HEREDITARY PANCREATITIS WITH LITHIASIS IN A 7-YEAR-OLD BOY

V.K. Gupta
T.P. Yadav
R. Khanna
K. Avtar
S. Mishra

Hereditary pancreatitis, a rare disease and first reported in 1952(1), is now considered the second most common inherited disease of the pancreas, involving an autosomal dominant gene with incomplete penetrance. Thirty five kindred have been reported in literature so far, most of the cases being of Caucasian ancestry(2-32).

Onset of symptoms occurs with equal frequency in both sexes at an average age of 10-12 years with range from 11 months to very old age(13,17,22). Calcification in pancreas usually occurs 8 years after the onset of first symptom of pain abdomen. Pancreatic calcification has been seen in hereditary pancreatitis as early as 13 years of age(33).

In the present reported case, the calcification of pancreas was seen at the age of 7 years and only after 3 years of onset of symptoms. Further, it is the third case from the Asian race and first from India.

From the Department of Pediatrics, Dr. Ram Manohar Lohia Hospital, New Delhi 110 001.

Reprint requests: Dr. Vijay K. Gupta, D 11/3, Officers' Flats, 14 Rajpur Road, Delhi 110 054.

Received for publication: April 9, 1994;
Accepted: September 28, 1994

Case Report

A seven year male child, a product of non-consanguinous marriage was brought with recurrent attacks of abdominal pain, diarrhea, failure to thrive for the last three years and progressive night blindness for the last 6 months. He had episodes of abdominal pain, each lasting for two to three days, the frequency decreasing from once a week initially to once a month later. Pain was moderate to severe, generalized without any radiation or vomiting, with no relation to meals, defecation or posture. The child used to pass 3-4 bulky, greasy and semiformed stools each day. There was no history of cough, dyspnea, exanthematous fever, recurrent jaundice, helminthiasis, abdominal trauma, bleeding from any site, joint pains and urinary trouble. Maternal grandfather used to have frequent attacks of severe abdominal pain (each attack lasting for 2-5 days), requiring repeated hospitalizations since a very young age. At least on three occasions he was diagnosed as acute pancreatitis with significant rise in enzyme levels. The pedigree is depicted in *Fig. 1.*

On physical examination, the child was

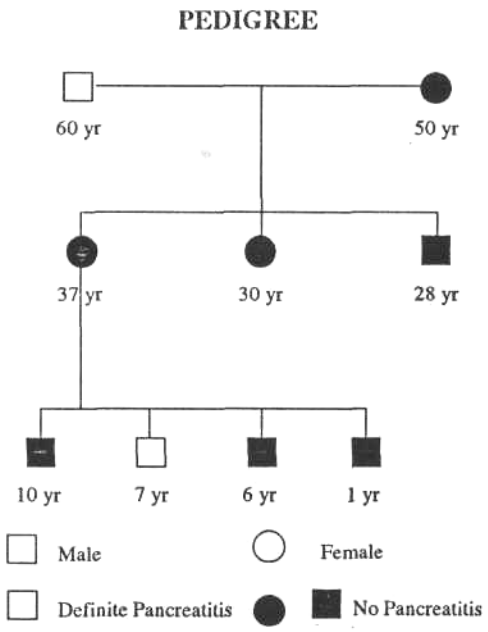

Fig. 1. Depiction of pedigree.

grossly malnourished with weight and height less than 5th percentile. He was pale with dry skin and Bitot spots. Examination of cardiovascular, respiratory, nervous system and abdomen was unremarkable. Hemogram revealed microcytic, hypochromic picture with hemoglobin 7.5 g/dl and reticulocyte count 2%. His total and differential leucocyte counts were normal. No aminoacids were detected in urine. There were large number of fat globules on microscopic examination of stools. Seventy two hours fecal fat content was 7 g% Tuberculin test was negative (<2 mm induration). Liver function tests were normal. His serum cholesterol and triglycerides were 156 mg/dl and 117.6 mg/dl respectively. Total serum calcium was 9.5 mg/dl. His fasting blood sugar was 90 mg/dl but glucose tolerance test was abnormal. Sweat sodium content was 26 mg/dl. TORCH test was negative. Serum amylase was 500 IU/1. X-rays of chest, skull and long bones were normal. Bone age was consistent with chronological age. Plain X-ray abdomen revealed calcification in the region of pancreas *(Fig. 2)* and ultrasound scan of abdomen confirmed calcified and atrophic pancreas *(Fig. 3)*. barium meal follow through study was normal. Plain X-ray abdomen of mother, father, siblings and maternal grandfather were normal. The Child died at home after 3 months of follow up.

