does not cross the blood–brain barrier and therefore does not counteract the central nervous system effects of the poison. However, it is a more effective antisialagogue than atropine. It is less likely to cause much tachycardia and blocks bradyarrythmias effectively.

Can I give only glycopyrrolate?

No, an animal study demonstrates early death in OPC poisoning appears to be a centrally mediated process. The peripherally acting cholinergic agents like glycopyrrolate will not prevent the early death. So initially start with atropine and slowly change into glycopyrrolate. This combination works better.

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Case Report

Reversal of Diabetes After Treatment of ACTH-dependent Cushing's Syndrome

Dr. V. Subashini Devi, Dr. Ranjit Unnikrishnan I, Dr. V. Mohan,

Abstract:

A 16 year old girl presented to us for evaluation of diabetes. On examination, she had stigmata of Cushing's syndrome, and laboratory evaluation confirmed the presence of ACTH-dependent Cushing's syndrome. Neuroimaging studies revealed a microadenoma of the pituitary gland, which was successfully resected. Following the procedure, the patient's diabetes resolved completely and the signs of steroid excess also subsided. This case highlights the importance of looking for secondary causes of diabetes and the dramatic results that can be expected on prompt treatment of such causes.

Keywords: Cushing's syndrome, diabetes, acanthosis nigricans

Cushing's syndrome (CS) refers to a clinical constellation of symptoms and signs produced by excess levels of circulating glucocorticoids. Varying degrees of glucose intolerance are a feature of CS. We present here a case of diabetes mellitus secondary to CS of pituitary origin, which resolved completely after treatment of the pituitary lesion.

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CLINICAL HISTORY

A 16 year old female school student presented to us for evaluation of uncontrolled blood sugars with complaints of polyuria, polydipsia and menstrual abnormalities. She was diagnosed to have diabetes two years ago at the age of 14, while investigating for eruptive skin lesions all over the body. She had a positive family history of type 2 diabetes and was on treatment with oral anti-diabetic agents, but the sugars had been poorly controlled. She has also been on antihypertensives for the past two years. She attained menarche at the age of 13 years, but she had oligomenorrhea from the age of 14. She gave no history of intake of drugs other than her antidiabetic agents and antihypertensives.

PHYSICAL EXAMINATION

She was obese, with a body-mass index (BMI) of 32.9 kg/m^2. Her pulse rate was 80/minute and blood pressure was 170/110 mm Hg in the sitting position. General examination revealed acanthosis nigricans over the neck, back, axillae and groins, lesions of acne vulgaris all over the body, buffalo hump, purplish striae and bilateral pitting pedal edema. Secondary sexual characteristics appeared normal. All systems were within normal limits.

In view of the above findings, a provisional diagnosis of Cushing's syndrome was made and she was investigated further as to the cause.

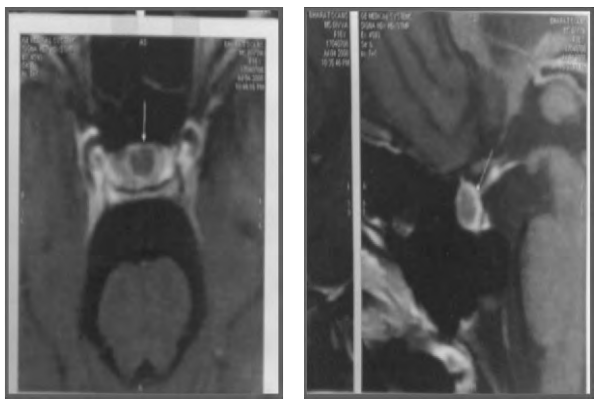
INVESTIGATIONS

At admission, she had fasting and postprandial blood sugar levels of 207 mg/dl and 449 mg/dl, respectively. Her glycosylated hemoglobin value was 10.2%, indicating poor glycemic control for the preceding two to three months. C-peptide assay revealed fairly good pancreatic beta-cell reserve. Serum insulin assay

and thyroid function test were within normal limits. She also had dyslipidemia, proteinuria and microalbuminuria. Measurement of serum electrolytes revealed severe hypokalemia (2.9 mEq/l).

Dexamethasone suppression test showed elevation of serum cortisol levels (43.9ug/ml;N-6.7 to 32.6). Serum ACTH levels were also elevated (129.00 pg/ml; N-<46). 17-hydroxy progesterone, dehydroepiandrosterone sulphate, free testosterone, and 24 hour urinary epiandrosterone levels were within normal limits. These results indicated that the patient had an ACTH dependent form of Cushing's syndrome.

Magnetic resonance imaging (MRI) scan of skull revealed 5.6 * 7 mm non-enhancing lesion in the midportion of pituitary gland with mild focal bulge in the roof and no evidence of pituitary stalk displacement, suggestive of pituitary microadenoma (Figure 1). MRI study of abdomen revealed no significant abnormality.



1a 1b

Figure 1 : MRI Scan showing pituitary space occupying lesion

MANAGEMENT

The above findings were suggestive of ACTH-dependent Cushing's syndrome due to pituitary microadenoma. She was referred to neurosurgeon and trans-sphenoidal excision of the adenoma was done.

Biopsy report was consistent with pituitary adenoma.

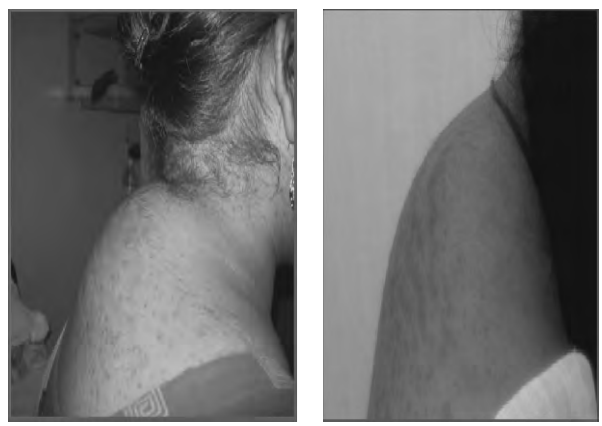
For control of diabetes, she was initiated on insulin and continued on the same perioperatively.

FOLLOW-UP

One month after surgery, blood tests showed normalization of levels of cortisol (10.56 ug/ml) and ACTH (32.8 pg/ml). Her blood pressure was 110/68 mmHg and she had lost 6.7 kg in weight. Her sugars and lipids had returned to normal and HbA1c had dropped from 10.2 to 6.6%. In view of this she was weaned off insulin and continued on oral antidiabetic agents alone.

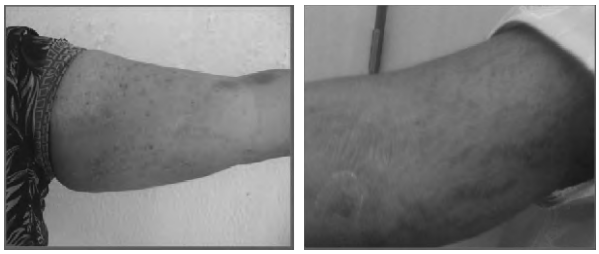
After 3 months, the blood sugars were found to be persistently normal on minimal doses of antidiabetic agents. Hence the medications were stopped and she was advised to be on diet control alone.

Two weeks after stopping the medications, she was reviewed in the diabetes clinic. She had lost a total of 14.2 kg of weight, acne had disappeared and buffalo hump and striae had diminished considerably (Figure 2 & 3). Her menstrual cycles had become regular. Her BP had dropped to 100/68 mm Hg without any antihypertensive therapy. An oral glucose tolerance test revealed normal values. HbA1c was 5.5% (non-diabetic range). C-peptide levels were also found to have improved.



2a 2b

Figure 2 : Prominent buffalo hump and acne vulgaris before (2a) and after treatment (2b)



3a 3b

Figure 3 : Striae before (3a) and after treatment (3b)

At present, the patient is off antidiabetic and antihypertensive medications and is doing well. In view of positive family history of diabetes, she has been advised to undergo OGTT once in a year. Although diabetes associated with CS is not uncommon, this case is of interest on account of the dramatic reversal of clinical features and laboratory abnormalities noted in this patient.

DISCUSSION

Secondary causes of diabetes have to be carefully looked for in any patient presenting with diabetes at a young age, in those with atypical clinical presentation or in absence of a family history. The importance of recognizing secondary diabetes lies in the fact that in many cases, the diabetes can be cured completely if the primary cause is treated. Conversely, failure to detect the primary cause will make control of blood sugars virtually impossible and put the patient at risk for diabetes complications, in addition to the long-term sequelae of the underlying problem.

Glucocorticoid excess is one of the more common secondary causes of glucose intolerance met with in clinical practice. Glucocorticoids cause glucose intolerance by increasing insulin resistance, most probably at the post-receptor level [1]. Some impairment of glucose tolerance is met with in 40-90% of patients with CS [2]. Overt diabetes develops only in 10-15%, especially in those with a positive family history of diabetes, like our patient [3,4]. The diabetes in CS resembles type 2 diabetes and ketosis is rare.

