

SECONDARY DIABETES DUE TO CYSTIC FIBROSIS WITH MULTISYSTEM INVOLVEMENT

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SUMMARY

An interesting case of cystic fibrosis with secondary diabetes is presented. Investigations revealed evidence of involvement of multiple organ systems.

INTRODUCTION

Cystic fibrosis is an autosomal recessive condition in which there is a generalized disorder of mucus secretion affecting most exocrine glands. It has been reported that the occurrence of cystic fibrosis is restricted to the Caucasian race and that the disease is almost unknown in India¹.

A report by Reddy *et al*² suggested that this might not be true, and that if looked for carefully, the disorder seems to exist in our country also. The authors have collected cases by routinely performing sweat chloride tests in patients with severe pulmonary disease. Here we present an interesting case of secondary diabetes due to cystic fibrosis with involvement of several organs.

CASE REPORT

Mr M, aged 33 years, was hospitalized for productive cough, hemoptysis, breathlessness and swelling of the feet. He had cough from childhood, but of increasing severity for the past three years. The sputum was purulent, copious (over 100 ml/day) and often associated with hemoptysis. He also complained of bulky frothy stools with occasional diarrhoea.

He was born of a full-term normal delivery. There was no history of measles, chicken-pox or pertussis in childhood nor any history of foreign body aspiration. Two of his siblings were reported to have died of severe respiratory infection. There was no history of bronchial asthma, tuberculosis or diabetes in the family. Clinical examination revealed a severely emaciated individual (37.2 kg, 157 cms). His body mass index was 16. There was central cyanosis, marked digital clubbing, and bilateral pitting pedal oedema. The JVP was elevated. The upper respiratory tract was normal. Examination of the chest revealed the trachea to be in the midline. There was diminished movements of the chest bilaterally, and a mild left parasternal lift. On auscultation scattered rhonchi and persistent coarse, leathery rales were present in both lung fields. The pulmonary component of

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the second sound was accentuated, indicating cor pulmonale. Hepatosplenomegaly was also present. The liver was firm in consistency and the spleen was palpable 2 cm in the long axis. The CNS examination was normal.

Investigations: Routine urine examination showed moderate glycosuria (1.5%), no acetonuria; urine deposits were normal. Stools examination was normal. WBC 10,800 cells/mm³ (P54 L35 E8 M3, ESR 35 mm/1st hour).

Sputum Culture: *Pseudomonas aeruginosa* grown, resistant to all antibiotics. *Mycobacterium tuberculosis* was not demonstrable in the smear. Sputum culture for anaerobes, fungus and *M tuberculosis* were negative.

Serum proteins 5.9 gm% with albumin 30% and globulin 70%. Serum bilirubin 1.0 mg%, SGOT 44 IU/L, SGPT 46 IU/L. Serum amylase 230 Somogyi units. Faecal fat (mean of three occasions): 14.2 gms/24 hours (normal 2-7 gms). Sweat chloride, estimated by pilocarpine iontophoresis method, was 102 mEq/L (Normal : 30-70 mEq/L). This confirmed the diagnosis of cystic fibrosis.

A standard oral glucose tolerance test using 75 gms glucose showed evidence of overt diabetes³: Fasting - 109 mg%, ½ hr - 140 mg%, 1 hr - 180 mg%, 1½ hr - 212 mg%, 2 hr - 210 mg%. Sugar was estimated in venous plasma by the O-Toluidine method. Radioimmunoassay of insulin (IRI)⁴ and C-peptide⁵ confirmed a low pancreatic beta cell reserve (Fig. 1).

A complete lipid profile⁶ showed low total cholesterol and LDL lipoprotein cholesterol levels : 150 mg%

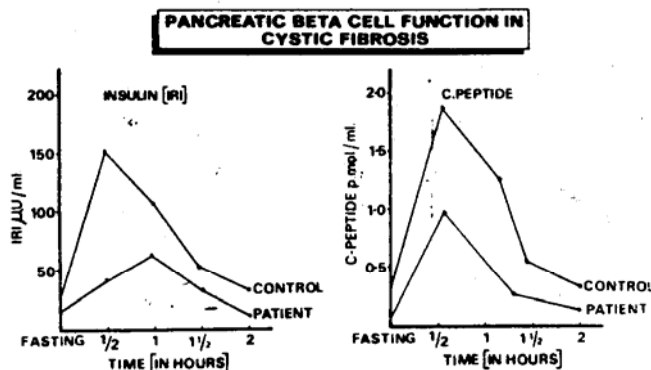


Fig. 1: Insulin (IRI) and C-peptide responses to oral glucose load.

and 80 mg% respectively. The HDL and VLDL lipoprotein cholesterol levels were 40 mg and 30 mg% respectively.

X-ray chest revealed evidence of extensive bilateral bronchiectasis and mild cardiomegaly (Fig. 2). The barium meal series was normal. Real time B mode ultrasonography of the abdomen showed evidence of gross fibrosis and shrinkage of the liver with dilated portal radicles (Fig. 3) and increase in echogenicity of the pancreas (Fig. 4). The head, body and tail measured 1.8 cms, 1.4 cms, and 1.0 cms. There was evidence of fibrosis and shrinkage in the pancreas, which measured only 5.4 cms (Normal : 6-8 cms).

