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Autoimmune Pancreatitis as a Very Rare Cause of Recurrent Pancreatitis in Children: A Case Report and Review of Literature

Niloufar Shashaani[1], Amirhossein Hosseini[1], Negar Imanzadeh[2], Naghi Dara[1], Rahman Matani[3], Aliakbar Sayyari[1*]

1- Assistant Professor of Pediatric Gastroenterohepatology, Pediatric Gastroenterology, Hepatology and Nutrition Research Center, Research Institute for Children's Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
2- School of Pharmacy, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
3- Department of Pediatric, Alborz University of Medical Sciences, Emam Ali Hospital, Karaj, Iran.
4- Professor of Pediatric Gastroenterohepatology, Pediatric Gastroenterology, Hepatology and Nutrition Research Center, Research Institute for Children's Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran.

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Corresponding Author
Amirhossein Hosseini
Assistant Professor of Pediatric Gastroenterohepatology, Pediatric Gastroenterology, Hepatology and Nutrition Research Center, Research Institute for Children's Health, Shahid Beheshti University of Medical Sciences, Tehran, Iran.
Address: Mofid Children Hospital, Mirdamad Avenue, Tehran, Iran.
Email: Amir1981hosseini@gmail.com
Tel: +989128887347
* Second Correspondin Author,
Email: drsayyari@hotmail.com

ABSTRACT

Autoimmune pancreatitis as chronic inflammation of the pancreas due to an autoimmune mechanism is a rare type of pancreatitis. A 14 years old girl presented with multiple episodes of abdominal pain, nausea with elevation of amylase and lipase suspicions of acute recurrent pancreatitis since 3 years of age. After through evaluation about secondary causes of recurrent and familial pancreatitis finally she responded to corticosteroid treatment. Although very rare but autoimmune processes should be considered in teenagers with recurrent pancreatitis.

INTRODUCTION

Autoimmune pancreatitis (AIP) is a rare distinctive type of pancreatitis that defined as chronic inflammation of the pancreas due to an autoimmune mechanism; autoimmunity is responsible for producing the pancreatic lesion [1, 2]. AIP diagnosis are mainly based on a combination of five cardinal features including pancreas histology and imaging findings, positive serology, presence of other autoimmune or inflammatory organ diseases, and prompt response to corticosteroids [3].

AIP in adults is a well-known condition and classified into two subgroups. Type 1 is more common in elderly Asian males, involves other organs and is associated with a raised immunoglobulin G4 (IgG4). Type 2 has been described in population from Europe and North America, with a normal serum IgG4 and is more commonly associated with the development of ulcerative colitis.

There are limited published cases and case series about AIP in children and pediatric gastroenterologists rely on the adult AIP guidelines or experience of other prior publish reports to diagnose and manage AIP in children [4, 5].

Review of literature about childhood AIP suggest that the clinical presentation of AIP is different in children compared with adults, and that exclusive use of adult criteria may lead to underdiagnoses of AIP in children and management and treatment such cases may need for specific strategy case by case.

Here we report a case of 14 years old girl who referred to us with history of recurrent pancreatitis that managed as AIP.

CASE PRESENTATION

A 14 years old girl presented to our medical center with history of multiple episodes of abdominal pain, nausea with elevation of amylase and lipase that resulted to admission to hospital and treat with suspicions of acute pancreatitis. First episode started in her third years of life. And approximate period time between each episode was at least six months. During this period of time, patient was asymptomatic and serum level of amylase and lipase were normal.

She had history of febrile seizure that start in her first year of life and that has been controlled by phenobarbital. Also she has a maternal relatives' history of ulcerative colitis, dermatitis and