It has also been reported that a significant proportion of hospitalized patients with type 2 diabetes patients have subclinical hypercortisolism [5]. Even in the presence of florid signs and symptoms, the diagnosis of CS in a diabetes patient is problematic. Many of the clinical and biochemical features of CS can be present in obese or overweight individuals, especially those with the metabolic syndrome. Diagnosis of CS in this situation requires the judicious use of clinical acumen, biochemical assays and imaging studies.

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Original Article

Chennai Slim and Fit Programme:

Awareness and perceptions related to obesity among urban children and adolescents

Dr. Shabana Tharkar., Dr. Vijay Viswanathan

Abstract

Background & Objectives The aim of the study was to assess the knowledge levels of children and adolescents on obesity and their lifestyle practices related to diet and physical activity.

Methods: About 1266 school children aged 8- 16 years were surveyed by an interviewer administered questionnaire. Scores were allotted for the knowledge questions and maximum attainable score was 8. Chi square or z test was done as appropriate to determine the significance testing between groups.

Results: The children generally had poor knowledge on obesity and its related factors. Eventhough most of them had heard of diabetes, knowledge on prevention was very scarce. The mean knowledge score of children from high socioeconomic status was 4.6 and those from low socioeconomic status were 3.1. Higher knowledge levels were seen among females and children from high socioeconomic status ($p<0.0001$). The practices of children were unhealthy and sedentary, only 35 % of the children had daily one hour physical activity.

Conclusion: The knowledge of the children on obesity and diabetes is grossly inadequate and awareness programmes are needed to improve their knowledge levels. They must be motivated to practice healthy lifestyle.

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Introduction

A lot has been discussed about the rising prevalence of obesity even among developing countries and its association with other co morbidities. (1).Childhood overweight and obesity is emerging as global epidemic and has become a major public health concern (2). The developing countries too are not spared and the burden of obesity disproportionately affects the Indian population. For instance, overweight and obesity is more in urban areas and is especially more among affluent class (3). The changing lifestyle and eating habits due to urbanization have lead to an increase in obesity among children and adolescents in India (4). It is inextricably linked to the surrounding environmental, behavioural and cultural aspects. There is an uptrend in urbanization in India resulting in increased purchase power and shift in lifestyle more towards sedentary kind besides increased consumption of calorie dense food. The children are exposed to many risk factors of overweight and obesity early in life, without realizing the health hazards in later life.

Excess body fat in children and adolescents have been found to be the cause for many clinical and biochemical abnormalities like insulin resistance, dyslipidemia, high leptin and high blood pressure all of which act as a trigger for the development of type 2 diabetes and cardiovascular diseases in adulthood (5-12). Since type 2 diabetes among Indians have reached epidemic proportions (13), it is imperative that children and adolescents are aware of its risk factors like family history, obesity sedentary lifestyle and unhealthy eating habits.

Research from our country suggests that the awareness on diabetes is inadequate among the general population aged more than 20 years (14). But there is virtually no data from India assessing awareness levels of diabetes and obesity among children and young adults. Understanding the behavioral patterns, the knowledge and awareness levels of the younger generation are important in planning intervention programmes. The aim of this study was to measure the awareness levels of children on obesity, their attitude and practices.

Methods

A total of 1266 (M:F, 673:593) school children from 8 to 16 years (IV grade to X grade), selected by stratified cluster sampling technique were interviewed by administering a well designed and validated proforma by trained research officers. To have a representative study sample, 2 private schools and 1 corporation school (government aided) were included in the study. Generally, private schools which have a higher fee structure mostly admit children from affluent society, while corporation schools were attended by children from low socioeconomic status. The study protocol was approved by the ethics committee of the institution.

The questionnaire was interviewer administered to the children of classes IV to X after getting permission and written consent from the school principals. Anthropometric measurements were recorded before administering the questionnaire. The instrument contained 3 parts- a) General characteristics b) anthropometric measurements – height, weight and waist circumference. c) Questions on knowledge related to diabetes, obesity, behavioural practices of children pertaining to diet, physical activity and TV watching.

The percentage of respondents who gave the correct answers to each question was assessed for total survey sample. Correct answers were awarded marks and total scores for knowledge and awareness were computed. The total attainable maximum knowledge score was 8. The scores obtained by the children were then compared with age, socioeconomic status and gender. Chi square / z test was done as appropriate to determine the significance testing between groups. A p value <0.05 was considered as significant.

Results

The comparative mean scores attained by children on knowledge of obesity and its risk factors are shown in Table 1. Highly significant differences in knowledge scores were seen among the children with respect to age, gender and socio economic status. Higher scores were obtained by children aged 13 years and older, female gender and children from high socioeconomic status ($p<0.0001$). The 50^{th} percentile for low socioeconomic status fell on score 3 whereas it was on score 5 for high socio economic status. Percentage of children scoring the least (score 0) and highest (score 8) were 5.2 and 2.4% among low socioeconomic status and 0.5 and 7.6% for high socioeconomic status children. The children had poor knowledge on obesity, only 32% of the them knew what obesity is. Even though 63.1 % of the study population was aware about diabetes, only 34.8 % knew that it could be prevented.

Table 1: Knowledge scores according to age, gender and socioeconomic status.

Variables n=1266		*Total n%*	*Mean Score*	*Std deviation*	*P value*
Age: (years)	8-12	702 (55.5)	3.6	1.9	<0.0001
	13-16	564 (44.5)	5.2	1.8	
Gender:	Male	673 (53.2)	3.9	1.8	<0.0001
	Female	593 (46.8)	4.8	2.2	
SES:	HSES	976 (77.1)	4.6	1.9	<0.0001
	LSES	290 (22.9)	3.1	1.9	

Table 2 shows details of knowledge on individual questions and the percentage of correct answers among children based on socioeconomic status. About 82 % of the adolescents (>=13 years) have heard of diabetes. However the knowledge on prevention of diabetes was low among all the study subjects. There was generally a low level of awareness on obesity. The children had poor knowledge about balanced healthy diet while junk foods and its ill effects were better known only to affluent children. Socioeconomic status had a significant impact on the level of awareness among children for all the knowledge based questions 1-7($p<0.0001$).

The knowledge scores, attitudes and practices related to diet and physical activity were assessed and are shown in table 3 stratified according to weight.

Table 2: Awareness levels according to socioeconomic status.

Variables		LSES		HSES	
		8-12 years *n*=177	13-16 years *n*=113	8-12 years *n*=525	13-16 years *n*=451
1.	Heard of diabetes: yes	62 (35.0)	92 (81.4)	274 (52.2)**	375 (83.1)
2.	Can diabetes be prevented: yes	11 (6.2)	51 (45.1)	158 (30.1)*	221 (49.0)
3.	Heard of obesity :yes	21 (11.9)	62 (54.9)	125 (23.8)**	196 (43.5)**
4.	Know about balanced diet: yes	14 (7.9)	32 (28.3)	204 (38.9)**	225 (49.9)**
5.	Know about junk food: yes	18 (10.2)	48 (42.5)	305 (58.1)**	377 (83.6)**
6.	Does physical activity promote good health: yes	117 (66.1)	90 (79.6)	471 (89.7)**	418 (92.7) **
7.	What is ideal body size?	120 (67.8)	95 (84.1)	352 (67.0)	374 (83.0)

χ^2 test done between similar age groups of two socio economic groups

* p value <0.05, ** p<0.0001

Table – 3 Descriptive details of attitude and practices among normal, overweight and obese children.

	Normal	Overweight	Obese
	985 (77.8)	172 (13.6)	109 (8.6)
(i) Knowledge score Mean (sd)	4.2 (2.0)	4.9 (2.0)	4.5 (2.0)
(ii) Attitude What will you do if you know that junk foods are harmful?			
(i) Avoid eating	270 (27.5)	59 (34.3)	32 (29.4)
(ii) Eat less	621 (63.0)	98 (57.0)	70 (64.2)
(iii) Will continue to eat	92 (9.3)	15 (8.7)	7 (6.4)
(iii) Practices			
Atleast 60 mins of daily physical activity	398 (40.4)	59 (34.3)	33 (30.3)
Consumption of Fried food upto 2 times per week	615 (62.4)	125 (72.7)	78 (71.6)
Fast food Upto 2 times per week	535 (54.3)	83 (48)	52 (48)
Eating out Upto 2 times per week	507 (51.5)	79 (46)	57 (52.3)

Values are shown as number (%)

Normal ≥ 50^{th} - < 85^{th} Percentile

Overweight ≥ 85^{th} – < 97^{th} percentile

Obesity ≥ 97^{th} percentile

(WHO BMI for age percentile charts 2007 are used as reference)

Discussion

To the best of our knowledge the awareness level of obesity and diabetes, its related lifestyle practices and behaviour among children and adolescents was being assessed for the first time in Chennai by this study. The present study showed that the level of knowledge and awareness on the above factors was however low and highly influenced by socioeconomic status ($p<0.0001$), hence confirming the existence of intra - urban differences in the awareness levels. Children and adolescents of higher socioeconomic status and those attending the private school had better knowledge than their counterparts from corporation school. It was observed from the study that the children were well informed about the good effects of physical activity but were not engaged in daily physical activity. Only 34 % of the over weight and 30% of the obese children were engaged in atleast 60 minutes of daily physical activity, which is suggestive of the sedentary kind of lifestyle of the younger generation. Prevention is the topic of interest today in order to control this escalating prevalence of obesity. Hence focus must be made on spreading awareness on the preventive aspects of the disease targeting not only children as audience but also involve the parents and teachers.

