Autoimmune pancreatitis with evolution to cholangitis : a case report

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Abstract

We report the case of a 47-year-old Caucasian male patient who presented with obstructive jaundice and mild epigastric pain. Autoimmune pancreatitis was diagnosed based on magnetic resonance imaging, biopsy and clinical evolution, and the patient was successfully treated with corticosteroids. However, a few months later ERCP showed an image compatible with sclerosing cholangitis. Again, treatment with corticosteroids was given, after which the bile ducts became normal. A few months later, again there was a relapse and azathioprine was started. After decreasing the dose of immunesuppression, we saw relapses of cholangitis and pancreatitis, with eventually evolution to chronic calcifying pancreatitis.

The aim of this report is to describe autoimmune pancreatitis as a cause of obstructive jaundice, and to illustrate that evolution to an immunesuppression-responsive cholangitis, with evolution to chronic calcifying pancreatitis is possible. Also, our patient had a small fluid collection, possibly a pseudocyst, an unusual finding in autoimmune pancreatitis, which disappeared during treatment. (Acta gastroenterol. belg., **2004**, 67, **346-350**).

Key words : autoimmune pancreatitis, sclerosing cholangitis.

In 1961 Sarles *et al.* discribed the concept of chronic pancreatitis associated with or caused by an autoimmune mechanism (1). Waldram *et al.* reported a case of chronic pancreatitis associated with sclerosing pancreatitis and sicca complex in 1975 (2). In Japan, Nakumura *et al.* first reported a case of pancreatitis associated with Sjögren's syndrome, successfully treated with steroid therapy (3).

Since this report several cases were described, and diagnostic criteria proposed (4). After treatment of the autoimmune pancreatitis, some of these patients developed a type of cholangitis, responsive to treatment with corticosteroids (9).

We report the case of a 47-year-old Caucasian male patient who presented with obstructive jaundice and mild epigastric pain. Autoimmune pancreatitis was diagnosed based on magnetic resonance imaging, biopsy and clinical evolution, and the patient was successfully treated with corticosteroids. However, a few months later ERCP showed an image compatible with sclerosing cholangitis. Again, treatment with corticosteroids was given, after which the bile ducts became normal. A few months later, again there was a relapse and azathioprine was started. . After decreasing the dose of immunesuppression, we saw relapses of cholangitis and pancreatitis, with eventually evolution to chronic calcifying pancreatitis.

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Case report

A 47-year-old Caucasian man was hospitalised because of jaundice associated with mild epigastric pain and weight loss of 8 kg in 1 month. There was no history of prior illness or alcohol abuse, he took no medication. Physical examination revealed only jaundice and some mild epigastric tenderness. Upon admission, laboratory examination showed a sedimentation rate of 28 mm/h (10-20 mm/h). Hematocrit, red cell count, white cell count and thrombocyte count were normal. Total bilirubin level was 9.8 mg/dl (0.2-1.3 mg/dl), alkaline phosphatase 640 U/l (35-95U/L), gamma-GT 167 U/l (13-45 U/l), SGOT 60 U/l (5-40 U/l), SGPT 85 U/l (7-56 U/l), amylase 550 U/l (30-110 U/l), lipase 266 U/l (13-300 U/l), CA 19,9 6,1 U/l (< 37 U/l). The C-reactive protein level was 3.6 mg/dl (< 0.7 mg/dl).

Abdominal ultrasound, endoscopic ultrasound, CT scan and MRI of the upper abdomen showed a diffuse oedematous pancreas, with a diffusely narrowed main pancreatic duct, and a small fluid collection in the tail of the pancreas. On T2 weighted images a hypointense rim was seen surrounding the pancreas (Fig. 1a). The main bile duct and the intrahepatic bile ducts were dilated, with a long narrow distal bile duct stricture (Fig. 1b). An ultrasound-guided fine needle biopsy of the pancreas showed fibrosis and lymphoplasmocytic infiltration, which is compatible with an autoimmune form of pancreatitis (Fig. 2). On ERCP diffuse narrowing of the main pancreatic duct was seen, and a biliary stent was positioned across the distal bile duct stricture. Brush cytology of the distal bile duct was negative for malignant cells. Additional laboratory examination showed normal levels of gammaglobulins, antinuclear factor, antimitochondrial and anti-pancreas antibodies were

