

Tropical chronic pancreatitis

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During the last 3 decades it has become increasingly apparent that a juvenile form of chronic calcific non-alcoholic pancreatitis is widely prevalent in several tropical countries. Although several terms have been proposed for this entity, it is now generally referred to as "Tropical Calcific Pancreatitis." The term Fibrocalculous Pancreatic Diabetes (FCPD) was introduced by the WHO study group report on diabetes, for the diabetes secondary to this form of pancreatitis.

Historical perspective :

In 1959, Zuidema from Indonesia was the first to describe cases of pancreatic calculi with diabetes in association with severe undernutrition. Subsequently reports from several tropical developing countries including India firmly established TCP as a distinct form of diabetes. Thanks to the pioneering work of Geevarghese, the high prevalence of TCP in southern India particularly in Kerala state become well known. Additional reports from Tamil Nadu and Orissa and other parts of India contributed further knowledge to this field.

Prevalence of TCP :

There is only one epidemiological study on TCP to date. Balaji studied a population of 28,507 and 518 subjects were identified who had one of the following three characteristics: abdominal pain suggestive of pancreatitis, diabetes mellitus or a history of weight loss (malnutrition). Using a combination of abdominal X-rays, ultrasound and NBT-PABA test, 28 cases of chronic calcific pancreatitis (CCP) and 8 cases of non-calcific pancreatitis (NCP) were identified. Thus 1:793 (0.12%) patients had chronic pancreatitis (CCP+NCP) and 1:1,020 patients had CCP (0.09%).

Clinical features:

TCP is a disease of youth. The mean age at diagnosis is about 20 years (range 10-40 years). There is usually a male predominance. Patients are invariably poor and present with extreme emaciation, protein energy mal-

nutrition, bilateral parotid enlargement, distension of abdomen and very rarely with a cyanotic hue of the lips. Multiple vitamin deficiencies and skin infections may be present. The disease usually starts with recurrent abdominal pain in childhood, pancreatic calculi are evident around adolescence and diabetes sets in by adulthood.

Abdominal pain : This is usually severe, epigastric in location and characterised by periods of remission and exacerbation. It radiates to the back on either side and is sometimes relieved by stooping forward. Powerful analgesics are needed for obtaining relief from the pain.

Steatorrhoea : About a third of patients complain of passing bulky, frothy or oily stools. The low frequency of steatorrhoea has been attributed to the low fat content of our diet.

Nature of diabetes and its complications :

Diabetes usually sets in a decade or two after the first episode of pain and over 80% of TCP ultimately develop diabetes. One of the characteristic features is that despite of severe hyperglycaemia requiring insulin for control, patients rarely become ketotic.

Being a secondary form of diabetes, it was earlier believed that patients with FCPD are not susceptible to specific diabetes complications. Our work and that of others has disproved this hypothesis. In our studies, we found that sight-threatening forms of retinopathy (maculopathy and proliferative retinopathy) nephropathy, neuropathy and cardiomyopathy occurred as frequently as in primary forms of diabetes.

Bio-chemical features :

Serum amylase is usually within normal limits but may be elevated during an acute exacerbation of pain. In advanced stages, serum lipase may be low. Serum cholesterol and triglyceride are usually low.

Exocrine pancreatic function :

Lundh meal tests have shown that 93% of calcific TCP have low tryptic activity. Yajnik et al from Pune using serum immunoreactive trypsin (IRT) levels to assess exocrine pancreatic function found that over 90% of TCP patients had subnormal IRT levels. We have recently shown that faecal chymotrypsin test is a simple marker of exocrine insufficiency in TCP patients.

Endocrine investigations :

The phenomenon of ketosis resistance has been referred to above. Our studies and that of others has shown that this is most likely due to partial preservation of pancreatic beta cell function, as shown by C-Peptide studies. Alternative explanations for absence of ketosis include low glucagon levels (pancreatic alpha cell dysfunction), low fat mass and decreased mobilisation of free fatty acids.

Radiology: Ultrasound: CT: ERCP Findings :

TCP patients have characteristic large, dense, discrete calculi usually seen to the right of first or second lumbar vertebrae. They are invariably intraductal and may be solitary or multiple. Sometimes the whole pancreas could be studded with calculi. In contrast, patients with alcoholic pancreatitis show small, ill-defined specks of calcification.

Ultrasonography and CT scan help to confirm the calculi, show ductal dilatation, fibrosis and irregularity of the gland. ERCP documents the degree of dilatation of pancreatic duct.

Composition of calculi :

Pitchumoni and colleagues have analysed the composition of calculi by X-ray diffractometry and found that formation of calculi takes place in multilayers and multistages. Formation of an inner protein nidus in the form of a cobweb is the first stage. Later calcite is deposited as tiny crystals.

GI Complications :

Apart from complications of diabetes, TCP's have several GI complications which include phlegmon, pseudocysts, pancreatic abscess and ascites. Obstructive jaundice is occasionally seen. This is attributed to the fibrosis involving common bile duct obstruction due to stone or to associated carcinoma of pancreas. TCP is considered a pre-malignant condition, as on follow-up many patients develop carcinoma of the pancreas.

Management of pain and chronic pancreatitis :

Steatorrhea when present can be reduced, but not totally alleviated by the use of pancreatic extracts and various enzyme preparations. Pain, if severe and intractable, may require surgical intervention. Sphincterotomy or side to side pancreatico-jejunostomy has been tried. Many patients have recurrence of pain after surgery.

Etiopathogenesis: This is still ill understood. Several theories have been proposed:

Undernutrition: Protein energy malnutrition has been suggested as an etiological factor. However this could well be the consequence of malabsorption and/or diabetes. The high prevalence of TCP in Kerala, where literacy rate is highest and infant mortality rate lowest in the country, suggests that malnutrition alone cannot be the cause of TCP.

Cassava hypothesis: The geographic distribution of TCP coincides with areas of consumption of cassava especially in Kerala. Cassava contains cyanogenic glycosides, which are usually detoxified by sulphur containing aminoacids. In rats, ingestion of cyanide has been shown to produce transient diabetes. But human evidence is still not sufficient to incriminate cassava as a cause of TCP. Moreover, this hypothesis does not explain the occurrence of TCP in areas like Madras, where cassava is not consumed.

Oxidative stress theory: This theory was proposed by Braganza. Several factors which cause chronic induction of cytochrome p 450, like xenobiotics (cigarette, alcohol, occupational, chemical etc) or suboptimal intake of micronutrient anti-oxidants results in defective oxidative detoxification of toxic products. This oxidative stress could lead to chronic pancreatitis. More work is needed to prove this hypothesis.

Criteria for FCPD :

No definite criteria have been laid down as yet for diagnosis of FCPD. Mohan et al have proposed the following criteria based on their own studies:

1. Diabetes must be present according to WHO criteria.
2. Evidence of chronic pancreatitis: The single most important criteria is the presence of pancreatic calculi on plain x-ray abdomen. In the absence of calculi atleast three of the following must be present.
 - a) Presence of structural pathology in the pancreas demonstrated by ultrasound, CT scan, ERCP or histopathology.
 - b) History of recurrent abdominal pain from childhood.
 - c) Other causes of chronic pancreatitis like alcoholism must be excluded.

Unresolved issues in TCP :

Studies aimed at establishing the prevalence and incidence patterns in different tropical countries are needed. The role of malnutrition should be more clearly defined. Role of environmental and toxic factors needs to be improved. These studies could not only lead to better understanding of chronic pancreatitis but also help to plan preventive strategies.

Suggested reading :

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