CASE REPORT

Autoimmune pancreatitis with concomitant autoimmune haemolytic anaemia

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SUMMARY

Autoimmune pancreatitis (AIP) is an infrequent cause of acute pancreatitis, being more commonly associated with chronic pancreatitis. AIP can be associated with other autoimmune manifestations, including Sjögren's, inflammatory bowel disease, primary biliary cirrhosis, rheumatoid arthritis, hypothyroidism and sarcoidosis. Rarely, concurrent autoimmune haemolytic anaemia (AIHA) is observed, as seen in our case report of a 33-year-old postpartum woman.

BACKGROUND

Acute pancreatitis is a common clinical presentation that often has a clear aetiology on relatively simple investigation. When first-line investigations prove negative, however, it is important to investigate other aetiologies rather than to declare the pancreatitis to be idiopathic in origin. In a case such as this, where the patient's South Asian origin and recent postpartum state threw up diagnostic red herrings, there was a delay in making the correct diagnosis and instigating appropriate treatment. Cases such as this highlight the importance of early involvement of other specialties—in this case infectious diseases and haematology—to offer advice once causes of pancreatitis that may be managed by the general surgical team are excluded.

Further complicating this presentation was the association with other autoimmune phenomena—in this case autoimmune haemolytic anaemia. The patient fits perfectly into the demographic for autoimmune phenomena, so this serves as a reminder that this should more readily be investigated as a cause for pancreatitis of unknown aetiology.

CASE PRESENTATION

A 33-year-old South Asian woman was admitted under the care of the hepatopancreatobiliary department at a tertiary university hospital. She complained of a 10-day history of severe epigastric pain, nausea and feverish symptoms. Medical history consisted of hypothyroidism, B12 deficiency and an episode of jaundice aged 16 with no diagnosed cause. She took regular levothyroxine and 3 monthly hydroxocobalamin replacement. She had no surgical or allergy history or history of recent foreign travel. Prior to this presentation she had had a normal diet, was a non-smoker and rarely drank alcohol and no concerns of weight loss or change of bowel

habit. The patient was 12 weeks post partum when she presented.

INVESTIGATIONS

Admission assessment and investigations revealed a soft, non-distended but tender upper abdomen. Blood workup showed a haemoglobin (Hb) of 113 g/L, white cell count $13.4 \times 10^9/L$ and C reactive protein (CRP) 141 mg/L (trends for these parameters are shown in [table 1](#)). Amylase on admission was 45 IU/L. Renal profile, other routine liver function tests, bone profile and full lipid profile were within normal parameters. Ultrasound sonography scan of her abdomen showed normal appearances of her liver, biliary tract and a limited view of her pancreas. Spleen and kidneys were of normal size and appearance. CT abdomen and pelvis with intravenous contrast on day 6 of admission showed free fluid in the abdomen with peripancreatic oedema correlating with acute pancreatitis.

Her admission lasted 4 weeks, throughout which she continued to have frequent temperature spikes up to 40°C despite antipyretics. Hb level dropped steadily to 50 g/L, while white cell count and CRP rose to $41.3 \times 10^9/L$ and 506 mg/L, respectively. Subsequent tests were negative for cytomegalovirus, double stranded DNA, C3 and C4, antineutrophil cytoplasmic antibody, mumps RNA, Rheumatoid Factor and parvovirus B19. The pertinent positive result was for IgG, which tested positive at 18.29 g/L—normal values 6–16 g/L (IgG4 1.35 g/L—normal values 0–1.3 g/L) (individual subclasses shown in [table 2](#)), making autoimmune pancreatitis the most likely diagnosis. A further CT abdomen and pelvis was performed with intravenous and oral contrast, showing a progressively oedematous pancreas and an increasing number of prominent porta hepatis, mesenteric, retrocrural and para-aortic lymph nodes. Serum quantiferon assays and bone marrow trephine performed did not correlate with tuberculosis (TB) or lymphoma.

The patient's developing anaemia corresponded with a rising lactate dehydrogenase (peak 2139 IU/L), raised ferritin (3269 ug/L), raised unconjugated bilirubin (33 umol/L) and depressed haptoglobin (<0.07 g/L) and haemopexin (0.11), indicative of intravascular haemolysis. Nucleated red cell counts were raised ($2.56 \times 10^9/L$), but reticulocyte level normal ($31 \times 10^9/L$). Paroxysmal nocturnal hemoglobinuria flow cytometry was negative.

