Hyperparathyroidism associated with chronic pancreatitis in a family

MARTIN C. CAREY AND OLIVER FITZGERALD

From the Department of Medicine and Therapeutics, University College, and St Vincent's Hospital, Dublin

Hereditary hyperparathyroidism, occurring as an isolated endocrinopathy was first described by Goldman and Smyth in 1936. They described primary hyperparathyroidism in two siblings. Jackson and Boonstra (1967) collected 21 families with 107 hyperparathyroid members from the literature, including eight unrelated families of their own, all discovered in a single centre over a 10-year period. This condition tends to occur in younger patients who frequently have symptomless hypercalcaemia; the more likely parathyroid pathology is either chief-cell hyperplasia or multiple recurrent adenomas than the sporadic form. Other endocrine involvement in three different families suggested to these authors that hereditary hyperparathyroidism is most likely a part of the Mendelian dominant syndrome of hereditary endocrine adenomatosis which is characterized by pleomorphic expression.

Since 1957 when Cope, Culver, Mixter, and Nardi defined an association between hyperparathyroidism and pancreatitis, many cases of pancreatitis complicating prolonged hypercalcaemia have been reported. Its incidence in primary hyperparathyroidism...

FIG. 1. Heredity of the family discussed in this paper in relation to both pancreatitis and parathyroid abnormalities.
Hyperparathyroidism associated with chronic pancreatitis in a family

Pedigree

Age Serum Ca- Urinary Calcium (normal
No. in no. Bulletin,

LABORATORY FEATURES

CLINICAL AND

exocrine techniques measured patients.

secretin-pancreozymin estimation and Nordin (1956) which modified the values were found. During the cortisone suppression test (1941). The glomerular filtration rate (GFR) was estimated by endogenous creatinine clearance. Routine clinical procedures were used for the other investigations.

RESULTS

The case summaries of the four siblings found to have a serum calcium level of 11-0 mg/\% or more are shown in Tables Ia and Ib. Cases III-7 and III-8 had chronic pancreatitis proven at laparotomy and in the case of III-5 the diagnosis rests on firm historical, clinical, and biochemical grounds. A three-day fat balance and stool nitrogen excretion and glucose tolerance tests were normal in all four. The cortisone suppression tests failed to reduce the serum calcium levels significantly. Routine urinary screening tests for porphobilinogen excretion were negative but a significant lysine-cystine aminoaciduria was found in each case. Skeletal radiographs revealed nothing significant and pancreatic calcification was not detected.

During neck exploration a lower left parathyroid adenoma, 1-3 cm × 0-75 cm, was found in III-5 and removed. Clinical response was dramatic and serum and urinary calciums are now normal. During neck surgery on the proposita (III-7) only three parathyroids were identified and all except one fifth of one was removed. A recent serum calcium level was 8-6 mg/\%. Histology of the excised glands was normal. Their other two sisters have refused parathyroid surgery.

The suspicion of pancreatitis in the five members who are dead (1-3, II-3, II-4) is tenable on the statements of their surviving siblings and offspring. Hospital studies for prolonged dyspepsia and pain in all three had not proven fruitful. Case III-6 is an alcoholic; his recurrent bouts of abdominal pain are typical of pancreatitis. Physical examination

No. in Pedigree Sex and Age Initial Serum Calcium (mg/%) Maximum Urinary Calcium (mg/24 hr) PEI (normal ±0-12) GFR (normal 125 ml/min) Aminoaciduria Neck Exploration

III-4 F 54 11-0 463 0-250 115 Lysine-cystine Not done

III-5 F 52 12-4 362 0-218 44-7 Lysine-cystine Single left lower parathyroid adenoma

