Autoimmune pancreatitis in Children: Case Report and Review of the Literature

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Abstract

Autoimmune pancreatitis (AIP) is a rare entity that is extremely uncommon in children. We report a case of AIP in an 8-year-old boy who presented with severe obstructive jaundice and hepatomegaly. Abdominal ultrasound and Magnetic Resonance Cholangiopancreatography showed a diffuse enlarged pancreas causing compression of the common bile duct with severe dilation of the gallbladder and intra- and extrahepatic bile ducts. Laboratory results revealed positive antinuclear autoimmune antibodies and normal serum IgG4. Based on the clinical findings and imaging the diagnosis of autoimmune pancreatitis was made, which showed excellent response to corticosteroid therapy.

Introduction

Autoimmune pancreatitis (AIP) is a rare chronic disease of the pancreas, first described in 1961 in adults by Sarles et al (1). It was described as a distinct form of chronic pancreatitis, usually characterized by obstructive jaundice and abdominal pain, with or without a pancreatic mass mimicking pancreatic cancer. In 2010, the diagnostic criteria for AIP were established by means of an international panel of experts including pancreas histology, imaging findings, positive serology, presence of other autoimmune or inflammatory organ diseases, and prompt response to corticosteroids. These criteria are otherwise known as the 'HISORt criteria' (2). The AIP entity in adults is divided into two subgroups, IgG4-related AIP (type 1) and non–IgG4-related AIP (type 2) (2). Type 2 is frequently associated with inflammatory bowel disease, whereas type 1 has often signs of extra-pancreatic involvement (3).

In children, AIP is rare and the distinction of two subgroups as described in adults is difficult to achieve. Data on pediatric AIP remain limited with only a few cases reported from all ethnic backgrounds and a median age of 13 years at diagnosis. Most cases show similarity to type 2 in adults (4). In the past pediatricians relied mostly on the adult criteria to diagnose AIP, but new studies and increased recognition of the disease have led to child-specific studies and recommendations (5,6). Here we present a case from our hospital in Curaçao to increase knowledge about this rare entity in the pediatric population.

Case presentation

An 8-year-old boy presented with a 10-day history of abdominal pain in the right upper quadrant, darker urine and pale stools. There was no diarrhea or vomiting and he had no fever. His past medical history was unremarkable. On physical examination he had icteric sclerae, which were present for 10 days as well. The abdomen was slightly distended but not tense, with a significant hepatomegaly for up to 11 centimeters below the costal margin. Biochemically he had elevated transaminases, gamma-glutamyltransferase and hyperbilirubinemia, but the INR, PT, aPTT and lipase were all normal. IgG was elevated as well, but IgG4 levels were normal (see Table 1).

Table 1 : Laboratory data on admission

Laboratory test (SI units)	Result	Normal range
Leukocytes (x10^9/L)	7.3	4.5-13.5
Hemoglobin (g/L)	156.6	127.8- 172.8
Platelets (x10^9/L)	437	150-400
CRP (mg/L)	<4	<10
AST (U/L)	731	13-40
ALT (U/L)	584	10-49
GGT (U/L)	417	<55
Alkaline-phosphatase (U/L)	891	86-315
Total bilirubin (µmol/L)	157	5-21
Direct bilirubin (µmol/L)	121	<5
Lipase (U/L)	56	10-60
IgG (µmol/L)	190	43-106
IgG4 (µmol/L)	1.80	0.15-12.6
PT (sec)	11.9	9.8-12.7
aPTT (sec)	27.3	25-39
INR	1.1	0.9-1.1

(CRP, C-reactive protein; AST, aspartate-aminotransferase; ALT alanine-transaminase; GGT, gamma-glutamyltransferase)

A viral screening was negative. ANA (antinuclear antibodies) screening was positive, with all other antibodies being negative. Abdominal ultrasound showed a distended gallbladder with a length of 11cm and dilation of the intrahepatic bile ducts and a dilated common bile duct (15mm). The pancreas was diffusely enlarged with a head of 2.5cm, body of 2.3cm and an enlarged tail measuring 2.3cm. Other abdominal organs were normal. No enlarged lymph nodes or signs of lymphoma

were observed. Subsequent MRI (magnetic resonance imaging) and MRCP (magnetic resonance cholangiopancreatography) confirmed the diffuse enlarged pancreas resulting in the distended gallbladder and bile ducts. There were no signs of a sclerosing cholangitis (Figures 1 and 2). Altogether this picture was suggestive of a pediatric autoimmune pancreatitis (AIP). Prednisolone was started in a dose of 2 mg/kg/day and within the following days he improved both clinically and biochemically. Because a concomitant autoimmune hepatitis could not be ruled out due to the significant hyperbilirubinemia and elevated liver enzymes, azathioprine was associated in a dose of 2 mg/kg/day. After four weeks, corticosteroids were tapered until eventually they could be discontinued after nine months in total. Azathioprine was continued due to possible concurrent autoimmune hepatitis, unfortunately this could not be confirmed due to the lack of expertise in children's liver biopsy on the island of Curaçao. Repeat MRI after six months of therapy showed no residual signs of pancreatitis and normalization of the gallbladder and liver size. He is currently still in follow-up with frequent clinical and biochemical controls.

