A CASE OF PYREXIA OF UNKNOWN ORIGIN

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The patient, a civil servant aged 51, was admitted to hospital in September 1951, complaining of attacks of shivering, sweating, epigastric pain, and general ill-health for the past nine months.

During the past year he had suffered from an intermittent purulent discharge from the right ear, and had noticed that he was partially deaf in this ear. In 1915 he had been admitted to a military hospital with ear trouble, and as a child he had suffered from ear disease. During and after the first World War he served in Germany, Poland and North Russia, where he suffered from louse infestation. There was no history of malaria, typhus or dysentery. He had an attack of jaundice as a young man.

The present illness began in January 1951, when he was confined to bed at home with an attack of 'gastric flu.' This was of sudden onset with shivering, sweating, and a sinking feeling in the epigastrium. There was no vomiting or diarrhoea. He believes he was febrile at the time, but did not record his temperature. A few weeks later two further attacks occurred, and in March he had another attack when travelling home in the train, when he felt hot, nauseated and perspired. There was blurring of vision, and he subsequently fainted for a short time. Later the same month he had a severe attack of epigastric pain of sudden onset associated with vomiting, which lasted for three days. He was admitted elsewhere as a possible perforated peptic ulcer, where the stomach was aspirated but no operation was performed. He was not jaundiced. A test meal and barium meal were found to be normal after the attack had resolved.

In July he had a further attack of shivering, sweating and faintness. During this time he lost a stone in weight, had a poor appetite, felt unwell and weak. At no time was he known to have been jaundiced, and he had not noticed pale stools or dark urine.

He was admitted to hospital in September 1951, when he was found to be running a low grade intermittent fever. On examination he was found to be a thin, sallow man; not clinically jaundiced or anaemic. There were no enlarged lymph glands. The cardiovascular system and respiratory system were normal; B.P. 140/80. The left ear was normal; the right drum showed a small perforation with purulent discharge. The tongue was clean, and the throat normal. The liver edge was palpable just below the right costal margin, but was not tender. The spleen and kidneys were not palpable. Rectal examination was normal. The central nervous system was normal.

The following investigations were carried out:

- E.S.R. (Wintrorbe) 40 mms. in the first hour.
- Blood count: Haemoglobin 13.4 grams per cent.
- White blood cells 8,600 per c.mm. Polymorphs 72 per cent. Lymphocytes 24 per cent. Monocytes 3 per cent. Eosinophils 1 per cent.
- The urine was normal. Occult blood on three occasions — negative. Agglutination tests for typhoid, paratyphoid, brucella abortus, and salmonella organisms were within normal limits.
- Liver function tests showed:
  - Serum alkaline phosphatase: 63.0 K.A units.
  - Thymol turbidity: 1.0 units. Van den Bergh reaction: Direct—positive. Indirect —1.6 mgs. per cent.
  - Repeated later the direct reaction was negative.
  - Serum proteins: Albumin—4.9 grams per cent.
  - Globulin—2.3 grams per cent.
  - Total—7.2 grams per cent.
  - Serum acid phosphatase: 3.0 units.

In view of the high serum alkaline phosphatase in the chest, pelvis and long bones were X-rayed and found to be normal. A barium meal suggested the presence of chronic duodenal ulceration. Cholecystogram showed no gall stones, but the gall bladder did not fill even after a second dose of pheniodol. Duodenal intubation was attempted but was unsuccessful.

Progress: Whilst in hospital he had one further attack of shivering and sweating when the temperature rose to 100°, and shortly afterwards the
Liver was found to be enlarged by three fingers breadth and tender, although later it returned to its original size.

He was seen by an E.N.T. Surgeon, Mr. Stratton, who was of the opinion that the right otitis media was of long standing and insufficient to cause the temperature and high B.S.R. A provisional diagnosis of subacute cholangio-hepatitis and possible pancreatitis was made. An insulin sensitivity test was normal as were serum calcium and phosphorus levels.

Laparotomy was performed in December, when the gall bladder and bile ducts were found to be distended. When opened, the bile appeared to be clean and no stones were found in the gall bladder or bile duct. There was stenosis of the ampulla of Vater and a probe could not be passed into the duodenum. No scarring was found in the bile duct, and there was no evidence of duodenal ulceration; the pancreas appeared normal. Numerous very large lymph glands were seen. Lymph glands and liver biopsy were taken. The post-operative period was uneventful.

Histological report on the specimens was as follows:

Sections of the liver (Figs. 1 and 2) shows a fairly heavy infiltration of the portal tract by lymphocytes with occasional eosinophils and plasma cells. In some areas neutrophil polymorphonuclear leucocytes are also present in moderate numbers. There is proliferation of the small bile ducts but they are not dilated. The liver lobules show a normal architecture and there is no histological abnormality of the hepatic cells.

The appearances are those of a mild degree of subacute cholangitis. Evidence of a biliary obstruction is lacking.

Section of the lymph node shows a mild degree of catarrhal adenitis only.

The patient therefore presented with a history of recurrent rigors and abdominal pain associated with low grade fever. After full investigation the only positive signs were a transiently enlarged liver, high E.S.R., raised alkaline phosphatase and a non-filling gall bladder. Operation confirmed the diagnosis of cholangio-hepatitis apparently secondary to stenosis of the ampulla of Vater, although histology of the liver showed little evidence of biliary obstruction.
Cholangio-hepatitis usually arises secondarily to obstruction of the biliary tract, and a mild degree is almost constant in cases of biliary obstruction. Rare cases have been described in which no obstruction of the biliary tract has been found. The clinical picture is very variable, but presentation as pyrexia of unknown origin (Charcot's intermittent biliary fever) is described and recognized, and Hobson and Rice-Oxley (1950) in a clinical study of the condition describe two such cases.

In the present case it is possible that the stenosis of the ampulla of Vater had resulted from the passage of a single stone, which would account for the severe attack of epigastric pain when the patient was sent to hospital as a possible perforated ulcer. It is noteworthy, however, that he was not jaundiced at this time, and no evidence of gall bladder disease or scarring was found in the bile duct at operation. It would, therefore, appear that the primary abnormality in this case was at the ampulla of Vater. Cases of functional biliary obstruction have been reported, and hypertrophy of the muscle surrounding the ampulla has been found in many such cases (Berg, 1923; Newman, 1933).

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