REFERENCES

1. Greenstein AJ. Janowitz HD & Sachar DS. The extra intestinal complications of Crohn's disease and ulcerative colitis. Medicine, 1976 55 : 401-12.
2. Johnson ML. & Wilson HTH. Skin lesions in ulcerative colitis Gut. 1969. 10 : 155-62.
3. Basler RSW. Ulcerative colitis and the skin. Medical Clinics of North Amercia. 1980, 64 : 941-51.
4. Smith JN. & Winship DH. Complications and extra intestinal problems in inflammatory bowel disease. Medical Clinics of North Amercia. 1980, 64 : 1161-71.
5. Newell LN. & Malkinsen FD. Commentary: Pyoderma gangrenosum Arch. Dermatology 1982, 118 : 769-73
6. Holt PJA. Davies MG and Saunders KC. *et al.* Pyoderma gangrenosum. Medicine, 1980, 59 : 114-33.

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INSULINOMA WITH SPECIAL FEATURES

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SUMMARY

A case report of insulinoma is presented for some special features. The patient had severe hypoglycaemic symptoms in fasting state for over 18 years. On oral G.T.T. there were no typical symptoms and the glucose tolerance was normal. The suspicion of insulinoma was strengthened because she had elevated fasting serum C-peptide. However, the corresponding insulin value was normal. On laparotomy, a peanut sized tumour was removed from the pancreas and histopathological examination confirmed that the tumour was insulinoma. Postoperatively, the patient is symptom free, but her insulin and C-peptide responses are subnormal. The plasma glucose values remain in the low normal range.

INTRODUCTION

The diagnosis of insulinoma depends on a high degree of clinical suspicion and documentation of fasting hypoglycaemia with symptoms which are relieved by administration of glucose. Confirmation of the diagnosis is facilitated by an elevated insulin/glucose ratio[1]. This case is being reported because of its many special features namely: 1) comparatively low insulin concentration with high C-peptide concentration 2) the insulin concentrations continued to be low with low concentrations of C-peptide after the removal of insulinoma and 3) one of the longest documented preoperative period without major catastrophe.

This is also the first case of proved insulinoma being reported from the Indian subcontinent.

CASE REPORT

Mrs. B.B., 54 years old housewife was referred to the centre for investigations for hypoglycaemia, on June 23, 1984. She gave history of frequent episodes of giddiness, palpitation, sweating and occasional fits with unconsciousness or semiconsciousness since 1966. She had been hospitalised on two occasions, treated with intravenous glucose and was advised laparotomy. The patient was afraid of the outcome of surgery and refused it on two occasions. The lowest fasting blood glucose recorded was 35 mg/dl in fasting state. She used to get hypoglycaemic attacks frequently at any time of the day or night and used to drink glucose solution frequently during day and night.

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Ultrasonogram performed a month prior to the reference to this centre showed no evidence of pancreatic mass and pancreatic echoes were uniform. Spleen, kidneys, liver and gall bladder were normal. There was no neurological deficit. First degree family history of diabetes was present, brother having diabetes. She had 8 child births and has 6 living children. The first episode of hypoglycaemia was noted 6 months after 7th child birth in 1966. She weighed 55.9 Kg. with a height 151 metres (BMI-24.5).

Investigations

Oral glucose tolerance test with 75 gms glucose load was performed. The results of plasma glucose (Ortho-toluidine method) immunoreactive insulin[2] (IRI) and C-peptide[3] (CP) are shown in Table 1. There was no hypoglycaemic symptoms during the GTT and the plasma glucose values were also normal. Fasting IRI was normal, although the stimulated response was on the upper limit of normal range. However, both the fasting CP and the stimulated CP responses were high. On subsequent days in the hospital the fasting plasma glucose values were 37 mg% and 41 mg% and the patient was uncomfortable during fasting. She was given oral glucose. Insulinoma was suspected in view of the high fasting CP. Surgery was done on November 9, 1984 and a peanut sized bluish tumour with capsule was removed from the head of the pancreas.

Pathology Report

The specimen was a discrete, well demarcated solitary tumour. The cut section appeared yellow and homogenous. Hematoxyline and eosin stained sections showed an encapsulated tumour with cells resembling normal islets arranged in solid nests of ribbons and festoons (Figure). The cells were eosinophilic and fairly

