

FAMILIAL PANCREATITIS WITH LITHIASIS

Pages with reference to book, From 275 To 278

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Chronic relapsing pancreatitis occurring in a familial fashion was first described by Comfort and Steinberg in 1952 and upto 1975 over 20 families with more than 100 established cases of pancreatitis have been reported in the literature. A report of two sisters suffering from pancreatitis with pancreatic lithiasis is being presented.

Case I. Propositus, a married female aged 33 years, presented during an attack of epigastric pain and vomiting on 15-8-1979. She gave history of similar attacks, lasting for 3-4 days and radiating to back, from the age of 10 years. Pain was occasionally accompanied by water-brash and vomiting which transiently relieved the pain. There are rumbling sounds in the abdomen at times. She passes 2-3 semisolid stools per day which are often "fatty" but develops constipation for a few days prior to the episode of abdominal pain. She gave history of passage of worms in the stool in childhood. When given a laxative at night for the preparation of oral cholecystogram in 1972, she passed a number of milky white, smooth, rounded stones in the stool next morning. They measured 275 upto 1 cm in diameter and were described by the patient as "some parasite is laying eggs in her abdomen". At that time she was diagnosed, at another hospital, as a case of chronic relapsing pancreatitis with pancreatic lithiasis.

On examination, she had an ill-defined epigastric mass and mild tenderness in left iliac fossa. Her investigations at that time revealed a Hb of 12.6 G%, and a normal total and differential leucocyte count, total bilirubin was 8.0 mg%, S.G.P.T. 40 umole/L, Alkaline phosphatase 50 umole/L, serum calcium 10 mEq/L, Inorganic phosphorus 4.1 mg%, serum amylase 100 S.U., glucose tolerance test showed fasting blood sugar 80 mg% and at half an hour intervals 120, 185, 165, 150 and 140 mg%. Fecal fat estimation on three consecutive days was 6.2, 5.9 and 6.0 Gram per 24 hours each. Oral cholecystogram revealed a normally functioning gall-bladder and multiple, round opacities in a horizontal line in the pancreatic region which were more dense and larger than those in the previous roentgenograms as shown in the accompanying figure.