Figure 1: Magnetic resonance imaging of the abdomen, showing the dilated gallbladder

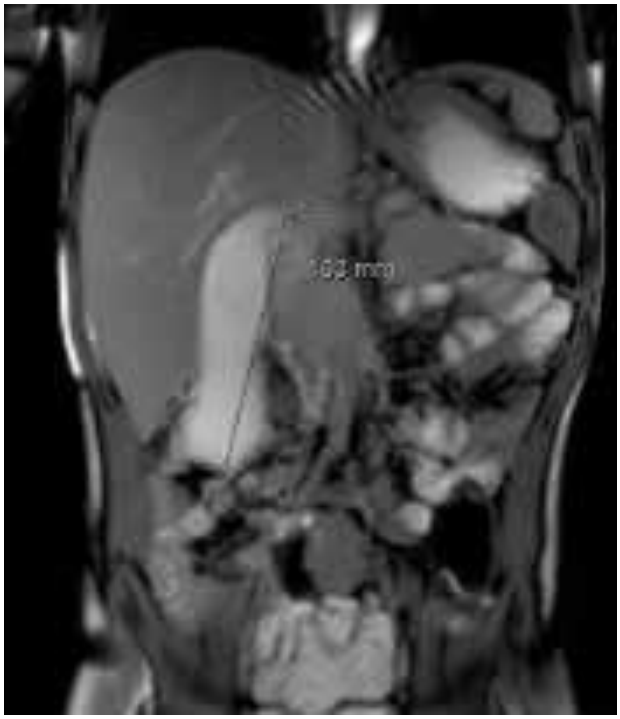
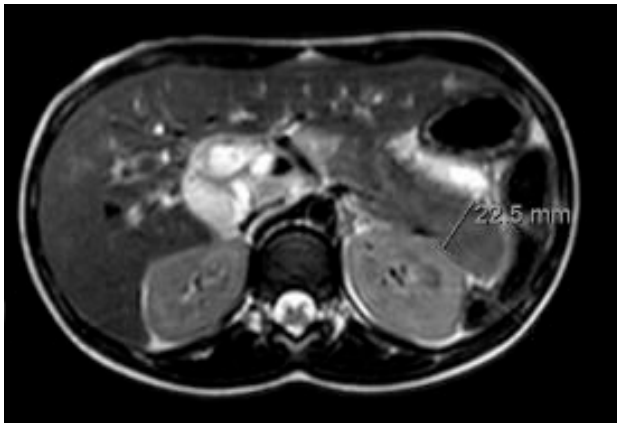


Figure 2: Magnetic resonance imaging of the abdomen, showing the enlarged pancreas with a typical "sausage-like" aspect



Discussion

The worldwide incidence for pediatric AIP is generally unknown, reflected by the previous approach to children with autoimmune pancreatitis, which was largely based on adult data (4). Thanks to the efforts of the INSPIRE group (the International Study Group of Pediatric Pancreatitis: In search for a cuRE) recommendations were made concerning the approach of diagnosis and management of AIP in children. Instead of the HISORt criteria used in adults, which include a pancreatic biopsy to rule out malignancy, the diagnosis in children relies on clinical findings and imaging, given the fact that the risk of pancreatic cancer in children is very low (7).

First step in the approach to a child with obstructive jaundice and/or pancreatitis is usually transabdominal ultrasound. This technique can adequately show pancreatic enlargement or mass formation and rule out other causes of obstructive jaundice. However, if AIP is suspected or when ultrasound resolution is limited, MRCP should be obtained, even in young children who will require sedation for the study (7).

The amylase and lipase levels are not included in the diagnostic criteria in children since these enzymes are normal at the time of diagnosis in 46-57% of children, as was the case in our patient. The same is true for IgG4, which was also normal in our case. Although it has a high diagnostic value in adults, elevated levels are uncommon in children (only in 22%) (4,7). Other autoantibodies have been described in adults with AIP. ANA positivity for example, was identified in up to 40% of adult AIP patients (8). In the pediatric population these autoantibodies have not been systematically studied and since they seem to lack disease specificity, they were not incorporated in the pediatric diagnostic criteria (5,7). Our patient showed positivity to ANA antibodies at presentation.

As for the treatment, current literature favors corticosteroids as first-line therapy in children. The majority of patients with AIP respond to glucocorticoids (80 to 99 percent) and most patients show significant improvement in clinical, biochemical and radiologic abnormalities. Relief of the pancreatic swelling can be observed as early as 2 weeks after the onset of AIP (9). It is suggested to start with oral prednisone, 1 to 1.5 mg/kg/day to a maximum of 40-60 mg given in one or two daily doses for 2-4 weeks, after that the prednisone should be tapered (7). Our 8-year old boy received 2mg/kg/day of prednisolone in two doses for a period of 4 weeks.

Follow-up in all cases is necessary to detect relapse, concurrent auto-immune diseases (e.g. Crohn's, ulcerative colitis, celiac disease, etc.) and possible impaired pancreatic exocrine function (7). Scheers et al. showed that the need for pancreatic enzyme replacement therapy and insulin-dependent diabetes mellitus occurred with a frequency of 16% and 11% respectively during a 21-month follow-up (4). In our patient there was no medical history of autoimmune disorders, nor in his family at presentation, although during his follow-up his mother has been screened for possible auto-immune hyperthyroidism. After 22 months of follow-up, he continues to attend the pediatric outpatient clinic to monitor for relapse or signs of exocrine/endocrine pancreatic insufficiency. Up to date he is doing well without lingering symptoms, although he is still under azathioprine therapy associated with low-dose budesonide since tapering of the corticosteroids resulted in a biochemical relapse of the transaminases. Concurrent autoimmune hepatitis is suspected in this case, which has been described in adult patients, but to our knowledge this has not yet in children been described (10).The signs of autoimmune pancreatitis are as for now completely resolved.

In **conclusion**, autoimmune pancreatitis in children is a distinct entity that responds well to corticoid therapy. Other than in adults, the risk of pancreatic cancer is low, which resulted in recent recommendations to diagnose the disease based on clinical findings and imaging, in particular MRCP.

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Conflict of interest

The authors declare that they have no conflict of interest.

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