Discussion

Hereditary pancreatitis is an autosomal dominant trait with 40 to 80% penetrance. At least 5 variants of this trait can be identified: (a) No associated defects; *(b)* Associated aminoacidemia (cystine, lysine,

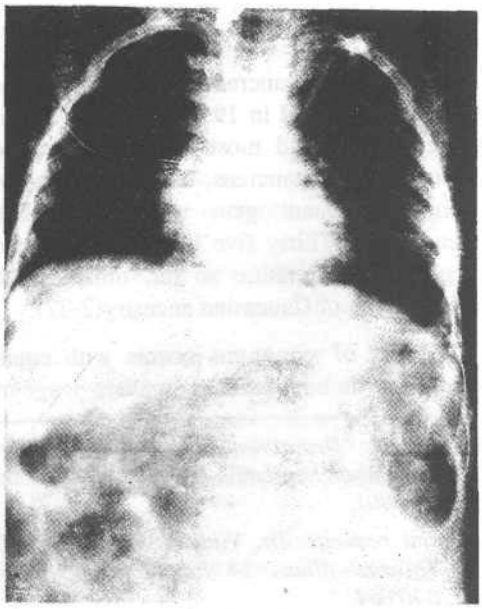

Fig. 2. Plain X-ray of abdomen showing calcification of pancreas.

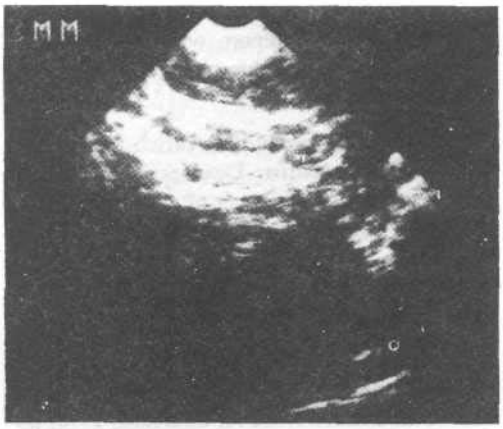

Fig. 3. Ultrasonogram of abdomen showing calcified and atrophic pancreas.

arginine, glycine)(34); (c) Anatomic abnormalities of pancreatic duct (chain of lakes, lacunar dilatation with strictures, ductal ectasia); *(d)* Embryological anomalies affecting pancreatic duct *(e.g.,* cyst formation of pancreatic duct as a result of stenosis of its terminal end); and (e) Hypertrophy of sphinchter of Oddi(35).

Due to cumulative insult to the pancreatic duct, resulting from chronic and relapsing nature of the illness, the pancreas becomes shrunken and indurated with calculi in its ductal system, with extensive interstitial fibrosis to near total loss of acinar tissue and relative sparing of islet cells. The most frequent presentation is with severe epigastric pain radiating through to the back, associated with nausea and vomiting, often precipitated by fasting, ingestion of fatty meals, alcohol or stress. Each episode lasts from 2 days to 2 weeks, is usually separated from the other episode by variable period of months or years or quiescence unless pancreatic deficiency develops. Episodes are usually not severe [hemorrhagic pancreatitis being a rarity(17)] and in fact, become less severe and less frequent with time, reaching a "plateau phase"(8,16,22). A few instances of painless pancreatitis manifested by pancreatic calcification, steatorrhea or diabetes mellitus have been reported in the relatives of patients with hereditary pancreatitis(17). Exocrine insufficiency occurred in 5 to 20% of patients(8,22). Our patient too had exocrine insufficiency.

