Relapsing Autoimmune Pancreatitis in a 14-Year-Old Girl

Masato Takase, Takehide Imai and Fumiko Nozaki

Department of Pediatrics, Graduate School of Medicine, Nippon Medical School Department of Pediatrics, Nippon Medical School Tama Nagayama Hospital

Abstract

We present a case of acute pancreatitis in a 14-year-old girl which fulfilled the diagnostic criteria of autoimmune pancreatitis (AIP) and responded to corticosteroid therapy. Imaging studies revealed that the main pancreatic duct was narrow in the head of the pancreas but had been dilated in the body at an earlier stage. The pancreatitis recurred twice when the prednisolone dose was reduced to 10 mg or less but responded each time to an increased dose and has been kept under control with low-dose prednisolone therapy for 3 years since onset. Repeated magnetic resonance cholangiopancreatography during steroid therapy revealed an improvement of the narrowing of the main pancreatic duct in the head and dilation of the duct in the body. AIP in younger patients has distinct clinical features, such as presentation with epigastralgia, back pain without jaundice, and elevated serum amylase levels. The serum level of IgG4 is rarely increased in young patients, indicating a different disease mechanism than for cases in elderly patients. Given the excellent response of this condition to steroid therapy, AIP should be considered even in young children and adolescents when the diagnosis of idiopathic pancreatitis is suggested.

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Key words: pancreatitis, adolescent, hypergammaglobulinemia, magnetic resonance imaging, prednisolone

Introduction

The causes of pancreatitis in children include trauma, structural anomalies, multisystem disease, drugs, toxins, infections, heredity, and metabolic disorders¹⁻⁴. However, in 8% to 23% of patients, no cause is found, and the pancreatitis is considered idiopathic²³. Autoimmune pancreatitis (AIP) is a type of chronic pancreatitis with a suspected autoimmune etiology which was first proposed by Yoshida et al. in 1995⁵. Although AIP occurs most often in elderly men, it can occur in younger persons⁶. Here, we report a case of AIP in a 14-year-old girl which was diagnosed according to the criteria proposed by the Japan Pancreas Society⁷ and was successfully treated with corticosteroid therapy.

Case Report

A 14-year-old girl visited a local physician complaining of acute abdominal pain in the right upper quadrant region since the previous day. Body temperature was slightly elevated (37.5° C), and a

Correspondence to Masato Takase, Department of Pediatrics, Nippon Medical School Tama Nagayama Hospital, 1–7– 1 Nagayama, Tama, Tokyo 206–8512, Japan

E-mail: mtakase@nms.ac.jp

Journal Website (http://www.nms.ac.jp/jnms/)

blood examination revealed a white blood cell count of $9,500/\mu L$ with moderate elevation of C-reactive protein. The symptoms did not improve with a 4-day course of an antibiotic. Upon a follow-up visit to the physician, the patient was found to have an elevated serum amylase level of 690 IU/L (normal range: 43-116 IU/L) and was referred to our hospital on the 7th day of the illness. At the time of her first visit, examinations revealed mild spontaneous pain and tenderness in the epigastrium and an elevated serum amylase level (454 IU/L). On ultrasonography (US), the pancreas was slightly enlarged from the body to tail with relatively homogeneous low-echoic area surroundings with some scattered high echoic spots inside, and the main pancreatic duct was enlarged (4.5 mm) in the body. With a tentative diagnosis of mild acute pancreatitis, the patient was followed-up on an outpatient basis and treated with camostat mesilate and scopolamine butylbromide, which appeared to provide some relief of the symptoms. Serum amylase levels were 150 to 239 IU/L during the follow-up period, and repeated US showed some improvement. However, because the increasingly severe abdominal pain prevented sleep, the patient was finally admitted to our hospital 6 weeks later. She had a history of egg and milk allergies during early childhood and had persistent, untreated mild atopic dermatitis. There was no history of preceding medication, blunt trauma, or foreign travel. No family history of pancreatitis or hepatobiliary disease was noted.

On admission, vital signs were normal, and physical examination of the head, neck, and chest yielded normal findings. Although there was no enlargement of the liver or spleen, severe tenderness was present in the epigastrium.

Laboratory Findings and Imaging Studies

Blood examination revealed a slightly elevated serum amylase level of 288 IU/L; other pancreatic enzymes, including lipase, elastase-1, trypsin, and pancreatic phospholipase A2, were significantly elevated. Total protein was elevated to 8.7 g/dL with an increased gamma globulin fraction of 23.1% (normal range: 9.0%–18.3%). Serum IgG was elevated to 2,104 mg/dL (normal range: 870–1,700 mg/dL),

although serum IgG4, at 54.1 mg/dL, was not elevated (normal range: 4.8–105 mg/dL). Anti-nuclear antibodies, anti-DNA antibodies, antiribonucleoprotein antibodies, anti-Sjögren syndrome (SS)-A/Ro antibodies, anti-SS-B/La antibodies, antismooth muscle antibodies, and rheumatoid factor were negative, and C3, C4, and CH50 were normal. Tumor marker CA 19-9 was not detected.

Computed tomography (CT) and magnetic resonance imaging (MRI) of the abdomen revealed enlargement of the head of the pancreas, and magnetic resonance cholangiopancreatography (MRCP) showed an enlarged main pancreatic duct in the body of the pancreas. However, the main pancreatic duct in the distal portion appeared to be narrow, indicative of mass-forming pancreatitis. Although the common bile duct was not dilated, the duct within the head of the pancreas was not visualized (**Fig. 1**).

