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Lipodystrophy, pancreatitis, and eosinophilia

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SUMMARY Two patients suffering from partial lipodystrophy, pancreatitis, and recurrent eosinophilia are described. In one patient the duodenum and the terminal ileum were narrowed, the appearances suggesting eosinophilic gastroenteritis: bilateral hydronephrosis was also present without ureteric obstruction. An association between lipodystrophy and renal disease is recognized; it is possible that there is also an association between lipodystrophy and pancreatitis, and eosinophilia with or without an intestinal lesion may be a further association.

Partial lipodystrophy is an unusual condition of unknown aetiology, sometimes familial, primarily affecting young females. There is progressive loss of fat from the subcutaneous tissues, usually starting in the face and gradually extending distally to the level of the knees. Many cases have been associated with renal disease (Eisenger, Shortland, and Moorhead, 1972), while some have hepatomegaly, mental retardation, or diabetes (Senior and Gellis, 1964). We wish to report two patients with partial lipodystrophy and pancreatitis, both of whom had recurrent eosinophilia, and one of whom probably had eosinophilic gastroenteritis.

Case 1

S.O.'G., a 27-year-old housewife, first presented when aged 5 years with thinning of the face and two years later partial lipodystrophy was recognized. There was no family history of this complaint. Subcutaneous loss of fat gradually extended over the next 10 years to involve the trunk, body, arms, and upper thighs.

At the age of 9 years recurrent attacks of abdominal pain, vomiting, and diarrhoea led to laparotomy. A clearly demarcated length of swollen and congested terminal ileum 15 cm long was found, with a few enlarged mesenteric glands. The attacks persisted and at a second laparotomy a year later the findings were identical. Three months later an elevated urinary diastase level of 500 Wohlegemuth units/ml was recorded during an attack of abdominal pain.

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During the next two years attacks of vomiting diarrhoea, and abdominal pain led to five further admissions to hospital. On two of these occasions the urinary diastase level was raised (200 and 500 Wohlegemuth units/ml). An intravenous pyelogram done during this period because of dysuria showed bilateral non-obstructive hydronephrosis with an apparently normal thickness of renal cortex. At the age of 15 years, transient glycosuria was noted though an oral glucose tolerance test was normal. The serum amylase was elevated at 480 Somogyi units/100 ml. Following further attacks of abdominal pain a third laparotomy at the age of 16 years led to the finding of a thickened, hard pancreas.

During the next three years abdominal symptoms led to four further hospital admissions, the only abnormal findings being raised white cell counts of between 10 000 and 14 000/c mm. On one occasion an eosinophilia of 10% was noted. At the age of 19 barium studies showed narrowing of the terminal ileum and a provisional diagnosis of Crohn's disease was made. A fourth laparotomy, however, revealed no evidence of this.

Her symptoms persisted, and at the age of 24 years barium studies demonstrated the presence of a duodenal stricture together with narrowing and apparent mucosal swelling of the terminal ileum (fig 1). Investigations also showed an elevated leucocyte count of 16 200/c mm (88% neutrophils), a faecal fat excretion of 15 g/day, and an abnormal glucose tolerance test. Because of the two abnormal areas in the small bowel, a fifth laparotomy was performed at which the duodenum and the last 30 cm of terminal ileum looked swollen and oedematous. Duodenal and ileal biopsies showed an increase in