Chennai is a metropolitan city in India which has experienced rapid urbanization in last two decades. Rapid epidemiological transition is currently sweeping across India, making the urban and peri urban areas more urbanized in terms of economy and luxury. This has a direct impact on food habits and lifestyle. Springing up of international standard fast food outlets and food zones are a major attraction to the adolescents and young adult population. Eating habits of the children from this study showed that there was widespread prevalence of consumption of fried food and fast food items and the children frequently dined out. An urban Indian adolescent usually consumed less of fruits, and greens, but more of industrialized snacks, sweets, savouries and cool drinks in replacement of breakfast and even lunch. These calories dense but zero nutritive value foods are causes of adiposity which in turn lead to cycle of events.

To summarize, the current study has shown that knowledge among the children on obesity and its effects is inadequate. The persistence of unhealthy practices among the children must be given attention. This study has thus highlighted the need to not only improve the awareness on prevention of childhood obesity among children but a need to motivate and reinforce them to practice healthy lifestyle is utmost essential.

Old habits die hard, hence the root of non communicable diseases – overweight and obesity must be tackled at an early age. This can be done effectively by education and awareness creation. Not only must awareness be created, but the children need to be motivated to practice healthy habits, as we understand from this study that even though the children were aware about the good effects of physical activity on health, very few played out door games daily. Certain guidelines and policies like school canteen policy, healthy food practices, inclusion of health related topics in curriculum and compulsory physical training classes must be introduced in the schools. There must be a multi sector approach from the government, school authorities and parents to introduce policies and guidelines to curb on the obesity menace and to help today's children to live a long healthy life tomorrow.

Acknowledgement

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Diabetes Research Centre. Conflict of Interest is none.

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Case Report

Polymerase Chain Reaction – Breaks the Dilemma in Meningitis

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Abstract

Tuberculosis continues to be a major cause of morbidity and mortality in developed and developing countries, despite the availability of effective chemotherapy. Despite its global importance, the diagnosis of extra- pulmonary tuberculosis (EPTB) remains an important clinical problem, primarily because of inadequate sensitivity of conventional bacteriologic methods for detecting Mycobacterium tuberculosis in extra pulmonary specimens. In this case report, a 45 year old female diabetic, hypertension, also a known case of Progressive systemic sclerosis, presented with fever, altered behaviour and drowsiness. Lab investigations showed normal blood routine, RFT & LFT. CSF analysis revealed only elevated proteins. CT brain done on the day of admission was normal and later repeated as the patient developed left facial palsy and lateral rectus palsy, which revealed communicating hydrocephalus. CSF was sent for Polymerase Chain Reaction for TB, which was reported as positive for Mycobacterium tuberculosis using IS6110 primer. Following treatment with ATT and steroids the patient has shown significant improvement and is symptom free after nine months of treatment with ATT. We recommend that CSF specimens be submitted for PCR testing whenever CSF analysis is inconclusive and clinical suspicion is sufficiently high to warrant empiric ATT therapy and conventional bacteriologic methods are negative.

***Key Words*:** Extra- pulmonary tuberculosis, PCR, M. tuberculosis.

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Introduction:

Tuberculosis is a rampant disease in developing countries such as India where the prevalence is reported to be high. In countries with a high incidence of tuberculosis, tuberculosis meningitis is typically a disease of young children that develops three to six months after primary infection. In countries with a low incidence of tuberculosis, tuberculosis meningitis more commonly affects adults, and although it may follow primary infection, it more frequently arises from the reactivation of a dormant sub cortical or meningeal focus. The diagnosis of extra-pulmonary tuberculosis in its different clinical presentation remains a true challenge. The disease's underestimation by clinicians and the use of insensitive conventional analytical methods have contributed to the difficulties in managing patients with EPTB. Early recognition of TB meningitis is of paramount importance because the clinical outcome depends greatly upon the stage at which therapy is initiated Thus the implementation of diagnostic methods with high specificity and sensitivity would improve the clinical outcomes

for EPTB patient's and should accelerate the application of appropriate public health control measures.

Case Report:

A 45 year old female, who was a known diabetic and hypertensive on treatment, also a known case of Progressive systemic sclerosis on treatment with steroids and pulse cyclophosphamide therapy; presented to emergency with history of fever of 1 week duration, which was intermittent and low grade, altered behaviour and drowsiness of 1 day duration. On examination she was drowsy but arousable, febrile, had a pulse rate of 96/min, respiratory rate of 24/min, and BP of 130/70 mm of Hg. She had glossitis and stiffening of skin over face and mouth. Patient did not have signs of meningeal irritation. Examination of other systems showed no abnormalities.

Lab investigations revealed a hemoglobin of 12.4gm/dl, total count of 10,910 cells/cu.mm, with polymorphs of 78.8%, normal platelets and ESR was 52 at one hour. RFT, LFT and coagulation profile was within normal limits and peripheral smear and QBC was negative for malaria parasites. In view of fever with altered sensorium lumbar puncture was done under strict aseptic precautions on the same day. CSF study revealed elevated proteins of 143 with normal sugar and chloride and no cells. CSF gram stain was negative and AFB stain was also negative. CSF culture was sterile for bacteria and fungi (table 1).

Table 1:

Parameters	Values
Hb	12.4g/dl
TC	10,910 cumm
Platelets	3.12 lakhs/cumm
ESR	52 at one hour
PT/ PTT / INR	15.5 seconds / 30.8 seconds / 1.14
LFT-	
Total bilirubin / Direct bilirubin	0.48 / 0.14 mg/dl
SGOT/SGPT	18 / 23 U/L
Alk. Phosphatase	75 U/L
Total proteins	7.4 g/dl
Albumin/globulin	3.8 / 3.6 g/dl
CSF-Proteins	143mg/dl
Sugar	40 mg/dl
Chloride	106
WBCs	Nil
RBCs	Nil
CSF Culture	No growth
India ink preparation	Negative for capsulated organism.
RFT	
BUN / Creatinine	10 / 0.9 mg/dl

CT brain done on the day of admission did not reveal any significant abnormality (figure 1; table 2).

Figure 1

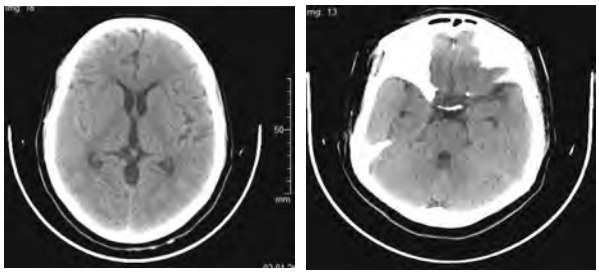


Table 2

CT –Brain is normal on the day of admission.

During the course in the hospital the patient developed left facial palsy and lateral rectus palsy. Patient required mechanical ventilation in view of low GCS on the fourth day of admission. CSF study was repeated which showed a rise in protein levels to 182 with normal sugar & chloride and absence of cells. CSF was sent for Polymerase Chain Reaction for TB. Patient was started on ATT and steroids on the same day. CT scan was also repeated which showed communicating hydrocephalus (figure 2; table 3). PCR test was reported as positive for Mycobacterium tuberculosis using IS6110 primer (figure 3; table 4).

Figure 2

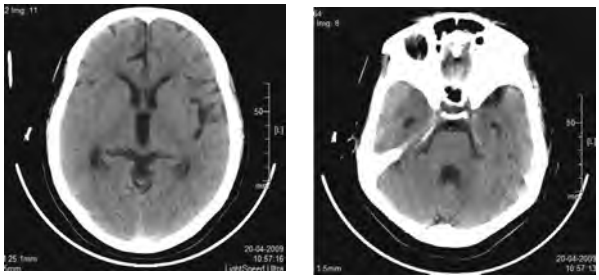
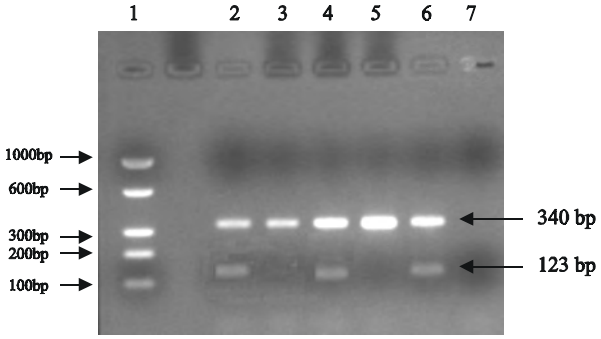


Table 3

CT - Brain shows communicating hydrocephalus.