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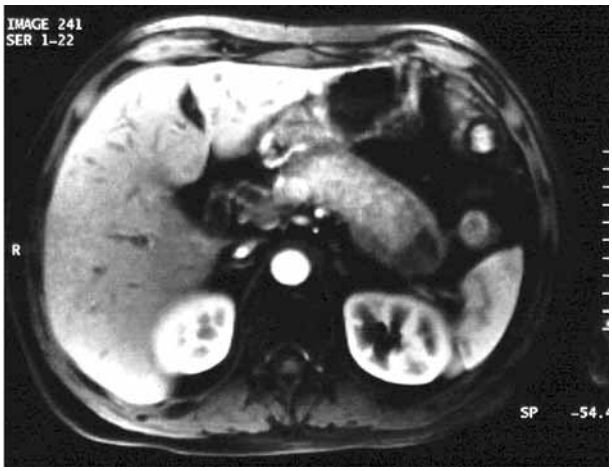


Fig. 1a. — MRI showing diffuse swelling of the pancreas, surrounded by a hyporeflective rim on T1 weighted images. This is pathognomonic for autoimmune pancreatitis. There is a small fluid collection in the pancreatic tail (arrow).

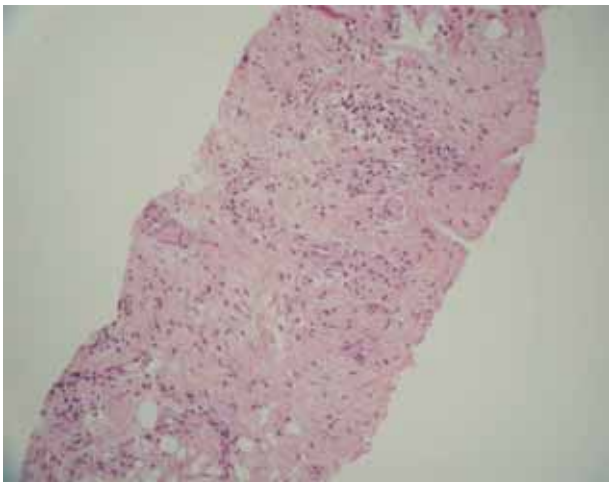


Fig. 2. — Biopsy of the pancreas showing fibrosis and lymphoplasmocytic infiltration.

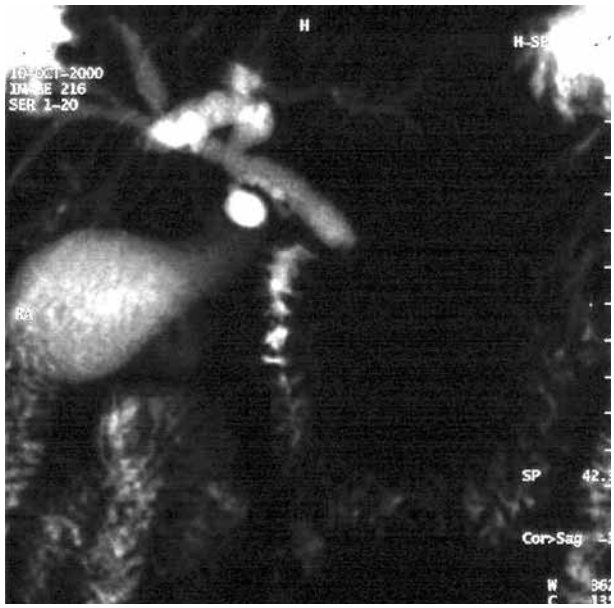
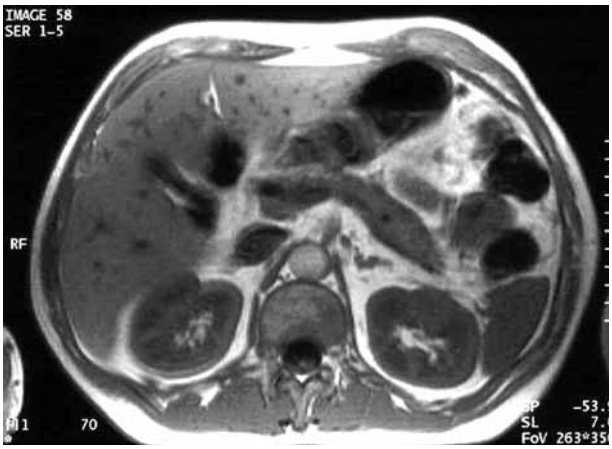