III-7 F 48 12-0 581 0-215 116-9 Lysine-cystine 3 normal parathyroids

III-8 F 46 11-4 291 0-108 77-5 71-0 Lysine-cystine Not done

Histology: normal
TABLE 1b

<table>
<thead>
<tr>
<th>Pedigree No.</th>
<th>Sex and Age</th>
<th>Relevant Symptoms and History</th>
<th>Pancreatitis</th>
<th>Comments and Associated Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>III-4</td>
<td>F 54</td>
<td>Recurrent pancreatic pain + flutaneous dyspepsia since age of 6; worse during pregnancies; headaches frequent</td>
<td>Suspected</td>
<td>Previously jaundiced on 2 occasions Recent cholecystogram and barium meal (1965) normal</td>
</tr>
<tr>
<td>III-5</td>
<td>F 52</td>
<td>Typical pancreatic pain + abdominal tenderness for 36 yr, very severe during menstruation and in pregnancies Biparietal headaches + polyuria for 12 yr, dysuria and constipation for 3 yr 1944—euthyroid goitre noted 1956—renal colic due to a solitary calculus 1957-67—chronic pyelonephritis</td>
<td>Definite</td>
<td>Small colloid goitre; renal insufficiency (blood urea 49 mg %, uric acid 6-8 mg %, viz. GFR) Clinical and biochemical response to parathyroidectomy Serum calcium 9-6 mg % Urinary calcium 55 mg/24 hours</td>
</tr>
<tr>
<td>III-7</td>
<td>F 48</td>
<td>Proposita: milk intolerance + pancreatic pain since childhood, worse during menses and in pregnancies; 10 lb weight loss Steatorrhoea + depression on first admission 1961—Laparotomy—nil found ?pancreas 1962—S-P test abnormal—chronic pancreatitis, Sphincterotomy + cholecystectomy 1966—Constant back pain—hypercalcaemia</td>
<td>Definite</td>
<td>Small cyst at thyroid istmus removed Normochromatic anaemia (Hb 10.4 g) postoperative serum calcium 12-5 mg % but level now 8-6 mg %</td>
</tr>
<tr>
<td>III-8</td>
<td>F 46</td>
<td>Periodic pancreatic pain accompanied by syncope since childhood; milk intolerance, constipation and latitudine 1932—acute abdomen; treated expectantly 1964—laparotomy: partial gastrectomy for a 'tumour proved to be an encapsulated area of fat necrosis saddling lesser curvature 1966—S-P test abnormal Sphincterotomy and cholecystectomy Subacute pancreatitis postoperatively Hypercalcaemia</td>
<td>Definite</td>
<td>Thyroid normal anaemia mild (Hb 11.0 g) Serum amylase 2.2 mg R.S./ml after laparotomy.</td>
</tr>
</tbody>
</table>

Amylase mg R.S/ml: 2-9 lipase STU/ml: 1-3 normal max.

showed widespread upper abdominal tenderness. A spot serum calcium, phosphate and amylase were normal.

In generation IV only those with complaints have been studied: calcium and amylase studies on IV-9, IV-12, and IV-13 were normal but in these the early onset of indigestion and abdominal pain and tenderness may be indicative of pancreatitis as gastroduodenal radiology was otherwise normal.

It is of interest that III-3 was found to have a toxic goitre in 1959 and was treated with 131I. During a cholecystectomy for cholelithiasis in 1963, the pancreas was palpably normal. A recent serum calcium level was 10-3 mg %. The Table indicates that III-5 and III-7 also had small goitres.

DISCUSSION

In this family there is a ready explanation for chronic pancreatitis in those members with hypercalcaemia. However, in those who survive with suspected pancreatitis the explanation is not easily apparent. If III-6 proves to have definite pancreatitis, his long history of alcoholism is the most likely precipitating cause as the serum calcium level is normal. One interesting finding in all those examined with pancreatitis was lysine-cystine aminoaciduria, a feature reported in 50% of the individuals in families with hereditary pancreatitis originally described by Comfort and Steinberg (1952) and recently summarized by Gross, Ulrich, and Maher (1962) which feature has hitherto been confined to six families under observation at the Mayo Clinic. We have not found any evidence in the present series of the severe pancreatic endocrine and exocrine insufficiency which is mentioned as typical of the latter condition, nor have we found the heavy pancreatic calcification which, in the adult in the absence of alcoholism, is nearly a sine qua non for...
Hyperparathyroidism associated with chronic pancreatitis in a family

703

the diagnosis of hereditary pancreatitis. Two possible explanations for the aminoaciduria in the present kindred is the independent coexistence of the incompletely recessive form of lysine-cystinuria (Harris, Mittwoch, Robson, and Warren, 1955) or it may be due to hypercalcaemic renal glomerulotubular damage as evidenced by an impaired GFR in two patients (Table 1b). The absence of radiological bone change in the presence of hyperparathyroidism may be attributable to increased calcium intake and/or absorption which is able to balance the urinary calcium loss. We found that the Ca++ content of the water from the district this family lived in, a limestone area, was 1.48 m-equiv/litre which is 20 times the calcium content of London drinking water.

In agreement with what Jackson and Boonstra (1967) have drawn attention to we have found that three individuals in this family had goitres; one patient developed hyperthyroidism. Perhaps in this family we are also dealing with hereditary endocrine adenomatosis, although evidence of other glandular involvement is wanting.

SUMMARY

A family with hereditary hyperparathyroidism and relapsing chronic pancreatitis is described. Parathyroid pathology was found in only one member. In another, subtotal resection of the parathyroids was carried out, causing a fall in serum calcium to a hypoparathyroid level. Two other hypercalcaemic members with pancreatitis have declined further study or surgery.

Drs Ailish Forristal (Kilkenny), Thomas P. Walsh (New Ross), and Michael G. O'Brien (Inistioge) assisted us considerably in studying this family. Professor Patrick FitzGerald carried out both neck explorations and Dr Robert Towers reviewed all the histological specimens. This study was carried out during the tenure of a full-time research fellowship of the Medical Research Council of Ireland awarded to one of us (M.C.C.).

Reprint requests to be sent to O.F.

REFERENCES


Hyperparathyroidism associated with chronic pancreatitis in a family.

M C Carey and O Fitzgerald

Gut 1968 9: 700-703
doi: 10.1136/gut.9.6.700