Figure 3



Lane 2: CSF
Lane 3 & 5 Other samples
Lane 4: CSF
Lane 6: Positive control
Lane 7: Reagent control

Table 4

PCR test is positive for Mycobacterium tuberculosis using IS6110 primer

Patient's condition slowly improved and was weaned off mechanical ventilation by tenth day of admission. Subsequently patient was shifted to ward on the fourteenth day. Patient continued to have left facial and lateral rectus palsy at the time of discharge (the twentieth day after admission). Patient was followed up second weekly thereafter and was completely symptom free after nine months of treatment with ATT She also recovered from the lateral rectus palsy. A repeat CT scan done after nine months was normal (figure 4; table 5).

Figure 4

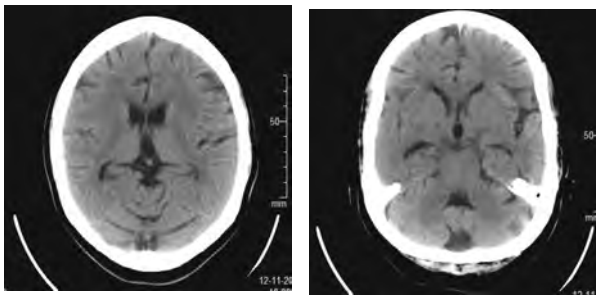


Table 5

CT- Brain is normal on follow up

Discussion

Tuberculosis is a protean disease affecting virtually all the organs and has a wide spectrum of clinical presentation depending on the anatomical site involved. TB meningitis is a challenge for clinicians because of the difficulty in making an early diagnosis and the severe consequences of delaying the treatment. Thus early recognition of TB meningitis is of paramount importance because the clinical outcome depends greatly upon the stage at which therapy is initiated. The diagnosis of extra – pulmonary tuberculosis remains an important clinical problem, primarily because of inadequate sensitivity of conventional bacteriological methods for detecting Mycobacterium tuberculosis in extra – pulmonary specimens.

PCR–based assays using the insertion–like sequence elements IS6110 are rapid and sensitive and has modified strategies for the detection of Mycobacterium tuberculosis.(1,2) Nucleic acid amplification can be utilized to identify tuberculosis infection in diverse clinical specimens including CSF, pleural fluid, ascitic fluid, urine and pericardial fluid. (1, 6, 7, 8)

PCR assay is more sensitive than the conventional methods, especially when low numbers of bacilli are present. Antibiotic therapy rapidly lowers the number of viable infecting bacilli and decreases the likelihood that culture assays are positive. However, as amplification methods can detect dead bacteria, the PCR assay remains positive until the killed bacilli are cleared. PCR has several advantages over culture, including confirmation of the presence of M. tuberculosis within 1 to 3 days as compared to 6 weeks with conventional culture techniques. DNA amplification can be used for tissue specimens which are already formalin – fixed and paraffin-embedded. (1, 3, 9) Furthermore, patients are often given treatment for EPTB based only on clinical suspicion, as treatment delays can negatively impact clinical outcomes.(8,12) PCR perhaps, is a highly sensitive technique that detects DNA from a single to few micro-organisms with overall sensitivity, specificity and positive predictive value of 97.87%, 100%,and 100% respectively (3).

Conclusion

PCR is a rapid method for detection of mycobacterium tuberculosis especially extra-pulmonary tuberculosis. Several studies have reported the usefulness of PCR using IS6100 primer to detect mycobacterium tuberculosis. With low reliability of the conventional techniques, implementation of more sensitive methods should be encouraged for specimens suspected to have few bacilli.

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Review Article

Medical Management of Renal Stone Disease

Dr. P.Soundararajan

Management of stone disease has changed from exclusively surgical management for stone removal to medical management to prevent stone occurrence and recurrence but also to facilitate dissolution or safe passage of stones in many clinical situations. Physicians and primary care providers should assume greater responsibility for long term stone management programmes and restrict select referrals to surgeons whenever necessary. Medical management is not only restricted to increased fluid intake but also to carryout investigations to find out the etiology of stones in every case and to prescribe suitable drugs and diet when required and to periodically check the effectiveness of drugs and diet by specific laboratory tests to avoid stone recurrence . Taking into consideration the high incidence of recurrence surgical treatment of urinary stones is an incomplete procedure. The goal of surgical treatment is the removal of existing stones while that of medical treatment is the prevention of recurrent stones formation. Continued application of medical and surgical approaches is mandatory for the full control of the disease. Stone disease management today involves huge financial burden on the patient care. Hence treating primary physicians need to play pivotal role in choosing appropriate investigations and selective mode of therapy in every stone patient in a cost effective manner.

Renal stone disease secrets

Primary physicians need to understand that most of the stones encountered in day today practice belong to the category of small stones less than 8 mm to 10 mm mostly in the collecting system which can be delivered by medical measures alone.

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Renal stone disease is a medical disease with surgical complications and consequences. Mechanisms of stone formation underlies abnormal urinary composition arising out of defective nephronal function involving excess glomerular filtration and are defective tubular secretion or reabsorption. To every patient one should ask oneself why stones form in a particular patient to get etiological clue to prevent stone recurrence in future. In case of untreated calcium oxalate stone the chance of recurrence is 10 % in one year, 35 % in 5 years, and 50% in 10 years.

Medical management consists of four parts

1. Clinical evaluation
2. Laboratory investigations and imaging studies
3. Dietary modifications
4. Treatment of abnormal stone risk factors

Renal stone disease by itself is not a sufficient diagnosis as much as the term edema or ascites or fever means, etiological diagnosis is mandatory for effective management.

Clinical Evaluation

Acute renal colic is the most common presentation, pain does not completely remit rather waxes and wanes and the location of stones modifies the pattern of pain. Nausea, vomiting may accompany. Rarely gross hematuria occurs without pain. Urethral stones can mimic gall stone, appendicitis, cystitis, pelvic organ pathology in females. Other conditions to consider as differential diagnosis are musculoskeletal pain, herpes, duodenal ulcer, abdominal aneurysm, gynec causes, and urethral obstruction due to blood clot, sloft papillae and urethral stricture.

Laboratory Investigations and Imaging Studies

For evaluation of kidney stone how much to be done and to what extent depends on several variables. First, what is the stone burden? First time stone former or recurrence stone former? Following points merit consideration, total number of stones, types of previous procedures and their success, residual stones, family history of stones , diet details and medication usage before the stone event . Because of non specific physical findings, laboratory findings and imaging studies play a crucial role in making the diagnosis. Helical spiral CT is the modality of choice because it does not need contrast agent and can detect stones as small as 10mm, even in uric acid stones traditionally considered radiolucent, ultrasonography can image only the kidney and proximal ureters. A plain X ray KUB can miss a stone in ureters or kidney even one that is radio opaque and provides no information on obstruction. X-ray KUB is used to locate urethral stone or growth of asymptomatic kidney stones and its sensitivity is limited. IVP requires contrast and can miss small stones. It is ordered less frequently now a day in tertiary care centers.

Dietary Modifications

All patients with stone disease are advised to follow strict dietary modification irrespective of their normal investigations many times.

High fluid intake: Patient is informed to measure urine out put once a week and then adjust the fluid intake to maintain urine output more than two litres/day. they are also advised to take maximum intake of fluid with in three hours after taking the meals, during periods of physical exercise, bedtime and once at midnight, plain water is good enough but potassium rich citrus fruit juices such as orange, grape fruit and berry are preferable to low potassium citrus fruits such as lime and lemon, orange juice for example represents a natural form of potassium citrate and posses alkalizing and Citra uric action 48. Limejuice, on the other hand, is composed largely of citric acid, and does not affect acid base balance appreciably, so it does not alter urinary PH and only modestly increases urinary citrate 49.Increasing fluid intake actually has been demonstrated to have positive effect on two urinary inhibitors, citrate and Tomm-Horsfall protein. Hydration augments urinary citrate excretion, which is thought to result from an increased fluid flux in the proximal tubule resulting in the delivery of more bicarbonate to the cells of this portion of the nephrons .Urinary dilution has been found to increase the inhibitory activity of Tomm-Horsfall protein on the calcium oxalate monohydrate crystal aggregation in the urine of the stone formers.

Restriction of Animal Proteins

Patient is informed to avoid non-vegetarian diet and the recommendation is of 8 oz or less of dry meat/day animal proteins are rich sulphur containing amino acids such as cystine and methionine, which on oxidation produces sulphate which forms a soluble complex with calcium in the nephron and limits the reabsorption of this cat ion, bone serves as a buffer and the resultant osseous dissolution provides more calcium to be excreted, chronic metabolic acidosis decreases calcium reabsorption with in the nephron, which further augments excretion of this mineral, increased protein consumption also augments glomerular filtrations , thus delivering more calcium to the nephron which promotes its excretion. Animal protein as a high purine content, which leads to increase in uric acid excretion. The associated acidosis resulted in a decrease urinary PH that could potential uric acid urolithiasis. Acidosis also enhances citrate reabsorption in the proximal tubule and thus decreases excretion of citrate in the urine.

Sodium Restriction

Patient is asked to avoid high sodium containing food with restriction of salt in the diet and salty shakers. Increased sodium intake may promote a variety of metabolic changes that may be detrimental to stone formers, including

increase in the urinary PH, calcium and cystine excretion and a decrease in citrate excretion.

Oxalate Restriction

Avoidance of nuts, spinachs,dark roughage,chocalate,tea, and vitamin C and advised to maintain recommended daily intake of calcium and to ensure that calcium consumption accompanies the ingestion of oxalate rich foods to prevent the absorption of oxalate.