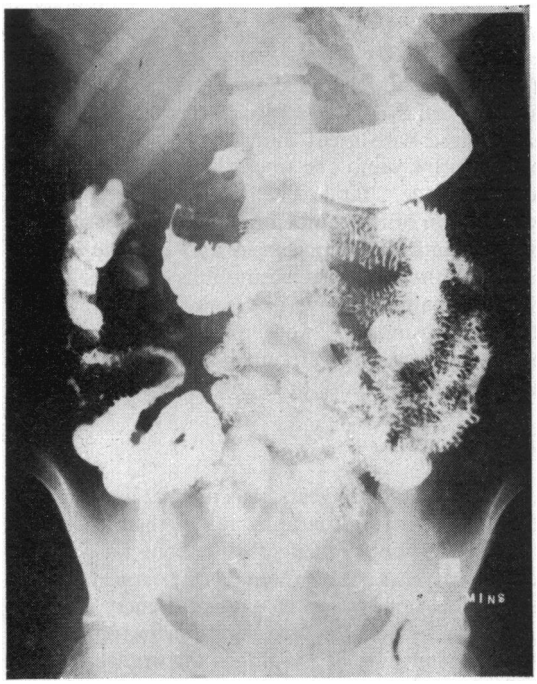

Fig 1 *Abnormal appearances of the duodenum, jejunum, and terminal ileum (case 1).*

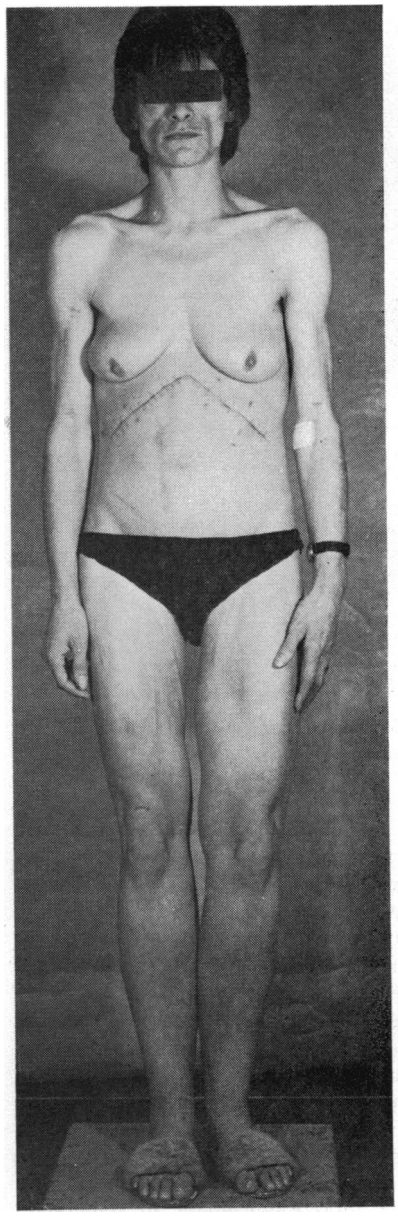

Fig 2 *Loss of subcutaneous fat over the arms, face, trunk, and upper part of the thighs (case 1).*

goblet cells and eosinophils in an otherwise normal mucosa. There were scattered eosinophils in the muscularis mucosa, with slight fibrous thickening of the subserosa and cuffing of the subserosal arterioles with polymorphs and eosinophils. No evidence of Crohn's disease could be found.

At the age of 27 years a transient episode of obstructive jaundice occurred and lasted for three weeks; an eosinophilia was again recorded (1050 and 1320/c mm). The patient had by now become dependent on analgesics because of constant severe epigastric and left hypochondrial pain which radiated through to the back. She passed up to four pale, bulky, and offensive stools daily, and had lost 13 kg in weight in the preceding three months. She also complained of repeated attacks of dysuria. Her appearance was classical of partial lipodystrophy (fig 2). A diagnosis of chronic pancreatitis was confirmed by the findings of pancreatic calcification on radiographs, steatorrhoea, a diabetic glucose tolerance test, no uptake of ^{75}Se-selenomethionine on a pancreatic scan, and very little recovery of the isotope from the duodenum at two hours (Youngs, Agnew, Levin, and Bouchier, 1971). Plasma amylase and calcium were normal; there was slight generalized aminoaciduria. The fasting plasma cholesterol, triglyceride, and lipoprotein levels were normal with a normal electrophoretic strip. Fasting growth hormone levels were raised. The plasma alkaline phosphatase was raised to 25 KA units/100 ml but liver function tests were otherwise normal and a liver biopsy was normal. A suction mucosal biopsy from the descending duodenum was normal. An intravenous pyelogram again showed bilateral non-obstructive hydronephrosis (fig 3). A micturating cystogram did not demonstrate ureteric reflux, but the bladder capacity was reduced and its wall was