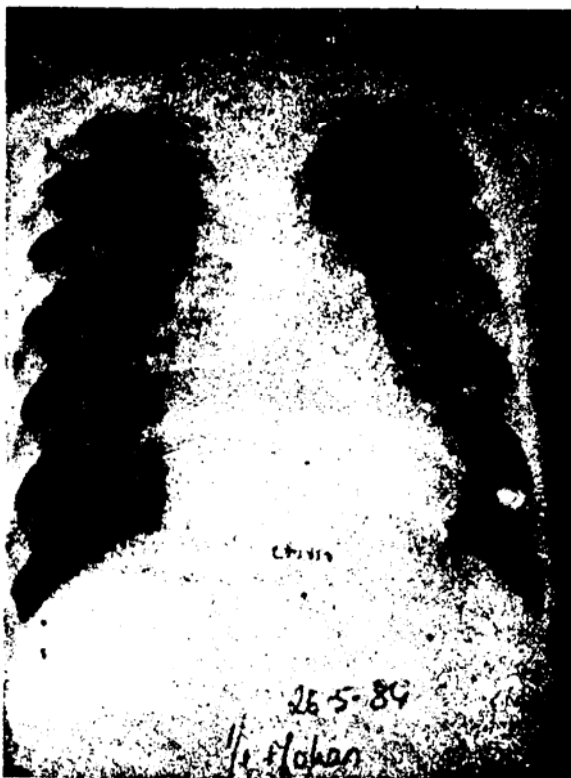


Fig. 2 : Evidence of bilateral bronchiectasis and cor pulmonale

Computerized spirometry revealed evidence of both obstructive and restrictive airway disease, with little improvement on salbutamol inhalation. Two dimensional echocardiography showed evidence of cor pulmonale with severe pulmonary hypertension.

Management: The diabetes was managed with high carbohydrate, high protein diet (2000 cal) along with 2.5 mg of glybenclamide in two divided doses. The respiratory infection was treated with appropriate antibiotics and the respiratory and cardiac failure were also treated. The patient was well-controlled when discharged at request.

DISCUSSION

This patient has classical features of cystic fibrosis. The interesting feature in this case is the occurrence of



Fig. 3 : Ultrasonogram showing evidence of cirrhosis of liver and dilated portal radicles.



Fig. 4 : Evidence of shrunken and fibrosed pancreas.

diabetes mellitus, which is relatively rare, occurring in only one of 130 cases of cystic fibrosis⁷. The absence of family history of diabetes, the mild nature of the diabetes, the severity of cystic fibrosis and the ultrasonographic evidence of pancreatic fibrosis are pointers that the diabetes is secondary to this condition. This is the first report of cystic fibrosis associated with diabetes from our country, to the best of our knowledge. The ultrasonographic features of the liver and pancreas in this condition are also presented for the first time.

This case is also interesting because of the multiple systems affected. The usual changes in the liver are focal biliary cirrhosis. Multilobular cirrhosis and portal hypertension occur in less than 2% of cases of cystic fibrosis¹. This patient had biochemical as well as ultrasound evidence of cirrhosis of the liver.

The involvement of the respiratory system is the usual presentation. In our patient this was severe enough to lead to cor pulmonale.

The gall bladder is another organ frequently affected in cystic fibrosis. In our patient the ultrasound showed a normal gall bladder. The intestines also sometimes show mucus plugs, and intussusception, volvulus

and rectal prolapse have all been reported. In this patient, the barium meal series was normal.

Immunoreactive insulin levels are usually low in patients with cystic fibrosis⁸ and this was found to be so in our patient also. C-peptide levels are a better index of pancreatic beta cell function. C-peptide values were also low in our patient, and this is the first report of C-peptide levels in cystic fibrosis.

To summarize, we have presented an interesting case of cystic fibrosis with secondary diabetes and involvement of the liver, pancreas, lungs and heart with complete clinical, biochemical, radiological and ultrasonographic work up.

REFERENCES

1. Forstner GG. Cystic fibro. . In: Keynes WM, Kerth RG Ed. The Pancreas. London: William Heinmann, 1981 169-188.
2. Reddy CRRM, Devi CS, Anees AM, Murthy DP, Reddy GE. Cystic fibrosis of the pancreas in India. J Pediatr 1969, 75 : 522-523.
3. National Diabetes Data Group: Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. Diabetes 1979, 28 : 1039-1057.
4. Hebert V, Lau KS, Gotlib CV, Bleicher SJ. Coated charcoal immunoassay of insulin. J Clin Endocrinol 1965, 25 : 1375-1384.
5. Heding LG. Radioimmunological determination of human C-peptide in serum. Diabetologia 1975, 11 : 541-548.
6. Susheela L, Shyamsundar R, Ramachandran A, Mohan V, Viswanathan M. Favourable alterations in serum total HDL and LDL/HDL cholesterol ratios after glucoregulation in newly diagnosed NIDDM. diabetologia Croatica 1983, 12 : 17-33.
7. Rosaih R, Schwachmann H, Kulczyeki L. Diabetes mellitus and cystic fibrosis of pancreas. Laboratory and clinical observations. Am J Dis Child 1962, 104, 625-634.
8. Wilmshurst EG, Soeldner DS, Hosclaw DS, *et al*. Endogenous and exogenous insulin responses in patients with cystic fibrosis. Paediatrics 1975, 55 : 75-82.