Restriction of Calcium

Moderate restriction of calcium is recommended and about 250ml of milk or milk products can be taken daily .in patients who are advised for long-term restriction of calcium intake, measurement of bone density, particularly in the spine is recommended.

Dietary Recommendation Role

Urinary Abnormality	Dietary Changes	Medication
High calcium concentration	Avoid excessive intake of calcium supplements	Thiazide
	Maintain adequate dietary calcium intake	
	Reduce intake of animal protein	
	Reduce sodium intake to < 3g/day	
	Reduce sucrose intake	
High oxalate concentration	Avoid high oxalate foods	
	Maintain adequate dietary calcium intake	High dose pyridoxine?
	Avoids vitamin C supplements	
High uric acid concentration	Reduce purine intake (i.e.	meat, chicken, fish)
Low citrate concentration	Increase intake of fruits and vegetables	Alkali (e.g. K Citrate)
	Reduce intake of animal protein	
Low volume	Increase total fluid intake	Not applicable

Calcium

Contrary to the popular belief there is no evidence that dietary calcium restriction is helpful in preventing stone formation and there is substantial evidence that routine calcium restriction is harmful, recent studies support the concept that dietary calcium intake is inversely associated with risk of stone formation. Mechanism by dietary calcium reduce stone risk is by calcium binding to oxalate in intestine there by blocking oxalate absorption.

The role of calcium supplement deserves comment because their use is common if someone who never had a stone the risk attributed to supplement is low. For a patient who had a calcium stone and wishes to continue taking calcium supplements 24hrs urine chemistry should be checked while the patients is taking and not taking supplements and advised accordingly. Decreasing intake of animal protein (meat, chicken, and sea foods) may be helpful.

Difference in timing of ingestion may explain the apparent contradiction between the protective effect of dietary calcium and detrimental effect of supplemental calcium. A protective effect would not be expected unless calcium supplements are taken with meals containing oxalate. A reported risk of supplemental calcium intake is a result of increased urinary calcium excretion without any change in oxalate excretion.

Patients who have low citrate in the urine should increase their intake of potential alkali (fruits and vegetables) and decrease intake of acid producing foods such as animal protein. For patients with high urine oxalate levels the benefit of low oxalate diet is less clear. Many foods contains only small amounts of oxalate but food that are high in oxalate are less common. An increase in calcium in diet may reduce oxalate absorption and thereby reduce urinary oxalate excretion.

I Pharmacological options:

When to use medications? If dietary modifications are unsuccessful in adequately modifying the urinary, drug therapy is indicated to achieve the same.

Drugs used in stone prevention are

1. Thiazide which are used to reduce urinary calcium excretion eg: chloroalidone and hydro chlrothiazide
2. alkali which is used to increase urine citrate excretion for e.g. potassium citrate
3. Allopurinol which is used to reduce urine uric acid excretion

Thiazide

For patients who have elevated calcium levels do not have an exceed calcium intake (not more than 1500 mg per day) Thiazides are shown to reduce stone recurrence while maintaining bone density with no risk of osteoporosis. Dosage required to reduce urine calcium excretion substantially higher than those used for treatment of hypertension (at least 25 mg per day and often 50 mg per day to 100 mg per day) randomised controlled trials have confirmed a 50% reduction risk of stone recurrence. Adequate sodium restriction (less than 3 gm per day is heavy to achieve, a higher sodium intakes leads to greater distal sodium delivery which minimizes or regulates the beneficial effect of thiazide. For patients who are unable to increase their fluid intake, thiazide may be helpful to increase in urine where it will reduce urine calcium concentration. Can we deliver stone by medical measures?

It depends on size of the stones and site of stone, whether obstructing or non obstructing the urethral passage. Stones less than 6 mm are likely to pass out through urine. Over 8 mm are unlikely stones in the distal ureters are more likely to come out than the in proximal ureters with the kidneys

II Pharmacological option for drugs to facilitate stone passage - called "MEDICAL EXPLOSIVE THERAPY"

Researchres recently have sought out pharmacologic means of increasing rates of stone passage and reducing both surgical intervention and financial costs. The use of hormones , non steroidal anti inflammatory drugs (NSAIDS) , calcium channel blockers , corticosteroids , and adrenergic alpha antagonist all have been proposed as a way to enhance stone passage.

Hormones, Progesterone

Numerous laboratory, as well as clinical studies has shown that sex hormones have a dilatory effect on the urinary tract, suggesting a possible therapeutic role for hormones in facilitating stone passage. Progesterone has been one of the most studied hormones. Progesterone is believed to cause dilation of the ureters by acting on the beta adrenergic receptors. It also as been shown to decrease the muscular activity of the ureters. Mikkelsen et al further studied this drug in a non randomized study of 24 patients with a ureters calculi. All patients were given intra muscular injection of 250 mg of hydroxyl progesterone and followed up until stone passage or surgical intervention. In all, 14 of 24 patients (59%) were able to pass their stone spontaneously, which is much higher than the previously reported rates for spontaneous stone discharge (18 % - 39 %). no side effects of hydroxyprogesterone were observed in any patient. The investigators concluded that hydroxyprogesterone treatment is simple, inexpensive, and is without side effects.

Glucagon

Glucagon is a well described smooth muscle relaxant of the gastro intestinal system. The actions of the glucagons on the urinary tract are not as well defined. In vitro and in vivo canine studies have shown that glucagons causes brief cessation of ureteral peristalsis. Lowman et al first published a preliminary report in 1977 describing 10 patients with ureteral calculi who were given one mg of intravenous glucagon. 3 patients had spontaneous passage of their stone in 4-8 hours. No side effects of the medication were reported. At this point at time, although

glucagon has proven effects to the urinary tract, expulsive therapy for urolithiasis remains largely untested.

NSAIDS

Prostaglandins impede ureteral stone passage through several interrelated mechanism. Prostaglandins are generated from arachidonic acid via cyclooxgenase (COX) activity. The 2 isoforms of COX are COX1 and COX 2. The studies of ureteral contractility have shown that prostaglandin F2 alpha and prostaglandins E2 increase contractility in obstructive ureters and that indomethacin (non specific inhibitor of COX) can inhibit generation of these contractions. Besides alteration in contractility, NSAIDS also treat renal colic by blocking the local release of pain – mediating prostaglandins.

Indomethacin

Al- walli first conducted the open study investigating the effect of indomethacin suppositories on both acute urinary colic and expulsion rates of stones resistance to convulsional analgesics and anti spasmodic.

Diclofenac Sodium

Diclofenac sodium has been studied in two clinical trials to date.

Calcium Channel Blockers

The primary anatomic unit of the ureters is the smooth – muscle cell, which functions in response to changes in calcium ion concentration. An increase in calcium concentration causes contraction. Conversely, a decrease in calcium concentration results in relaxation.

Nifedipine

Six studies evaluating nifedipine as a medical expulsive therapy have been reported to date. Borghi et al conducted the first randomized, double – blind, controlled trial using nifedipine.

Adrenergic Alpha Antagonist

Alpha receptor antagonists have long been used to treat symptoms of benign prostatic hypertrophy and prostatitis. Their mechanism is via smooth-muscle relaxation of the prostate and bladder neck via inhibition of alpha 1a receptors, resulting in increased urinary flow. Tamulosin is uro selective for the alpha 1a and alpha 1d receptors, resulting in an overall lower side effect profile compared with the non selective agents. In the ureters, alpha 1 adrenergic receptor antagonists inhibit basal tone and also decrease peristaltic frequency and amplitude. Consequently, intra ureteral pressure decreases and fluid transport increase. Given its receptor specificity and vitro findings, its seems plausible that tamulosin would be useful in the treatment of obstructive ureteral calculi.

Tamulosin

Several clinical trials have shown that alpha 1 blockers not only are useful for stone expulsion, but for control of stone colic as well.

Tamulosin versus Nifedipine

Recently, Hollingsworth et al provided further validation by reporting a Meta –analysis assessing the efficacy of drug therapy in facilitating spontaneous passage of ureteral stones. They also concluded that the addition of corticosteroids might have a small advantage, but the benefit of drug therapy is not lost in those patients in whom corticosteroids might be contraindicated.

Multiple clinical trials have shown that tamulosin improves stone passage rates, decreases stone – expulsion times, and reduces the need for analgesic therapy, hospitalization, and surgery. The non selective adrenergic alpha blockers also appear to be effective as well.

Medical expulsive therapy for ureteral stone provides other non surgical options for patients with ureteral stones. Multiple randomized clinical trials have shown that medical expulsive therapy is clinically efficacious, safe, and will tolerate.

Conclusion

The medical management of urolithiasis is a rational approach based on the abnormal

parameters detected on full investigations. However, in clinical practice it is very difficult as the patient may have all normal urinary parameters or multiple deranged parameters.

In patients with all normal urinary parameters (idiopathic) the patient is advised for the dietary restriction and kept on periodic surveillance. In patients with multiple deranged parameters the drug approach in a permutation combination rationale is applied with periodic surveillance of the parameters at repeated intervals for the dose modification or temporary discontinuation of the drug therapy. Both surgical and medical treatment is necessary for the complete management of patients of urolithiasis.