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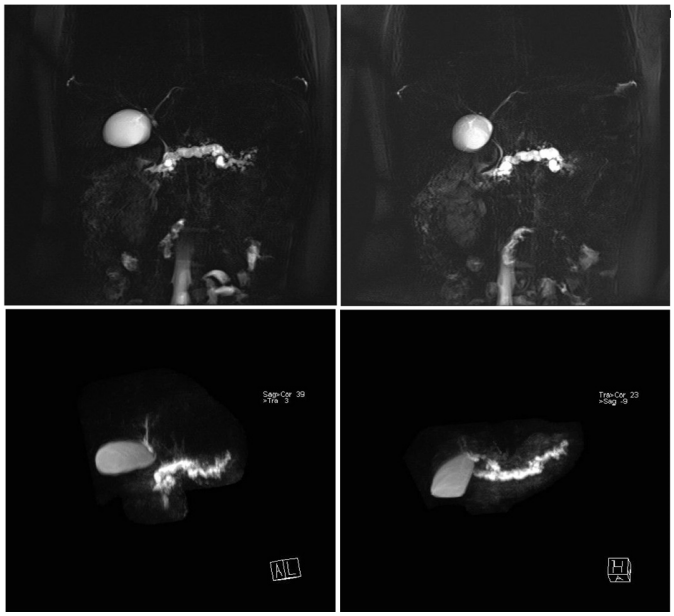

Figure 1. MRCP T2-weighted three-dimensional (3D) cholangiogram reconstruction showing significant dilation and tortuosity of MPD, possibility of multiple small cystic structures around pancreatic duct, small filling defects within pancreatic duct, a hypointense capsule-like rim around it and Stricture of the distal CBD within the pancreatic head. (MRCP: Magnetic resonance cholangiopancreatography, MPD: main pancreatic duct, CBD: Common bile duct). Although most of these features are not specific for P-AIP, the presence of more than one should raise the suspicion for P-AIP.

rheumatoid arthritis.

She was referred to our center for further investigations. She had ongoing epigastric pain and nausea and elevated amylase and lipase serum level. Her total IgG were within normal range. All autoantibodies were in normal ranges and genetic evaluations about common mutation in familial pancreatitis were negative.

Liver ultrasound scan on presentation showed dilated extrahepatic bile ducts and non- homogenous pancreas with hyperechoic foci's. Also there was dilation of pancreatic duct at the level of the pancreatic head and body.

MRCP confirmed marked intra-and extrahepatic cholangiopathy with smooth inflammatory stricture of the distal bile duct within the pancreatic head and neck. There was rim-like enhancement around the uncinate process of the pancreas as well as smooth stricturing and dilatation of the pancreatic duct suggestive of AIP as a potential etiology (Figure 1).

Endoscopic retrograde cholangiopancreatography (ERCP) was performed to assess patency of pancreaticobiliary system and ampullary endoscopic biopsies that revealed no positive findings.

Based on clinical and paraclinical findings, AIP diagnosed. The patient was commenced on full dose of 40mg prednisolone OD (1 mg/kg/day) for two weeks followed by tapering down to 5mg/day and then 2.5mg /day over three month, after this period, prednisolone was stopped.

In post-treatment follow up the patient has been asymptomatic since then with no episode of pancreatitis and no complication of pancreatic insufficiency, such as diabetes, until now.

DISCUSSION

Diagnosis of AIP in children can be established based on the combination of clinical symptoms at presentation and imaging findings. Therefore, some investigators have suggested using a combination of laboratory testing, imaging, histological findings, association to other autoimmune disease, and response to corticosteroid treatment to establish the diagnosis.

In the retrospective analysis of the literature involving 38 children with AIP, abdominal pain was most common symptom following by obstructive jaundice and weight loss [6]. Nausea and vomiting, fatigue and abnormal stool were other less frequents clinical symptoms patients.

Although there is no specific imaging finding in AIP, but combination of radiological finding with the clinical symptoms can be helpful in diagnosis of AIP. Transabdominal ultrasound scan (USS) is often the first available imaging modality. Focal and global pancreas enlargement are most common findings in USS respectively [6].Other USS findings includes bile duct dilation and liver fatty changes. Our findings in USS were non-homogenous pancreas with hypoechoic foci's and dilation of pancreatic duct.

Magnetic resonance cholangiopancreatography (MRCP) finding also included of focal and global enlargement that presented with hypointence areas on T1-weghted images. Other common findings are irregularities of the main pancreatic duct and a narrowed CBD (stricture or tapering). Main pancreatic duct irregularities and distal CBD narrowing are nonspecific findings and might also be seen in patients with CP or biliopancreatic diseases of any other etiology or even in primary sclerosing cholangitis type 1 [6, 7].