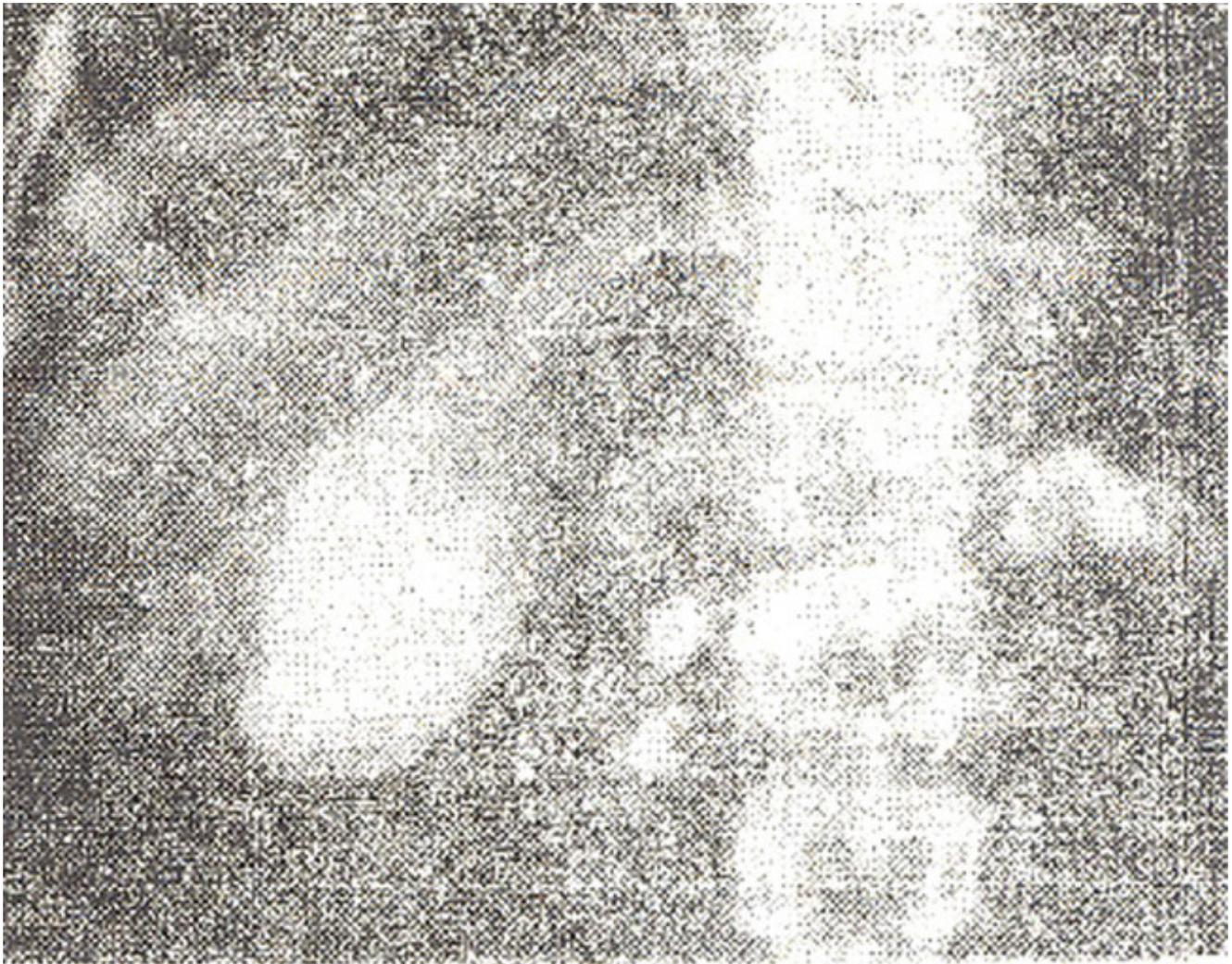


Figure showing oral cholecystogram and Pan-creatic Calcifications.

Her previous investigations which were carried out to determine the cause of abdominal pain are as follows. In 1967, when 21 years old, an I.V.P. revealed normally functioning kidneys and no calcifications in the pancreatic region. In 1972, these were Hb 12.3 G%, T.L.C. 10,000/cmm, Urine for Salkowitch test was negative, serum amylase 100 S.U., serum calcium 8.3 mEq/L and 7.5 mEq/L on two occasions, serum inorganic phosphorus 2.6 mg% ,alkaline phosphatase 30 .0 Babson units and fasting blood glucose 80 mg%. Oral cholecystogram and Barium meal were normal except for horizontal pancreatic calcifications.

Her father had diabetes and mother is hypertensive but there is no history of abdominal pain in both. She has two sons of 12 years and 5 years of age and one daughter of 7 years of age. At present all the three are symptom free.

Case II. 17 years old sister of the propositus started having attacks of epigastric pain 3 years back. Pain is usually moderate and relieved by spasmolytics and during the attack of pain she develops vomiting. Vomitus contains "oily droplets". There is no history of steator-rhoea or diarrhoea. She is not diabetic. Her total serum lipids were slightly raised. Plain X-ray abdomen shows a horizontal row of pancreatic calculi similar to that of the propositus.

Discussion

Distinguishing features of the previously reported families have been described in the accompanying table. Chronic relapsing pancreatitis is different from that of the non-hereditary type in that many members of a family are affected, age of onset is lower, disease is inherited as autosomal dominant gene and the pancreatic calcification is quite common in this type of pancreatitis. Although the initial report of Comfort and Steinberg (1952) showed an increased female preponderance (5 out of 6 were females) compared to a male/female ratio of 6:1 in non-hereditary pancreatitis, later reports have revealed no significant preponderance of either sex.