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Table 1 Trends in haematological and biochemical parameters during admission

Day of admission	Haemoglobin (g/L)	White cell count $\times 10^9/L$	C reactive protein mg/L
1	113	13.4	141.3
2	109	11.9	222.4
3	91	13.6	290.3
4	89	15.5	336.1
5	94	15.9	344.8
6	83	17.2	409.1
7	74	17.4	506.8
8	77	27.0	467.0
9	61	26.8	467.0
10			409
11	50	41.3	340.7
12	88	36.6	212.4
13	91	28.7	208.2
14	99	22.9	129.0
15	99	23.2	130.4
16	86	21.1	114.1
17	85	18.6	97.2
18	85	15.7	83.0
19	73	14.3	52.1
20	98	14.7	
21	98	13.1	
22	80	15.7	
23	93	13.1	
24	89	10.9	15.1
25	92	11.0	
27	94	9.0	
42 (outpatient)	116	9.0	8.8

DIFFERENTIAL DIAGNOSIS

- Gallstone pancreatitis;
- Acute pancreatitis caused by: hyperlipidaemia; mumps; hypercalcaemia; drug-induced; idiopathic; autoimmune;
- Parvovirus B19 infection;
- TB;
- Lymphoma.

TREATMENT

The patient was initiated on high-dose steroid therapy (65 mg prednisolone once a day), to which she responded well, and was discharged to be followed up by the haematology team for weaning of steroid therapy.

OUTCOME AND FOLLOW-UP

The patient was discharged with a 14-day supply of 65 mg prednisolone and followed up in haematology clinic to begin steroid weaning. Over 6 weeks, the patient was weaned from her steroid therapy, then discharged from follow-up. Her Hb remains stable,

Table 2 IgG subclass results

IgG subclass	Normal range (g/L)	Value (g/L)
IgG 1 subclass	3.2–10.2	11.73
IgG 2 subclass	1.2–6.6	5.62
IgG 3 subclass	0.2–1.9	0.79
IgG 4 subclass	0–1.3	1.35

and a repeat CT abdomen and pelvis shows complete resolution of inflammatory changes, with no residual abnormality.

DISCUSSION

Autoimmune pancreatitis represents a heterogenous disease that may be classified into two types. Type 1 autoimmune pancreatitis is found to have IgG4-positive antibodies, whereas type 2 autoimmune pancreatitis is negative for IgG4 antibodies.^{1,2} The case presented is that of type 1 autoimmune pancreatitis (AIP), with associated autoimmune haemolytic anaemia (AIHA). AIP is associated with other autoimmune phenomena, including Sjögren's, inflammatory bowel disease, primary biliary cirrhosis, rheumatoid arthritis, hypothyroidism and sarcoidosis and AIHA.^{3–5} In addition, pancreatitis of other aetiology (systemic lupus erythematosus, mumps, Epstein-Barr virus) have also been associated with AIHA.^{6–8} Other haematological complications are also seen in acute pancreatitis including Haemolytic-Uraemic Syndrome (HUS), Disseminated Intravascular Coagulation (DIC) and Thrombotic Thrombocytopenic Purpura (TTP).^{9–12} Lastly, pancreatitis can arise itself in the context of raised serum calcium and lipids, often seen in haemolysis.^{13,14}

Although results are suggestive of an initial pancreatitis, followed by haemolysis in this patient, reports of massive haemolysis triggering acute pancreatitis exist.^{15,16} It is postulated that a proinflammatory milieu is generated by the presence of large amounts of haem in the bloodstream, with subsequent cytokine and reactive oxygen species release triggering pancreatitis.¹⁷ On admission, this patient's haemoglobin was 113 g/L, suggesting the haemolysis to be secondary to the acute pancreatitis. The pathophysiological process by which acute pancreatitis leads to haemolysis is less well understood, though a uniting autoimmune aetiology seems apparent.

Although two reported cases from Japan, and one from Canada, describe autoimmune pancreatitis with associated autoimmune haemolytic anaemia, this is believed to be the first reported case in the UK.^{4,5}

Learning points

- Once common causes of pancreatitis are excluded, further timely investigation is required to investigate and exclude rarer causes.
- Patients prone to autoimmune phenomena may often suffer from more than one autoimmune condition.
- Autoimmune pancreatitis remains a rare but treatable cause of pancreatitis and should be considered in the differential diagnosis of pancreatitis.

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