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Case Report

Hashimoto's Thyroiditis with Evan's Syndrome-An Interesting Association

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Abstract

Here we report the case of a 48-year-old female patient admitted with exertional breathlessness and easy fatiguibility. She was diagnosed as having severe autoimmune hemolytic anemia (AIHA) with autoimmune thrombocytopenia (Evans Syndrome) and was found to have coexisting Hashimoto's thyroiditis. We prescribed prednisolone and thyroxine administration. Hashimoto's thyroiditis is often associated with other non endocrine autoimmune diseases. However, there is no report of Evans' syndrome co-existing in patients with overt hypothyroidism and Hashimoto's thyroiditis, and thus is the first such reported case from India.

Introduction

Chronic, autoimmune thyroid diseases are sometimes combined with autoimmune hematologic diseases, such as pernicious anemia, autoimmune hemolytic anemia (AIHA) and idiopathic thrombocytopenic purpura (ITP). Hashimoto's thyroiditis is one of the most common autoimmune diseases. It is due to autoantibody formation and lymphocyte infiltration of the thyroid glands. Since Evans reported the first case of AIHA associated with ITP, there have been several case reports of Evans' syndrome occurring simultaneously with an autoimmune thyroid disease [(1)] ,nine cases of Evans' syndrome occurring with Graves' disease have been reported[(2)(3),(4),] and two case of Evans' syndrome with Hashimoto's thyroiditis and hypothyroidism has been reported worldwide[(5)].Here we report a case of Evans' syndrome developed together with Hashimoto's thyroiditis and overt hypothyroidism in a 48-year-old woman.

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Case report

A 48 year old female was admitted with complaints of giddiness and exertional dyspnea for 1 month. There is no history of palpitations and chest pain. She did not have any history of hypertension and diabetes. General examination revealed pallor, icterus and thyroid enlargement. On abdomen examination showed 3 cm hepatomegaly, splenomegaly .Examination of other systems were within normal limits. On evaluation she had an Hb of 3.8gm%, platelet count of 3,000/mm3., TC: 10,300. Reticulocyte count was 4%.ESR was 40mm of mm/1st hr. Urine analysis showed urobilinogen positivity. S.bilirubin was 4.1mg %. (direct: 1.6, indirect2. 5).SGOT and SGPT were within normal limits. Peripheral smear showed anisopoikilocytosis, polychromasia with thrombocytopenia. Bone marrow aspirate showed erythroid hyperplasia. USG Abdomen revealed hepatosplenomegaly. A clinical diagnosis of hemolytic anemia with thrombocytopenia was made. ANA, HIV ELISA was negative. X-ray chest showed cardiomegaly. As neither platelet count nor hemoglobin increased with repeated blood transfusions, autoimmune lysis was suspected. Hence Coombs test was ordered. Coombs test (direct) was positive. Hence the autoimmune etiology was proved and a diagnosis of Evans syndrome was made. Since the patient had a thyroid

enlargement, thyroid function test was done. Thyroid function test showed low T3,T4 and high TSH consistent with hypothyroidism. Since an autoimmune disease already was established by positive Coombs test, cause of hypothyroidism was also suspected to be autoimmune. Hence, Anti Microsomal antibody (thyroid) was done, which was strongly positive (>600, normal<34).There was difficulty in determining blood grouping due to auto agglutination. Hemoglobin as well as platelet count failed to improve with blood transfusions. Patient was started on oral steroids- prednisolone 1mg/kg and Eltroxin 100 micrograms. After 10 days of treatment, Hb improved to 5.6 gm%, and platelet count showed marginal improvement to 9,000.She did not have any external bleeding. Patient was discharged on oral steroids and Eltroxin.

Discussion

Hashimotos thyroiditis (or Hashimoto's thyroiditis) is part of the spectrum of autoimmune thyroid diseases. Hashimoto's thyroiditis is characterized by the destruction of thyroid cells by various cell- and antibody-mediated immune processes. Patients with Hashimoto's thyroiditis have antibodies to various thyroid antigens, the most frequently detected of which include anti – thyroid peroxidase (anti-TPO), antithyroglobulin (anti-Tg), and to a lesser extent, TSH receptor-blocking antibodies. Nevertheless, a small percentage of patients with Hashimoto's thyroiditis (approximately 10-15%) may be antibody negative. The most common and early presenting symptoms of hypothyroidism, such as fatigue, constipation, dry skin, and weight gain, are nonspecific. In the presence of suggestive symptoms and physical findings, a serum TSH test is needed for the diagnosis of primary hypothyroidism, and it serves to assess the functional status of the thyroid. The presence of thyroid autoantibodies, typically anti-TPO and also anti-Tg antibodies, delineates the cause of hypothyroidism as Hashimoto's thyroiditis or its variant. The treatment of choice for Hashimoto's thyroiditis (or hypothyroidism of any cause) is thyroid hormone replacement. The drug of choice is orally administered levothyroxine sodium, usually for life.

Evans syndrome is a combination of immune thrombocytopenia and autoimmune hemolytic anemia (AIHA). Evans syndrome is a diagnosis of exclusion. Confounding disorders, such as infections, rheumatologic diseases, and malignancies can present with autoimmune cytopenias, must be ruled out. Autoantibodies are directed against antigens specific to red cells, platelets or neutrophils. In Evans syndrome, the direct antiglobulin result (i. e, Coombs test result) is almost invariably positive (often weakly) and may be positive for IgG, complement, or both. Indirect antiglobulin test findings may also be positive in 52-83% of patients. Prednisone therapy, the most commonly used first-line therapy, often effectively controls acute episodes, although relapses may be frequent when patients are weaned off prednisone. Other therapies effective in small series include danazol, cyclosporine, azathioprine, cyclophosphamide, and vincristine. Splenectomy may improve CBC counts and decrease the steroid requirement, although relapses are common. Hashimoto's thyroiditis and Evans' syndrome are autoimmune disorders. Yet the combined disorders have still not been classified in Autoimmune polyglandular syndromes (APS). There are two distinct types of autoimmune polyendocrine syndromes with characteristic clinical manifestations. APS (autoimmune polyendocrine syndrome) type I, typically recognized in early childhood, is a rare autosomal, recessive disorder. Defects in the autoimmune regulator gene have been shown to cause this disorder. In contrast, the more common syndrome, APS type II, typically manifesting in adulthood, has polygenic inheritance. APS type II is less well defined, but is strongly associated with several specific HLA class II gene polymorphisms .The chronic development of organ-specific autoimmunity necessitates the evaluation of patients with Evans' syndrome over

time. This suggests further that autoimmune hemolytic anemia and idiopathic thrombocytopenic purpura with Hashimoto's thyroiditis might share a common pathogenetic pathway, the defect of which leads to Evans' syndrome and should be classified as a new third APS type.

In summary, we report a case of Hashimoto's thyroiditis complicated by Evans' syndrome, and suggest that Evans' syndrome could be a high risk factor for autoimmune thyroiditis. Patients with Evans' syndrome should be evaluated by thyroid function tests, including those for thyroid auto-antibodies, to prevent the development of overt hypo- or hyperthyroidism. .

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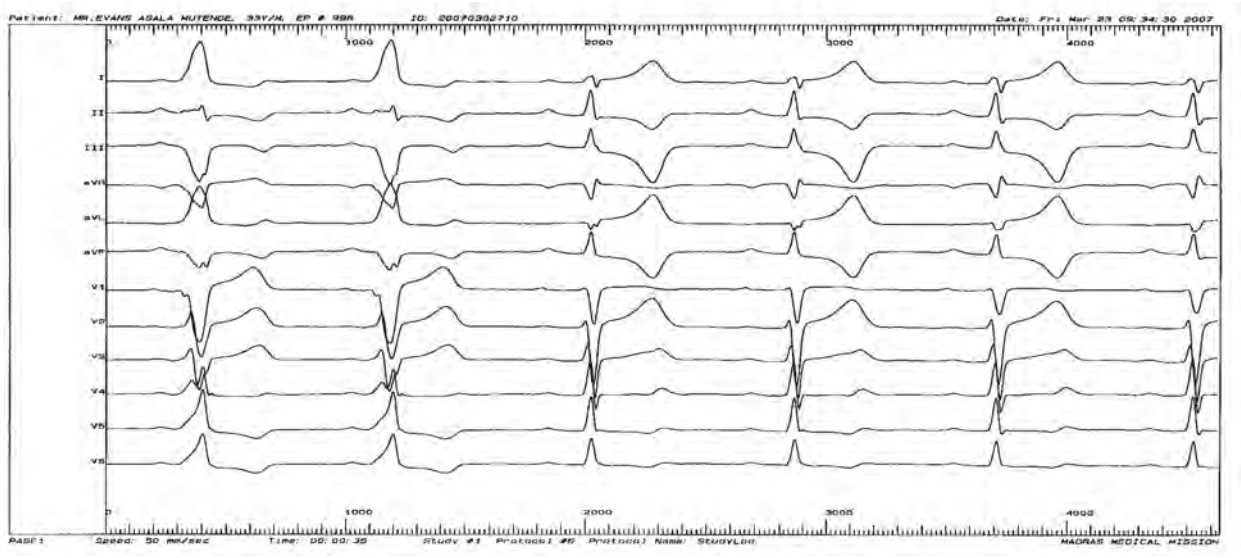
ECG Section

Diagnose the ECG Abnormalities

Dr. Ulhas M. Pandurangi MD, DM



The Previous issue (Volume 1, Issue 2, September-December 2009) quiz answer:

What is the complete diagnosis?