In the present family, nothing can be definitely said about the hereditary pattern of the disease because of the smallness of the family, involvement of only two members of the family and young age of the offsprings of the propositus who have not yet shown any manifestations of the disease. Familial, but not necessarily hereditary, occurrences of chronic relapsing pancreatitis have previously been described (Jackson, 1958; Beall et al., 1960; Poulsen, 1950). Alcohol, hyperlipaemia and cholelithiasis were described by Gross and Comfort (1957) to be unimportant factors in the etiology of this condition. The occurrence of abdominal pain suggesting pancreatitis has been reported during convalescence from measles (Gross et al., 1962) mumps (Gross and Comfort, 1957; Zelman, 1944) and scarlet fever (Veghelyi, 1949), the explanation of which is still not clearly understood. Various associated conditions, with an unexplained significance, have been reported in a few families with hereditary pancreatitis. These included aminoaciduria, particularly of lysine and cystine (Comfort and Steinberg, 1952; Gross and Comfort, 1957; Gross et al., 1962; Cornet et al., 1962; Carey and Fitzgerald, 1968) hypercalcaemia (Carey and Fitzgerald, 1968), gastrointestinal bleeding (Sibert, 1975) and pleural effusions (Cornet et al., 1962; Nash, 1971). Another feature of the hereditary pancreatitis is the increased incidence of pancreatic calcifications (Logan et al., 1968) suggesting increased possibility of pancreatic cancer in these cases. Paulino et al (1960) found that only 24% of the patients with non-hereditary chronic pancreatitis exhibited calcifications and the carcinoma of pancreas appeared in 25% of the patients but never in the absence of calcific pancreatitis. The number of so far reported pancreatic cancers, as shown in the table,

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No.	Name of Study	Definite cases Male — Female	Suspected cases Male — Female	Age of onset Range (Mean)	Steatorrhea (definite cases)	Diabetes (definite cases)	Calcification (definite cases)	Aminoaciduria	No of operated cases	Cancer or Pseudocysts	Important features of the study
1.	Comfort and Steinberg (1952)	4 M 0 F 4	2 M 1 F 1	5-23 (12.75) years	1	2	4	Yes	2	Cyst-1	<ol style="list-style-type: none"> 1. First family reported in literature. 2. Clinical manifestations similar to non-hereditary chronic pancreatitis but age of onset is earlier and sex incidence is different. Here 5 out of 6 cases are female compared to a M/F ratio of 6:1 in non-hereditary chronic pancreatitis. 3. Stones form with varying rapidity and time lapse between initial attack of pain and stone formation. They vary in size from mm-cm, arranged in main pancreatic ducts which are enlarged, particularly in head then the tail. 4. Inheritance is probably due to a dominant autosomal gene.
2.	Gross and Comfort (1957)	"C" family 3 M 3 F 0	2 M 1 F 1	5-23	1	1	3	Yes	2	0	<ol style="list-style-type: none"> 1. Observations confirmed the original impression that the disease is inherited as autosomal dominant gene. 2. Alcohol, hyperlipaemia and cholelithiasis appear unimportant in etiology. It is suspected that inherited defect is metabolic.
		"K" family 6 M 1 F 5	8 M 3 F 5	(12)	3	3	4	Yes	2	Cyst-1	
3.	Gross (1958)	3 M 2 F 1	0 M 0 F 0	(13.7)	1	0	1	Yes	1	Cyst-1	
4.	Gross et al (1962)	6 M 5 F 1	4 M 3 F 1	(13)	3	1	3	Yes	3	Ca-1 Cyst-1	<ol style="list-style-type: none"> 1. Mode of inheritance appears same but poor penetrance of the gene and incomplete recessiveness cannot be excluded. 2. About half of the cases, with or without pancreatitis, studied so far were found to have aminoaciduria.
5.	Cornet et al (1963)	8	9	4-7	—	—	—	Yes	8	Cysts-3	<ol style="list-style-type: none"> 1. First report of a French family. 2. Found dilatation and ectasia of the ductules. Possibly later is the primary defect with attacks of sclerosing and calcifying pancreatitis occurring secondarily.
6.	Davidson et al (1968)	6 M 5 F 1	5 M 4 F 1	5-15	4	5	6	No	—	Ca-2	<ol style="list-style-type: none"> 1. Only one of the 13 members of the family without pancreatitis had a high urinary alpha-aminoacid level of 289 mg/24 hrs.
7.	Logan et al (1968)	5 M 2 F 3	1 M 1 F 0	3-29 (15.6)	0	3	2	Occasional	3	Ca-1 (on autopsy)	<ol style="list-style-type: none"> 1. Raised possibility of relationship of pancreatic cancer and hereditary pancreatitis because of high rate of calcifications. 2. Aminoaciduria may be a manifestation of acute pancreatitis, whether familial or not, rather than a genetically related defect.
8.	Whitten et al (1968)	2 M 0 F 2	0	(2)	0	1	1	No	1	0	<ol style="list-style-type: none"> 1. First case of a 5 years old girl reported in pediatric literature. 2. Possible etiology, congenital ectasia of pancreatic ducts or congenital hyperplasia of sphincter of Oddi. 3. Treatment suggested; Total pancreatectomy with insulin and enzyme replacement.
9.	Carey and Fitzgerald (1968)	3 M 0 F 3	8 M 5 F 3	—	1	0	9	Yes	2	0	<ol style="list-style-type: none"> 1. Hypercalcaemia was found in 4 cases (3-definite and 1 suspected pancreatitis), one of whom had pancreatic adenoma. 2. No diabetes or pancreatic calcification in any of 4 but significant lysine-cystine aminoaciduria found.
10.	Nash (1971)	3 M 2 F 1	1 M 1 F 0	—	—	1	3	No	0	0	<ol style="list-style-type: none"> 1. Propositus (a girl of 14) had massive pleural effusion as well, with pleural amylase content of 100,000 S.U./100 ml.
11.	Sato and Saitoh (1974)	3 M 0 F 3	1 M 0 F 1	(14.7)	—	2	3	No	3	0	<ol style="list-style-type: none"> 1. Report of the third family from Japan, first two being published in Japanese journals, 7 females and 1 male had pancreatitis in these three families. 2. All the three cases treated by side to side pancreaticojejunostomy in this series.
12.	Sibert (1975)	9	15	(12.6)	0	1	1	No	5	Abscess-1	<ol style="list-style-type: none"> 1. Fourth and the largest family described in Great Britain. 2. Attacks of pain appear to cease in this family by the age of 40 years. 3. Three patients (1-definite and 2-suspected pancreatitis) have had unexplained abdominal bleeding.
13.	Present Case Report	2 M 0 F 2	0	(10)	1	0	2	—	0	0	<ol style="list-style-type: none"> 1. First case of familial pancreatitis reported from Pakistan. 2. Stones were passed in the stool.