The diagnosis of hereditary pancreatitis should be suspected if one or more relatives in two or more generations develop pancreatitis at an early age (10 years versus 40 years for nonhereditary pancreatitis). In our case, the maternal grandfather had recurrent attacks of acute abdominal pain since early childhood and was diagnosed thrice as acute pancreatitis.

Pancreatic enzymes are usually elevated in various body fluids during an episode; however, the values may be normal. Abnormally thickened duodenal folds, displacement of stomach or widening of duodenal loop may be seen on barium meal study. Ultrasonography may show enlargement of pancreas, dilatation of ducts, mass lesion, stones, pseudocyst formation or even obliteration of splenic vein. ERCP visualizes the ductal system and is important specially if calcification is not visualized radiologically(11,29).

Pancreatic calcification is the most frequent complication affecting 33 to 50% of patients(8,13,22,31) with large calcium oxalate concretions, mostly in pancreatic duct(22,23,36). Symptomatic pseudocysts of pancreas are rare(8,10,36,37) but pseudocysts may be seen ultrasono-graphically in 80 to 90% of patients(5). The most feared complication is intra-abdominal carcinoma which is reported in 15% of definite and 9% of suspected patients of hereditary pancreatitis(13). Even family members

without apparent pancreatitis have higher incidence of intra-abdominal carcinoma(22). Malignancy should be suspected if there is a change in pattern of pain, weight loss, icterus, thrombotic phenomenon or lassitude. CT scan guided angiography or even CT or ultrasound guided biopsy may be required. Rarely, obstructive jaundice(18), extrahepatic portal hypertension(8,22,38) (due to obstruction of common bile duct and splenic or portal vein thrombosis(8-16,31), hemorrhagic ascites or pleural effusion may occur(18).

REFERENCES

1. Comfort MW, Steinberg AG. Pedigree of a family with hereditary chronic relapsing pancreatitis. Gastroenterology 1952, 21: 54-63.
2. Appel MF. Hereditary pancreatitis: Review and presentation of an additional kindred. Arch Surg 1974, 108: 63-65.
3. Crane JM, Amoury RA, Hellerstein S. Hereditary pancreatitis: Report of a kindred. J Pediatr Surg 1973, 8: 893-900.
4. Davidson P, Costanza D, Swieconek JA, Harris JB. Hereditary pancreatitis: A kindred without gross aminoacidura. Ann Intern Med 1968, 68:88-96.
5. Fried AM, Selke AC. Pseudocyst formation in hereditary pancreatitis. J Pediatr 1978, 93:950-953.
6. Gerber BC. Hereditary pancreatitis: The role of surgical intervention. Arch Surg 1963, 87:70-80.
7. Girard RM, Archambault, A. Hereditary chronic pancreatitis. N Engl J Med 1980, 303: 286-287.
8. Gross JB. Hereditary pancreatitis. *In:* Ed. Pancreatitis. Gambill EE. St. Louis CVMosby, 1973, pp 109-114.
9. Gross JB, Comfort MW. Hereditary pancreatitis: Report on two additional families. Gastroenterology 1957, 32: 829-854.
10. Gross JB, Gambill EE, Ulrich JA. Hereditary pancreatitis: Description of a fifth kindred and summary of clinical features. Am J Med 1962, 33: 358-364.
11. Gross JB, Jones JD. Hereditary pancreatitis. *In:* The Exocrine Pancreas: Proceedings of Symposium held at Queen's University, Kingston, Ontario, Canada, June 1969. Eds. Beck IT, Sinclair DG, London J and A, Churchill, 1971, pp 247-270.
12. Gross JB. Ulrich JA, Maher FT. Further observations on the hereditary form of pancreatitis. *In:* Ciba Foundation Symposium on the Exocrine Pancreas: Normal and Abnormal Functions. Eds. de Reuck, AVS, Cammeron MP. Boston, Little Brown Co, 1961, pp 278-305.
13. Kattwinkel J, Lapey A, di Sant' Agnese PA, Edwards WA. Hereditary pancreatitis: three new kindreds and a critical review of the literature. Pediatrics 1973, 51: 55-69.
14. Logan A, Schlicke CP, Manning GB. Familial pancreatitis. Am J Surg 1968, 115: 112-117.
15. Malik SA, Van Kley H, Knight WA. Jr. Inherited defect in hereditary pancreatitis. Am J Dig Dis 1977, 22: 999-1004.
16. McElroy R, Christiansen PA. Hereditary pancreatitis in a kinship associated with portal vein thrombosis. Am J Med 1972, 52: 228-241.
17. Riccardi VM, Shih VE, Holmes LB. Nardi GL. Hereditary pancreatitis: Nonspecificity of aminoaciduria and diagnosis of occult disease. Arch Intern Med 1975, 135: 822-825.
18. Hardy M, Cornet E, Dupon H, Gordeef A. Chronic pancreatitis associated with