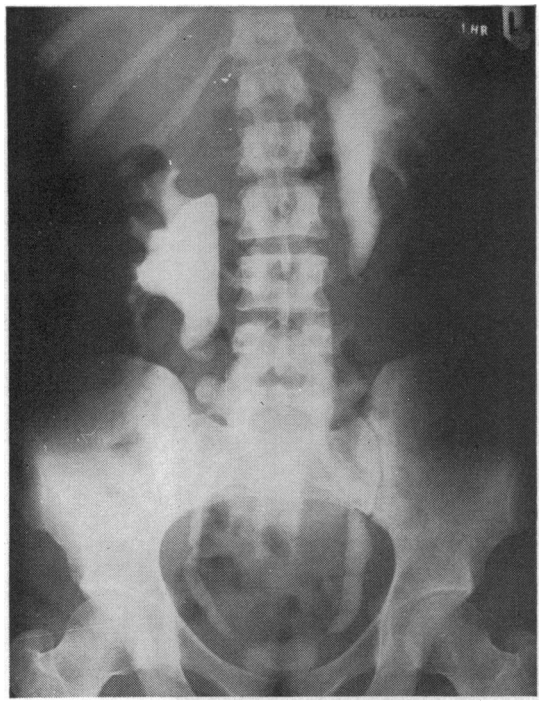

Fig 3 *Bilateral hydronephrosis with dilatation of the ureters but no evidence of ureteric obstruction (case 1).*

thickened and irregular; biopsy of the bladder mucosa was normal. Plasma immunoelectrophoresis showed an increase in IgG; no thyroid or gastric autoantibodies were detected.

The incapacitating pain was ascribed to chronic pancreatitis and subtotal pancreatectomy was advised. At laparotomy, the pancreas was hard and nodular, especially the head of the gland around the common bile duct which was dilated and thickened; subtotal pancreatectomy was performed. Adhesions were present around the duodenum, the wall of which was not thickened, and the terminal ileum which was a little dilated proximally. The excised tissue showed dilatation of the main pancreatic duct and almost total replacement of pancreatic exocrine glands by fibrosis.

The pain in the back and left upper quadrant of the abdomen was relieved by the operation and analgesics were successfully withdrawn. Diabetic control proved difficult at one stage due to an acquired resistance to beef insulin (200 units/day), but sensitivity to pork insulin was normal (30 units/day).

Some pain in the right upper abdomen persisted after operation and about two years later this pain became impossible to relieve with simple analgesics. Failure to control persistent and severe pain made it necessary to attempt removal of the remaining pancreatic tissue. Dense adhesions were present around the duodenum and pancreatic remnant; the head of the pancreas with the duodenal loop was excised with great difficulty and with damage to the portal vein. The operation was followed by uncontrollable, fatal haemorrhage. Histological examination of the duodenum and ampulla of Vater showed epithelial hyperplasia and chronic inflammation with numerous eosinophils in some areas. The pancreatic tissue was chronically inflamed and fibrosed; eosinophils were present in the inflammatory exudate but were much less prominent than in the gut. Permission for necropsy was refused.

Case 2

S.H., a woman of 23 years, was normal until the age of 5 years but photographs taken then showed a progressive loss of facial subcutaneous fat over the next three years. She presented the typical picture of partial lipodystrophy with absence of subcutaneous fat over the face (fig 4), arms, and trunk. On the upper part of the thighs fat was absent but on the lateral side of the left thigh the subcutaneous fat was slightly increased; the subcutaneous fat over the legs below the knees was normal. Muscular development, particularly of the legs, was well marked. There was no family history suggesting lipodystrophy.