has not been found to be as high as was anticipated in this condition. The pancreatic calculi appear to be the result and not the cause of this disease because a variable time lapse has been observed between the initial attack of abdominal pain and the appearance of the stones (Comfort and Steinberg, 1952). In our case the propositus developed the calculi after more than eleven years of the onset of symptoms

whereas her sister had them only after three years of the initial attack of pain. It is emphasised that this condition should also be considered in differential diagnosis of recurrent attacks of unexplained abdominal pain when other features of the disease are found even in the absence of pancreatic calculi. The exact inherited defect has not yet been completely understood although several hypotheses have previously been suggested like an inborn metabolic defect (Gross and Comfort, 1957), abnormal embryological defect affecting the anatomical arrangement of pancreatic ducts (Nash, 1971), hypertrophy of sphincter of Oddi (Roebechek, 1967) congenital hyperplasia of sphincter of Oddi and congenital ectasia of pancreatic ducts (Whitten et al., 1968) and dilatation and ectasia of the pancreatic ductules as evidenced on surgery (Cornet et al., 1962).

Treatment of this condition is either palliative, by alleviating pain with spasmolytics or opiates, replacement of exocrine enzymes and controlling diabetes if present, or surgical which in various series consisted of sphincterotomy (Roebechek, 1967), side to side pancreaticojejunostomy (Sato and Saitoh, 1974) and total pancreatectomy with insulin and enzyme replacement therapy (Whitten et al., 1968), depending upon the state of pancreas at the time of surgery.

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