A capsule-like rim enhancement of the pancreas was infrequent in children but its occurrence appears to be pathognomonic for the disease [6]. A pancreatic head enlargement or nonencapsulated mass lesions were other frequent findings. It should be note that lymphoma, pancreatoblastoma or solid pseudopapillar epithelial neoplasms that are often encapsulated and express cystic and solid components should be ruled out after a focal pancreas enhancement.

Increased serum IgG4 is very suggestive of AIP in adults, but IgG4 serology and immunostaining is rarely positive in children with AIP. This marker is of limited value as only 22% of the children had IgG4 levels above the upper limits of normal (ULN). In comparison, about 65% of adult AIP type 1 and 25% of adult AIP type 2 patients have elevated IgG4 levels. This suggests that children may more commonly follow the disease presentation of AIP type 2 or may have a distinct AIP pattern that may not necessarily fall into either category.

A diagnosis of AIP can be confirmed by the histopathological identification of pathognomonic and well-described features of an autoinflammatory process in the pancreas tissue specimen. Most common findings in AIP patients are a combination of lymphoplasmacytic infiltration, pancreatic fibrosis, and granulocyte infiltration of the pancreatic duct epithelium and lumen (also called granulocytic epithelial lesion). Frequent finding of granulocytic epithelial lesion in pediatric pancreas tissue specimen would be consistent with type 2 AIP as per adult criteria.

However, because of the increased clinical recognition of AIP as well as a growing familiarity with AIP-type imaging findings, adult gastroenterologists often times waive a histopathological diagnosis and start a trial with corticosteroids that itself is used as a diagnostic criterion to confirm the diagnosis of AIP [3,4].

Although granulocytic epithelial lesion is more frequently found in the pancreas of children with AIP compared with adults. If adult AIP criteria were applied to the pediatric AIP population, children would most likely be classified as having type 2 AIP. However, as histology of pancreas biopsies in children with AIP have not yet been validated in relation to the disease phenotype [3], we cannot at this point exclude the possibility that AIP in children may yet follow a distinct disease pattern.

In our patient, the diagnosis of AIP was based on the MRCP and ERCP imaging finding, although negative autoimmune antibodies and normal levels of immunoglobulins especially IgG and subclass 4 were obtained. These results are similar to those in the patients presented by Toomey et al.[8] who diagnosed AIP based on the abdominal US and CT imaging features of a solid mass in the pancreatic body despite normal serum IgG and elevated CA19-9 levels and patient presented by Refaat et al. [9] who diagnosed AIP based on the MR and MRCP.

We agreed with Finkelberg et al. [10] who state that diagnosis may be made in the absence of diagnostic laboratory finding

A total of 27% of children and 10–20% of adults [5] diagnosed with AIP have concurrent immune/inflammatory diseases, especially ulcerative colitis. It remains to be elucidated whether the pancreas inflammation drives the intestinal inflammation in these cases or whether the intestinal inflammation spreads to the pancreas.

The therapeutic approach to AIP has significantly evolved over time. In the early days, surgery was undertaken to confirm the nature of a pancreatic mass and/or drain an obstructed bile duct. ERCP was used for CBD stenting in children with obstructive jaundice.

The current standard treatment for AIP is corticosteroid therapy [11]. The corticosteroid induction dose used in children (1–1.5 mg/kg/day) as captured in our study was higher than the recommended dose (0.6–1 mg/kg/day) in adults with AIP. Of the children, 92% including our patient clinically improved with corticosteroids. Interestingly, 17% of the AIP patients had disease resolution without any treatment. Although corticosteroid use seems beneficial in the short term in adults with AIP, it remains unclear whether it has an impact on the long-term outcome of patients. In the absence of any comparative or outcome studies in children, we believe that a time-limited corticosteroid treatment courses to treat the acute symptoms of pancreatitis, which may also prevent long-term complications of pancreatic insufficiency, is justified. As in the one-year follow up, our patient did not suffer from pancreatic insufficiency and complications such as diabetes and son on.

However, further studies are needed to determine whether the advantages of steroid therapy outbalance the potential side effects of this therapy, particularly in children. In this regard, it will be helpful to obtain control imaging about 3 months after starting corticosteroids to evaluate for normalization of the pancreatic imaging findings, confirming the diagnosis of AIP.

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