At the age of 8 years, she was first admitted to hospital with an acute episode of abdominal pain, though there was a history of similar attacks of pain during the previous year or two. At laparotomy the pancreas was oedematous, fat necrosis of the omentum was observed and confirmed by biopsy, no abnormality was found in the small intestine.

Recurrent attacks of abdominal pain occurred during the next 15 years, with admission to hospital on 14 occasions. Between attacks the patient was well. Repeated investigations showed a normal biliary system, liver and pancreatic function tests. The serum amylase was elevated during acute attacks of pain. Eosinophilia was noted (maximum recorded 3500/c mm) on at least eight occasions during admission to hospital, but normal eosinophil counts were observed during periods of good health. No evidence of parasitic infestation was found.

After a particularly severe attack of pancreatitis at the age of 23 years the pancreas was reinvestigated to determine whether or not surgical exploration should be undertaken. Tests of pancreatic function, including glucose tolerance, faecal fat, and measurement of tryptic activity in duodenal juice (Lundh test), gave normal results. Growth hormone

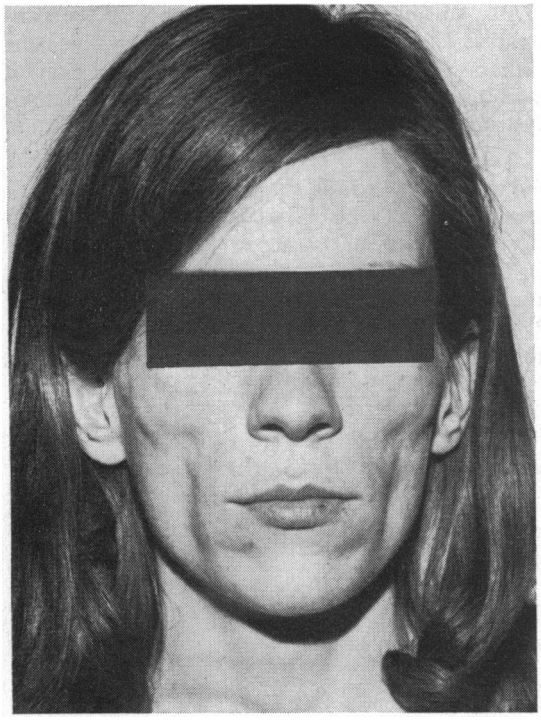

Fig 4 *Typical facial appearance of lipodystrophy (case 2).*

and insulin levels during a glucose tolerance test were normal. Blood lipid studies showed normal fasting cholesterol, triglyceride, and lipoprotein levels with a normal electrophoretic strip. Coeliac angiography demonstrated normal vasculature of the pancreas. At duodenoscopy (Dr P. B. Cotton) the stomach, the first two parts of the duodenum and ampulla of Vater appeared normal, as were biopsies obtained from the duodenal bulb and third part of the duodenum. Retrograde cholangiopancreatography demonstrated normal calibre of the main pancreatic duct and the ducts in the head, with minimal irregularity of some of the branch ducts of the tail. There was delay in pancreatic duct emptying and some contrast remained 12 minutes after injection.

In the absence of structural change, there did not appear to be any clear indication for surgical treatment and conservative treatment was continued. Since eosinophilic gastroenteritis usually responds to corticosteroid therapy this treatment was tried during three attacks of pain associated with raised plasma amylase and eosinophilia. There was no definite benefit or change in the eosinophil count.

Later that year a single attack of left renal pain occurred. An intravenous pyelogram showed no excretion of dye by the left kidney, though excretion had been normal previously. Left retrograde pyelography demonstrated dilatation of the left pelvis but no calculus was visible. Intravenous pyelography nine months later was within normal limits.