Fig. 1b. — MRCP showing narrowing of the distal main bile duct (between the arrows) with upstream dilatation of the bile ducts. The pancreatic duct is diffusely narrowed, and almost invisible.

negative, thyroid function tests were normal and there were no clinical sings of other autoimmune diseases. As the findings were suggestive for autoimmune pancreatitis, and as there was no evidence for a malignant lesion, we treated our patient with 32 mg methylprednisolone once daily, after 4 weeks gradually decreasing the dose. The patient became asymptomatic, liver enzymes, bilirubin and amylase normalised. The endobiliary stent was replaced after 3 months. At that moment, the stricture of the distal bile duct was already less narrow. Another 3 months later MRCP showed complete normalisation of the pancreas and the bile ducts (Fig. 3), the fluid collection in the pancreatic tail had disappeared. Removal of the endobiliary stent was planned shortly afterwards, but at that moment the patient complained of itching. He had no fever or chills. Total bilirubin level was 2.6 mg/dl (0.2-1.3 mg/dl), SGOT 60 U/l (5-40 U/l), SGPT 158 U/l (7-56 U/l), alkaline phosphatase 986 U/l (36-95 U/l), gamma-GT 514 U/l (13-45 U/l), CA 19,9 2420 U/l (< 37 U/l). LDH, amylase and lipase were normal. The IgG4 level was 96,1 mg/dl (7.2-73.2 mg/dl). ERCP revealed irregular narrowing and dilatation of the bile ducts, with a longer stricture in the proximal main bile duct (Fig. 4). The image was compatible with primary sclerosing cholangitis (PSC). A colonoscopy to exclude inflammatory bowel disease and anti-neutrophil cytoplasmatic antibodies was negative. Because of the history of autoimmune pancreatitis, we presumed a possible autoimmune aetiology of the PSC-like bile ducts. We performed a liver biopsy revealing normal bile ducts, there were no signs of sclerosing cholangitis. Again we treated our patient with methylprednisolone, starting at 32 mg once daily, and gradually decreasing the dose after 4 weeks. After 3 months of corticosteroid therapy, ERCP showed normalisation of the bile ducts (Fig. 5), but 4 weeks after cessation of the corticosteroids the cholangitis relapsed. Again, there was a good response to corticosteroids, and azathioprin 1mg/kg was started. After 1 month we started to decrease the dose of the corticosteroids, but three weeks after cessation of the steroids, the cholangitis again relapsed. We elevated the dose of the azathioprine to 2,5 mg/kg, and corticosteroids were again associated and gradually decreased after 4 weeks. The patient was free of symptoms for 7 months, but afterwards our patient again suffered from abdominal pain and laboratory findings showed an elevation of the amylases and lipases. MRCP was performed, which showed a stenosis of the main panceatic duct with pancreatic fibrosis and dilatation of the Wirsung duct in the corpus and tail of the pancreas. The



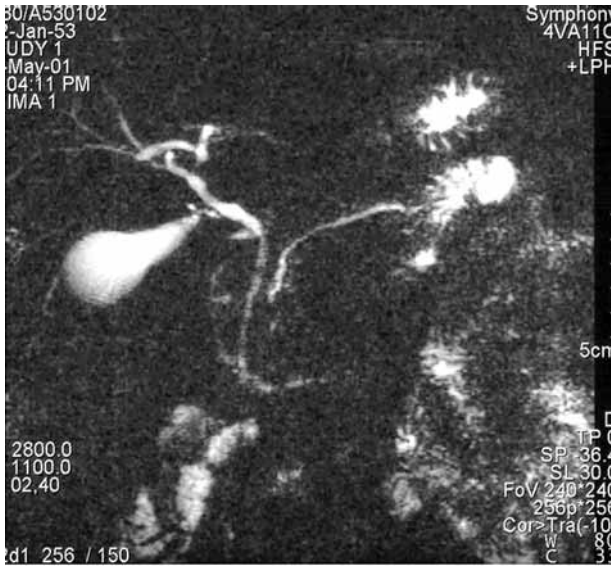


Fig. 3. — MRCP after treatment with corticosteroids, showing almost complete normalisation of the pancreas, bile ducts and pancreatic duct.