1. *Hypertrophic Left Ventricular Cardiomyopathy*
2. *Hypertrophic Biventricular Cardiomyopathy*
3. *WPW Syndrome*
4. *Acute Coronary Syndrome*

The correct answer is Hypertrophic Biventricular Cardiomyopathy

Note:

Answer in the next issue.

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Case Report

Isoniazid-induced Pellagroderma and the *N*-Acetyltransferase Gene Genotype

Prof. Jayakar Thomas

Introduction

Pellagra is a disorder stemming from nicotinic acid deficiency and is still prevalent in certain parts of the world. It is characterized by mucous and cutaneous lesions as well as gastrointestinal symptoms. Significant neuropsychiatric conditions have been described in many patients with pellagra. Isolated skin involvement is called pellagroderma. The anti-tuberculosis agent isoniazid can induce pellagra. Isoniazid is metabolized by arylamine *N*-acetyltransferase, and individuals with a less active form of this enzyme do not acetylate and break down isoniazid efficiently and are more susceptible to pellagra [1]. A case of isoniazid-induced pellagroderma in an individual is reported.

Case report

Miss B, a 23-year-old, well-nourished nun had been receiving a 300-mg dose of isoniazid daily with other anti-tuberculosis drugs for 5 months against her pulmonary tuberculosis, which she had suffered for the last 3 years. She had developed photosensitive dermatitis, with erosion in both forearms (Figure 1) and in the neck region since 6 weeks before presenting to the out-patient department. The lesions were typically erythematous, scaly and over her neck were lesions of the typical Casal's necklace (Figure 2). She had no gastrointestinal or psychiatric symptoms. A diagnosis of isoniazid-induced pellagroderma was made. Isoniazid was stopped and she was given daily oral administration of a 200-mg dose of nicotinic acid. Her skin lesions gradually improved and disappeared after 8 weeks.

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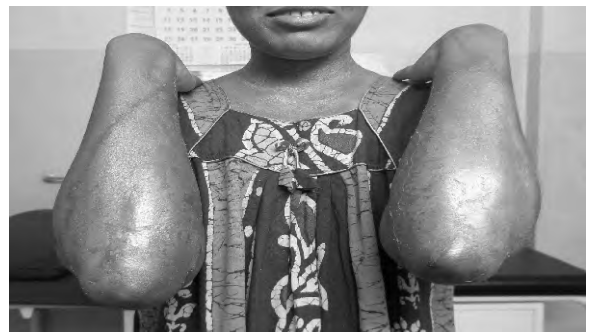

Fig. 1

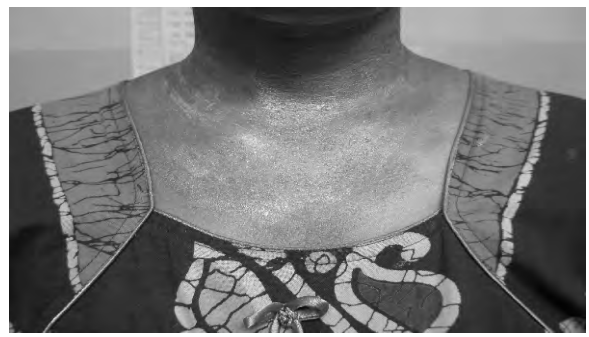

Fig. 2

Discussion

To determine the *N*-acetyltransferase genotype, genomic DNA is extracted from whole blood. A polymerase chain reaction is performed to amplify the entire coding region of the gene. The polymerase chain reaction product is extracted and used as a template for sequencing by using a dye-terminator cycle-sequencing method [2]. But these laboratory investigations are not possible in our setting. In this patient also the *N*-acetyltransferase genotype might be a major risk factor for isoniazid-induced pellagra, considering that the frequency of the slow acetylating type is 8% in the Asian population[3].

Conclusion

The *N*-acetyltransferase genotyping test is simpler and easier to perform than the conventional phenotyping test. Therefore, in patients receiving isoniazid, the genotyping test may be helpful in preventing isoniazid-induced pellagra. In India, where tuberculosis is rampant and isoniazid is almost always used, these tests should be made easily available.

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Review Article

Practical Management of Snake Bite

Dr. Palaniappen

Snake bite poisoning is a leading cause of premature death of young earning member of family in rural areas. There are about 216 species of snakes identifiable in India of which 52 are known to be poisonous. The Poisonous Snakes are **Elapidae** – Common Cobra, King Cobra, and Common Krait. **Viperidae** – Russell's viper, Echis carinatus (Saw scaled viper or Carpet Viper).

Pit Viper. **Hydrophidae** - Sea Snakes. Saw Scaled Viper or Carpet Viper (Suruttaipaambu)

Colour is pale brown or dark brown, Trident or Arrow type or bird foot print shaped mark seen on head with constricted neck. Body is covered with rough serrated flank scales. Major Clinical Features are Spreading cellulitis, Painful Lymphadenopathy, Hemostatic Abnormalities, Renal Failure – Rare, No Neurological Manifestation. In Russel's Viper (Kannadiviriyan) typical rows of oval scales arranged in two rows is characteristic of Russel viper. Local envenomation features are spreading cellulitis, painful lymphadenopathy, and compartmental syndrome. Development of wet gangrene, due to compartmental syndrome or vascular occlusion. The Systemic envenomation features are Hypotension, shock, hemostatic failure, renal failure common, Neurological manifestation may or may not be seen.

Common Indian Krait (Kattuvirian)

Krait is 10 times poisonous than cobra. Small white dots at the head end while complete

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circle of white band of whole width is till the end of tail. Hexagonal white bands arranged in pairs. Kraits usually strike a person while sleeping on the ground. The major clinical manifestation is no local signs or minimal local signs. Predominantly neurological manifestations. Early morning paralysis, hemostatic abnormalities rare. neurological manifestations of krait: autonomic stimulation – causes (20 – 30 minutes), abdominal colic, bradycardia, sweating, vomiting, hypokalemia, raised bp. post synaptic acetyl choline receptor block: (30 minutes to 18 hr's) ptosis, pooling of saliva, dysphagia, dyspnea, inter nuclear opthalmoplegia, appearance of neck, weakness of neck muscle, respiratory paralysis, diaphragmatic paralysis, vertical gaze reflex preserved ; horizontal gaze reflex absent. Deaths like features are non reacting dilated fixed

pupils, areflexia. No respone to painful stimulai is not a sign of irreversible brain damage (due to venom induced pupillary muscle paralysis)

Cobra bite

Cobra venom is potent cardiotoxic, neurotoxic, hematotoxic, cytotoxic the fangs are small and sharp. Small molecular venom - rapidly enters into the circulation. Clinical features are severe pain at the site, fang's marks covered with blood clots, rapid swelling due to myocytolysis, ecchymosis & blebs. Cobra bite sudden death – causes. Fear of cobra bite, ventricular arrythmias or cardiogenic shock, massive mi, adrenal haemorrhage envenomation itself: cardiotoxicity, respiratory paralysis. Cardio respiratory envenomation features are sinus bradycardia, a-v block, hypotension, sudden respiratory arrest, anoxic cardiac arrest. neuroenvenomation features of cobra bite - blurring of vision, loss of accommodation, rapid ptosis, bulbar palsy, respiratory depression, hematotoxic effects are minimal.

Sea snakes

Occurs in fisherman duringfishing. Venom contains neurotoxin, myotoxin, haematotoxin. No local manifestation at the site of bites. Cardiac arrest due to liberation of potassium into circulation due to myotoxic effect. Massive liberation of myoglobin into circulation causes ATN & ARF. The first aid are r - reassure the patient; i - immobilisation; g.h - get to hospital immediately, t - Tell the doctor any systemic symptoms such as ptosis that manifest on the way to hospital. Reassurance - keep the person calm. Unnecessary panic will only raise the PR, BP rapid entry of venom into the system.

Immobilization

Like fracture management if hand or arm bite - use a piece of cloth to support the arm. Leg bite - use splint - for support - bandage both legs together. Don't tie tightly. Crepe bandage applied with the pressure enough that one can easily introduce one finger between skin & bandage. Remove any rings or constricting items because the affected area may swell. Restrict movement & keep the affected area below the heart level to reduce the flow of venom. Be careful while transporting the dead snake – a snake can actually bite for up to an hour after its dead (from a reflex). Don't allow the patient to become over exerted, don't try to suck out the venom, don't cut the area with a knife or razor, and do not use ice or cold packs. Don't wash the wound, don't allow the patient to walk or run. Don't use electric shock therapy; don't give anything by mouth (NPO). Don't apply any drugs or chemicals on the wound. Don't raise the site of the bite above the level of the patient's heart. Don't use the suction devices; don't remove the tourniquet if the patient is brought in with the tourniquet until wide bore IV access is obtained. Drawback of tourniquet is risk of serious local necrosis. Immediate removal of tourniquet causes respiratory failure venous clot surge causes embolism and death. If you suspect venous clot with the help of BP cuff release the tourniquet pressure slowly.