Discussion

There is little doubt that these two patients showed the changes of partial lipodystrophy, as described by Senior and Gellis (1964). The diagnosis of chronic pancreatitis in case 1 and recurrent acute pancreatitis in case 2 was established by examination of the pancreas and by appropriate investigations.

Recurrent eosinophilia was noted in both patients and in case 2 was associated with episodes of pancreatitis. In case 1, a diagnosis of eosinophilic gastroenteritis is likely with narrowing of the duodenum and terminal ileum, and infiltration of the gut wall by eosinophils. No lesion of the gut has been demonstrated in case 2.

Partial lipodystrophy is commonly associated with renal disease (Eisenger *et al*, 1972), usually a form of glomerulonephritis, but in three of the 14 patients with this association described by Senior and Gellis (1964) there was bilateral hydronephrosis and hydroureter without obstruction, as in case 1, and they refer to four other reported cases. One example of bladder involvement in association with eosinophilic gastroenteritis has been described (Burhenne and Carbone, 1966), the thickened bladder wall being infiltrated with eosinophils. In case 1, the bladder wall appeared thickened on radiographs but cystoscopy and mucosal biopsy showed normal appearances.

No association between partial lipodystrophy and pancreatitis is recognized, though Boucher, Cohen, Frankel, Stuart Mason, and Broadley (1973) have described a woman of 26 years with partial lipodystrophy who had a typical attack of acute pancreatitis at the age of 21, and another patient with partial lipodystrophy and recurrent pancreatitis is known (Senior, personal communication).

Besides our two patients, one other patient with lipodystrophy, recurrent abdominal pain, and eosinophilia has been described (Boucher *et al*, 1973; Boucher, B. J., and Wright, J. T., personal communication, 1974). This boy presented with a history of abdominal pain and vomiting at the age of 14 years. He was noted to have eosinophilia (1200-2200/c mm). Barium meals were normal and laparotomy one year later showed lack of intraabdominal fat as the only abnormality. Total lipodystrophy was diagnosed two years after he was first seen and by this time the eosinophil count had fallen to about

500/c mm. A gastric mucosal biopsy contained no excess eosinophils; plasma amylase was not raised. There were no urinary symptoms and an intravenous pyelogram was not performed. Corticosteroid treatment was given; by the age of 21 years the patient was well and not receiving treatment.

There is possibly an association between pancreatitis and eosinophilia (Juniper, 1955) and a single patient with a long history of eosinophilic gastroenteritis and terminal pancreatitis has been recorded (Weisberg and Crosson, 1973).

The pancreatitis in case 1 could have been due to involvement of the pancreatic duct in duodenal disease. It is of interest that in a recently reported series of 10 patients with Crohn's disease involving the duodenum, three had associated pancreatitis (Legge, Hoffman, and Carlson, 1971). This explanation cannot account for the pancreatitis in case 2 nor in another patient whose duodenum was normal (Senior, personal communication). Pancreatitis is known to be associated with hyperlipoproteinaemia (types I and V) but this was not present in our two patients, nor in the patient described by Boucher *et al* (1973). Eosinophilia is frequently associated with allergic disorders such as asthma or urticaria, and a high proportion of patients with eosinophilic gastroenteritis have such a tendency (Klein, Hargrove, Sleisenger, and Jeffries, 1970; Leinbach and Rubin, 1970). Case 1 developed resistance to beef insulin but we observed no other immunological disorders. It is tempting to speculate that the recurrent eosinophilia in case 2 is associated with oedema of the pancreatic ducts or acini.

The aetiology of lipodystrophy is unknown though an abnormality of B-adrenergic receptors in dermatomes of part or all of the body leading to increased lipolysis has been suggested (Boucher *et al*, 1973). An abnormality of B-receptors in the pancreatic islets has also been postulated by the same authors to account for an increased secretion of insulin in some patients. Any links between lipodystrophy, pancreatitis, and eosinophilia are obscure.

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