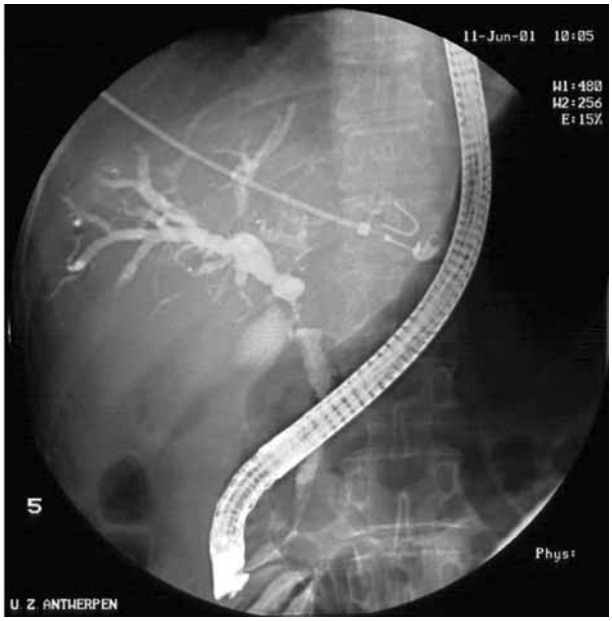


Fig. 4. — During follow up, ERCP showed multiple narrowing of the bile ducts with sacculary dilatations as seen in primary sclerosing cholangitis. There is a new, longer stricture (arrow) at the level of the common hepatic duct.

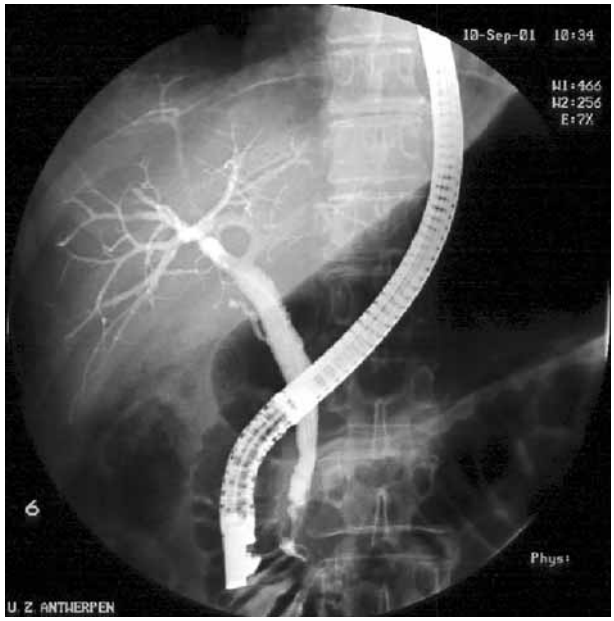


Fig. 5. — ERCP after treatment with corticosteroids, showing normalisation of the bile ducts.

main pancreatic duct was dilated and stented (Fig. 6). After two months, the azathioprine was stopped because of evolution to chronic calcifying pancreatitis, seen on endoscopic ultrasound and MRCP. After four weeks the patient again had abdominal pain and an elevation of the amylases and lipases. There was a good clinical and biochemical response after treatment with azathioprine and corticosteroids.

Discussion

Several authors, mostly Japanese, have reported on patients with chronic pancreatitis that appeared to be autoimmune mediated (1,2,3,4,5,6,9). It was Yoshida *et al.* who first proposed criteria for diagnosing autoimmune pancreatitis : increased serum levels of gammaglobulins and IgG, presence of autoantibodies, diffuse