Laboratory investigations

The 20- min whole blood clotting test (20 wbct): gold – std bed side test, take a new clean dry glass test tube and not washed with soap, a few millilitres of venous blood is left undisturbed in the test tube for 20 min. The tube is then tilted gently (should not be shaked) and if the blood is still liquid - coagulopathy positive, clotted – coagulopathy negative. Clotted blood sediment with liquid serum should not be mistaken for positive coagulopathy. Repeat 20wbct. (a) Positive wbct on admission ~~> repeat 6th hourly. (b) Negative wbct on admission repeat every ½ hourly for 3hours, then hourly for 3 hours, then 6th hourly two consecutive tests, 24th hourly. If wbct test is positive in between then repeat wbct 6th hourly. other investigations: ELISA, hemogram, blood urea and serum creatinine, PT and APTT, FDP and ABG, serum electrolytes, urine examination, ECG, EEG.

ASV: immunoglobulin purified from the serum or plasma of a horse or sheep. Indian ASV is polyvalent against the big – 4 species, not included in hump nosed pit viper, malabar pit viper, sea snakes. Liquid ASV - cold chain & r powder ASV - keep in cool. ASV is double edged weapon. ASV administration criteria- e/o neurotoxicity, coagulopathy, severe current local envenomation (sclv), cardiovascular abnor. Hypotension, shock, cardiac arrythmia, abnormal ECG, persistant severe vomitting or abdominal pain.

SCLE: Swelling rapidly crossing joint or involving half the bitten limb in the absence of tourniquet. Persistent swelling even one hour after the removal of tourniquet and there is no window time for giving SCLE

Prophylactic regimen for ASV reactions

1. ASV test dose not recommended
2. Prophylactic regimen not routinely practiced.
3. Avoid adrenaline – proarrythmic, sudden death
4. Hydrocortisone injection peak action starts after 20 minutes
5. Avoid pheniramine maleate – making n.e. features

Treatment of hemotoxic envenomation: Total required ASV 10 – 23 vials, dose – 1: 10 vials ASV diluted with 5% dextrose rushed in 1 hour. Neutralizes free circulation .v (50%). dose 2: mild e. 2 vials ASV. moderate e. 5 vials ASV. Severe e. 8 vials ASV. Given over 4hours and 2hours drug free period (dose 1 and 2), dose 3: severe e. 5 vials ASV given over 4hours & 2hours drug free period. dose 4 : (5 – 10 vials ASV) titrate according to the patient need ; fatal bleed, pulmonary haemorrhage, frank hematuria, bleeding from venopuncture site, bleeding from bitten site, divc, given over 4hours and 2hours drug free period

Discussion: dose 2, dose 3 & dose 4 are useful for neutralizing; slow releasing tissue bound venom (50%), 2hours drug free interval will stimulate liver for clotting factors synthesis, severe coagulopathy - FFP (fresh frozen plasma) (positive 20wbct), fresh blood (thrombocytopenia) -- really useful.

Remember: hump nosed pit viper doesn't respond to routine Indian the big – 4 ASV,plasma paresis useful to save the life and ASV resistance.

Treatment of Neurotoxin envenomation—A.S.V.Dosage, Total Required ASV 0 – 20 Vials

a) Dose 1: 10 vials ASV diluted with 5% dextrose rushed in 1 hour.

b) Dose 2: if the symptoms have not improved second dose of ASV (10 vials) should be restarted according to the patient need. (1-3 hour) – Given over 1- 4 hours period. Neuro envenomation should be assesed 1/2 hourly for 3 hours. Anticholinergic therapy will postpone the respiratory failure[3]. After 15 min inj neostigmine 1 mg (2 amp) & inj glycopyrolate (2amp) 0.4 mg+ & inj atropine 0.6 mg (1 amp) stratum, neostigmine (2 amp) + glycopyrolate (2amp) in ns drip given in 4 hours can be continued for 24 – 48 hours. Stop the drip if 2 consecutive, 4th hourly clinical observation of neuroenvenomation is negative[4]

Reports

1. If the patient is in respiratory failure – received 10 vial of ASV & supported on a ventilator – no need to continue ASV
2. Cases are reported neuroenvenomation and managed only with the help of ventilator without ASV
3. Reversibility of post synaptic neurotoxic envenoming is only possible in the first few hours.

A.S.V. not available????

1. Blood and blood products
2. Neostigmine, atrophine, glycopyrolate combination.
3. Mechanical or artificial ventilation

Neuroenvenomation – artificial ventilation indications: decreasing level of consciousness, pooling of saliva, inability to lift the neck, inability to abduct the shoulder, spo2 < 90 % with o2

Haemodynamic instability: ASV –children / pregnancy: children should be treated exactly the same dose of ASV as adults. Snake bite pregnant patient is treated the same manner as the non pregnant patient. Lactating mothers can continue lactation

Anaphylactic reaction: approximately 10-20% patients treated with ASV develop either early or late reaction. the earliest symptoms are vomiting sensation, warm sensation in ears or head, itching behind the ears, urticaria, itching all over the body, dry cough, abdominal colic, diarrhoea, tachycardia and fever.

Life threatening reaction

Hypotension, bronchospasm and angio oedema, frequent monitoring is needed. Treatment of ASV reaction: stop ASV temporarily, desensitisation of ASV reaction. For adults: inj.adrenaline 1.5cc of mixture im (1cc adrenaline + 4cc ns = 5cc mixture), inj.pheniramine maleate (22.5mg) 1cc iv ; inj.hydrocortisone (100 mg) iv, oxygen, fluid management and for children : inj.adrenaline 0.5 cc of mixture (1cc adrenaline + 4cc ns = 5cc mixture) inj.pheniramine maleate 0.1-0.3mg/kg iv, inj.hydrocortisone 2mg/kg. The dose can be repeated after 10 – 15 minutes if the patient's condition has not improved. Majority of cases respond to two doses of adrenaline, if the patient not responding then IV adrenaline drip or 1ml 1: 1000 adrenaline diluted in 20ml of saline to be administered over 20minutes by slow drip and restart the ASV slowly.

Antibiotics

Mild to moderate envenomation: 3rd generation cephalosporin, quinolone infusion, metronidazole infusion. Severe envenomation: cefoperazone + sulbactum or piperacillin + sulbactum combination, quinolone infusion, metronidazole infusion ---- duration : 3 – 10 days

Switch over to oral antibiotics once patient recovers from acute crisis.

Analgesia: tab.paracetomol, inj.tramadol, tab.chymoral forte, nsaid's, should be avoided, regional anesthesia

Causes of AKI in snake bite

Severe persistant hypotension, divc, spreading cellulitis, septicemia, atn due to snake venom, myoglobinuria, hemoglobinuria, hemolytc uraemic syndrome immune mediator kidney injury. prerenal azotemia: fluid challenge, positive ionotrophics, intermittent i.v. frusemide inj., c.v.p. monitoring.

Early management of AKI due to ATN

Meticulous hourly urine output monitoring, hourly urine output < 30ml suspect acute renal impairment; if renal failure (ATN) occurs reduce iv fluids. Switch over to 25% dextrose (17microdrop/mt = 4pints over 24hr's)

Early A.K.I. management

Fluid restriction (previous hour output + 20ml); appropriate antibiotics like pipzo, ofloxcin, metronidazole ; oral fluid diet restriction ; best diet – soft bland diet. Early renal failure can be managed with inj. frusemide or torsimide 200 to 500mg continuous IV drip; positive iontrophic support inj.dobutamine or dopamine, taper dopamine drip till blood pressure is maintained for 130/90 mm HG for 24 hr's .inj.metaclopromide or ondensetran antiemetics according to patient need. Stress peptic ulcer prophylaxis according to your preferance like. inj. PPI inhibitors or h2blockers or sucralfate, peritoneal dialysis or hemodialysis and plasmaparesis. Mortality in snake bite due to AKI: incidence 1 – 10 %; causes - acute cortical necrosis, delay in administration of ASV, snake bite with extremes of age group.

Fasciotomy

Before fasciotomy hemostatic abnormalities should be corrected, multiple subcutaneous 2cm fasciotomy over foot, 3cm above medial malleolus; 3 cm above lateral

malleolus; posterior aspect all are in a circle. This will prevent all 3ways of toxic fluid containing lymphatic system drainage.

Carry home message

20wbct gold std. test, meticulous monitoring, FFB & fresh blood transfusion, supportive measures, early multiple fasciotomy, brown limb_a.k.i., black limb -_amputation or death

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Consultant in charge, snake venom research laboratory& herpetarium
University of Colombo, Srilanka

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Dr. S.N. Narasingan, Chennai
(2007-2008)

We Congratulate Our Past Chairman Dr.S.N.Narasingan for being Elected as a Fellow of the Royal College of Physicians, (FRCP) Glasgow.

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