familial dilatation of the pancreatic ducts; 6 operated cases. Bibl Gastroenterol 1965, 7: 189-216.

19. Leger L, Pare R, Soprani A, Petit FH. Pancreatite chronique familial; 13 cas, 5 families. J Chir (Paris) 1978, 115: 129-130.

20. Pestel M, Lambert C. Estienne B, Estienne M, Godeau P. Pancreatite chronique calcifinate familiale. Ann Med Intere (Paris) 1972, 123: 481-486.

21. Nash FW. Familial calcific pancreatitis: An acute episode with massive pleural effusion. Proc R Soc Med 1971, 64: 17-18.

22. Sibert JR. Hereditary pancreatitis in England and Wales. J Med Genet 1978, 15: 189-201.

23. Sibert JR. A British family with hereditary pancreatitis. Gut 1975, 16: 81-88.

24. Sibert JR. Hereditary pancreatitis in a Newcastle family. Arch Dis Child 1973, 48: 618-621.

25. Sibert JR. Pancreatitis in children: A study in the North of the England. Arch Dis Child 1975, 50: 443-448.

26. Bergestrom K, Hellstrom K, Kallner M, Lundh G. Familial pancreatitis associated with hyperglycinura. Scand J Gastroenterol 1973, 8: 217-223.

27. Lilja P, Evander A, Ihse I. Hereditary pancreatitis—A report on two kindreds. Acta Chir Scand, 1978, 144: 35-37.

28. Scuro LA, Dobrilla G, Angelini G, Cavallini G, Vantini I, Barba A. Hereditary pancreatitis: Report of the first kin dred in Italy. Acta Hepatogastroenterol 1973, 20: 70-76.

29. Vantini **I.** Piubello **W.** Ederle **A,** Adamo **S,** Cavallini G, Scuro LA. Hereditary pancreatitis: Morphological pictures (ERCP) in the youngest member of a family. Acta Hepatogasteroenterol 1979, 26: 253-256.

30. Lawson JA. A Dutch family with hereditary pancreatitis. Ned Tijdschr Geneeskd 1981,15: 309.

31. Sato T. Saitoh Y. Familial chronic pancreatitis associated with pancreatic lithiasis. Am J Surg 1974,127: 511-517.

32. Mian TA, Zuberi SJ. Familial pancreatitis with lithiasis. JPMA 1980, 30: 275-278.

33. Gross JB. Ulrich JA., Jones JD. Urinary excretion of amino acids in a kindred with hereditary pancreatitis and aminoaciduria. Gastroenterology 1964, 47: 41-48.

34. Paul, AD; Saint's Agnese—The Pancreas. *In:* Nelson's Textbook of Pediatrics. Eds-Vaughan VC, McKay RJ. 10th Asian. Edn. Philadelphia, WB Saundcrs Co. 1975 pp 820.

35. Robechek PJ. Hereditary chronic relapsing pancreatitis: A clue to pan creatitis in general? Am J Surg 1967, 113: 189-824.

36. Perrault J, Gross JB, King JE. Endoscopic retrograde cholangiopancreatography in familial pancreatitis. Gastroenterology 1976, 71: 138-141.

37. Freed J, Poley JR, Smith El, Altman A, Riley HD. Pancretitis in children. J Okla State Med Assoc 1975, 68: 153-160.

38. Bartholomew LG. Comfort MW. Chronic pancreatitis without pain. Proc Staff, Meet Mayo Clin 1957, 32: 361-364.