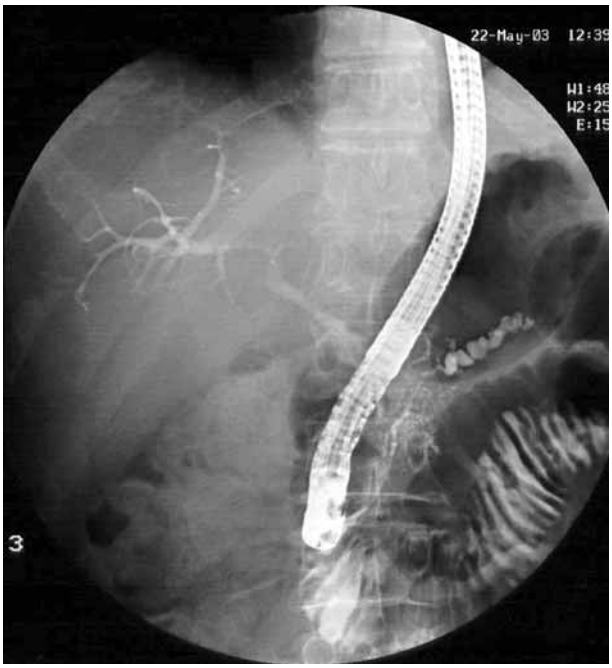


Fig. 6. — ERCP showing stenosis of the main panceatic duct with pancreatic fibrosis and dilatation of the Wirsung duct in the corpus and tail of the pancreas.

enlargement of the pancreas, diffuse irregular narrowing of the main pancreatic duct on ERCP, fibrotic changes with lymphoplasmocytic infiltration of the pancreas, absence of acute attacks of pancreatitis, narrowing of the main bile duct with upstream dilatation and elevated cholestatic liver tests, possible association of other autoimmune diseases, no pseudocysts and effective clinical response to steroid therapy. The diffuse irregular narrowing of the main pancreatic duct is thought to be particularly characteristic of the disease (6). It is explained by the presence of marked cellular infiltrates around the pancreatic ducts, which contributes to the swelling of the pancreas (7).

Our patient did not have the laboratory findings typical for autoimmune pancreatitis, we could only show an elevated IgG 4 level, as described by others. This IgG4 level was measured 6 months after initial diagnosis (8,9). He also showed a pancreatic pseudocyst, which is not typical. However, as the histological findings were compatible with the diagnosis and more important, as Irie *et al.* described the diffuse swelling of the pancreas surrounded by a hypointense rim on T2 weighted MRI-images as being pathognomonic for this disease (10), we diagnosed autoimmune pancreatitis. There were no arguments for malignancy, neither on imaging investigations nor histologically. There were no arguments for other autoimmune diseases. Our patient had a small fluid collection, possibly a pseudocyst in the tail of the pancreas, but there was no alcohol abuse and no history of acute pancreatitis. We treated our patient with corticosteroids, resulting in normalisation of the pancreas and bile ducts on radiological imaging, confirming the diagnosis of autoimmune pancreatitis. The fluid collection disappeared.

During follow up our patient expressed PSC-like bile duct anomalies on ERCP. We performed a liver biopsy, but no alterations in the intrahepatic bile ducts like those seen in PSC were present. Other authors described patients with the same characteristics (11,12,13), having proliferation of bile ducts and infiltration of chronic inflammatory cells into portal areas without piecemeal necrosis or lobular hepatitis. Though we could not demonstrate these anatomopathological changes in our patient, again we treated him with methylprednisolone and we saw complete remission of the abnormalities in the bile ducts.

Our observations suggest that autoimmune pancreatitis should be considered in patients with obstructive jaundice and a diffusely oedematous pancreas, with the characteristic image on MRI, even in the absence of the biochemical criteria as proposed by Yoshida. Our patient even has a small pseudocyst ; nevertheless, there were no arguments for another diagnosis than autoimmune pancreatitis, and the pseudocyst disappeared during treatment.

After treatment with corticosteroids, evolution to an image compatible with sclerosing cholangitis on ERCP and/or irregular narrowing of the main pancreatic duct is possible, but this cholangitis is also responsive to corticosteroid therapy, also suggesting an autoimmune cause (14).

We saw several relapses of autoimmune pancreatitis after cessation of the corticosteroids and azathioprine was started. The relapses after cessation of the corticosteroids suggest that immunesuppression should be given for a (undefined) long period, perhaps lifelong in our particular patient.

Our patient showed evolution to chronic calcifying pancreatitis, about three years after the first onset of the acute pancreatitis. Other case reports did not mention evolution to chronic calcifying pancreatitis or relapses after cessation of the immunosupression, but the follow up time did not exceed 2 years in the published reports. For this moment it is not clear whether we can prevent evolution to chronic calcifying pancreatitis with adequate immunesuppression.

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