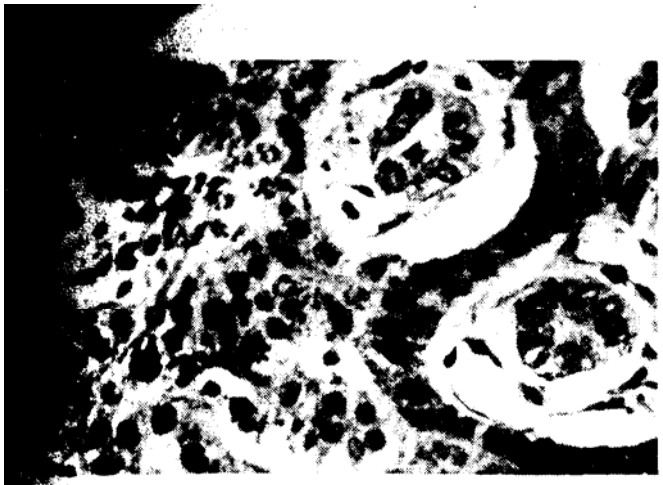

Fig.: Section of the tumour showing normal islet cells arranged in solid nests.

granular with ovoid or spherical nuclei without nucleoli. Highly vascular stroma with thin walled vessels were seen between cords of cells. Areas of fibrosis and amyloid were observed. No area of nuclear pleomorphism or mitosis was seen.

Post-operative period

The patient was comfortable and was free of hypoglycaemic symptoms after the surgery. GTT was repeated on 26th April, 1985 when she returned for a check-up (Table 1). It showed a flat glucose curve with low IRI and CP responses. Post prandial plasma glucose, IRI and CP were repeated, 3 months later on 27.7.1985. This also showed low pp glucose with low IRI and CP values. Her IRI and CP responses remained subnormal and the plasma glucose was also low.

DISCUSSION

In the diagnosis of insulinoma hypoglycaemic symptoms along with low plasma glucose and elevated insulin/glucose ratio are considered to be the most reliable criteria. Service *et al*[4] from Mayo Clinic have recorded the largest series of insulinomas. Many workers feel that measurement of serum C-peptide has no specific advantage over the measurement of insulin/glucose ratio in the diagnosis of insulinoma[1]. Service *et al*[5] have stressed upon the use of the C-peptide suppression test in the diagnosis of insulinoma.

In the diagnosis of the case reported here, the most convincing evidence was the high concentration of serum CP in the fasting state. The corresponding IRI value was within normal limits and not suggestive of endogenous hyperinsulinaemia. The reasons for the disparity between IRI and CP values are speculative. It may be that the degradation of IRI is increased in the patient. It may be that the degradation of IRI is increased in the patient. It is also likely that the sensitivity for endogenous insulin is quite high. Normal insulin concentration and I/G ratio, thus do not exclude the possibility of insulinoma. A similar case was reported by Harrisson[1]. The patient, a young child was reported to have profound, hypoglycaemia with low insulin values of 3 to 5 uU/ml. Interestingly, our patient has subnormal insulin and CP values after the removal of insulin secreting tumour; however her plasma glucose values are always in the low normal range. This is probably an indication for enhanced insulin sensitivity in this patient who is now absolutely symptom free. The other possibility for low plasma glucose could have been incomplete removal of the tumour. However, the low CP and IRI values do not support this possibility.

This case is, therefore, reported for its peculiar features, viz. 1) Elevated fasting serum CP with normal IRI and 2) the picture of elevated insulin sensitivity subsequent to the removal of the insulinoma and 3) for one of the longest pre-operative periods with symptoms of hypoglycaemia.

The patient is leading a normal life for the past 2 years after the surgery and has stopped buying glucose.

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REFERENCES

1. Harrisson. T.S. Insulin secreting lesions of the pancreas. The Pancreas. Keynes, WM Keith, R.G. Eds. London, William heinmann Medical Books. 1981 : 221-40.
2. Herbert V, Lau KS, Gotilieb CV, Bleicher SJ. Coated charcoal immunoassay of insulin. J. Clin. Endocrinol. 1965; 25 : 1375-84
3. Heding, LG. Radioimmunological determination of human C-peptide in serum. Diabetologia 1975; 11 : 541-8.
4. Service FJ, Dale AJD, Elveback LR, Jiang NS. Insulinoma: Clinical and diagnostic features of 60 consecutive cases. Mayo clinic Proc. 1976; 51 : 417-20.
5. Service FJ, Horwitz DL, Rubenstein AH, Kuzuya H, Mako Reynolds C, Molnar GD. C-peptide suppression test for insulinoma. J. Lab. Clin. Med. 1977; 90 : 180-4.

TABLE 1: **RIA OF INSULIN AND C—PEPTIDE**

Date	Plasma Glucose mg/dl						IRI uU/ml						CP p mol/ml					BMI
	F	30'	60'	90'	120'	180'	F	30'	60'	90'	120'	180'	F	30	60	90	120'	
Before Surgery																		
23.6.84	79,	109,	127,	100,	100,	87	12,	68,	86,	135,	140,	46	1.6	1.8.	2.3.	2.3,	2.3,	24.5
After Surgery																		
26.4.85	64,	96,	39,	64,	88		17,	22,	28,	22,	14		0.14,	—.	0.18,	0.3,	0.3	23.0
27.7.85	PP	66							20						0.31			24.0