Clinical Course

The abdominal pain and serum amylase level did not improve through fasting or intravenous administration of a proteolytic enzyme inhibitor (Fig. 2). Because of the high serum levels of gamma globulin and IgG and the narrowing of the main pancreatic duct indicated by imaging studies, we began treatment with intravenous prednisolone (30 mg/day) during the second week. The symptoms gradually subsided, and the serum amylase level had normalized at 70 IU/L by the fourth day. The serum level of IgG had decreased to 1,811 mg/dL after 2 weeks and had further decreased to 1,436 mg/dL after 4 weeks. The dosage of oral prednisolone was maintained at 30 mg/day for 4 weeks and then was tapered to 20 mg/day. The symptoms resolved completely, and the serum amylase level remained within normal limits until the patient was discharged from the hospital after 50 days of admission. Followup MRCP shortly after discharge revealed a normal, smooth main pancreatic duct from head to tail (Fig. 3a).

However, abdominal pain recurred when the prednisolone dose was reduced to alternate-day administration of 10 mg. A blood examination revealed an increased serum amylase level (723 IU/



Fig. 1 Images of CT and MRCP on admission a: CT performed the day after admission revealed an enlarged pancreas head (arrow).

b: MRCP performed 2 days after admission revealed marked dilation of the main pancreatic duct in the body and irregular narrowing in the head (**arrowhead**). Although the common bile duct was not dilated, the duct was not visualized within the head of the pancreas.

L), which indicated the recurrence of pancreatitis. The patient was re-admitted and given intravenous prednisolone at a dosage of 30 mg/day, which led to immediate relief of symptoms and normalization of the serum amylase level (70 IU/L). She was discharged after 2 weeks. MRCP performed shortly after discharge revealed slight widening of the main pancreatic duct in the body (**Fig. 3b**). On follow-up visits, the dose of prednisolone was tapered more slowly to maintain the normal serum amylase level and the absence of symptoms.

When the dose of prednisolone was reduced to 10 mg/day after 4 months of follow-up, the patient complained of discomfort after meals. A blood examination revealed that the serum amylase level had risen again to its highest level (1,319 IU/L).

Serum IgG (1,413 mg/dL) was not elevated, and no anti-nuclear antibodies were found. The patient was admitted for the third time. Intravenous prednisolone at a dosage of 30 mg/day with fasting and administration of a proteolytic enzyme inhibitor led to prompt improvement of symptoms and laboratory findings. During this admission, abdominal US revealed nonhomogeneous а intrapancreatic echo, and MRCP showed irregular narrowing of the main pancreatic duct in the head (Fig. 3c). Endoscopic retrograde cholangiopancreatography (ERCP) performed shortly after symptom relief confirmed narrowing of the main pancreatic duct in the head and tail (Fig. 3d).

The patient continued to be treated with prednisolone at a dosage of at least 10 mg/day for the next 2 years. Although she had not been readmitted to the hospital, she had several bouts of epigastralgia and back pain along with a slight increase in serum amylase level (up to 300 IU/L). However, the symptoms have been controlled by increasing the prednisolone dose (up to 20 mg/day) for 2 to 3 days.

Discussion

Pancreatitis is uncommon in children. However, its diagnosis and management remain difficult, given its multiple causes, the limited effectiveness of treatments, and the potential for severe and persistent morbidity.

Autoimmune pancreatitis (AIP) is a recently identified clinical entity with а suspected autoimmune etiology⁸. Since the concept of AIP was first proposed by Yoshida et al⁵ in 1995, many cases have been reported worldwide, and AIP has become widely accepted as a distinct form of pancreatitis^{9,10}. This condition occurs most often in elderly men, although the reason remains unknown. Thus, the present case of an adolescent girl with AIP is unusual. Our literature search for autoimmune pancreatitis yielded only a few cases in children and adolescents¹¹⁻¹⁴. Indeed, the clinical presentation of the present case differed from that of typical AIP, which can include mild or absent epigastric pain or back pain, obstructive jaundice, and normal or



Fig. 2 Clinical course indicating the trend of serum amylase levels along with the dose of prednisolone



Fig. 3 Images of MRCP and ERCP during the course of the illness

a: Follow-up MRCP performed shortly after discharge from the first admission revealed a normal smooth main pancreatic duct from head to tail. The distal portion of the common bile duct was also better visualized.

b: MRCP performed shortly after discharge from the second admission revealed slight dilation of the main pancreatic duct in the body.

c: MRCP performed after the third admission indicates irregular narrowing of the main pancreatic duct in the head with an almost normal caliber in the body.

d: ERCP performed shortly after discharge from the third admission confirming irregular narrowing of the main pancreatic duct within the head.

slightly increased serum levels of amylase. Thus, similar cases of pancreatitis in young patients might be misdiagnosed as idiopathic pancreatitis and remain untreated with corticosteroids or could result in unnecessary surgeries.

Clinical diagnostic criteria for autoimmune pancreatitis were proposed by the Japan Pancreas Society in 2002 and revised in 20067. There are 3 criteria: 1) diffuse or segmental narrowing of the main pancreatic duct with an irregular wall and diffuse or localized enlargement of the pancreas on imaging studies, such as abdominal US, CT, and MRI; 2) high serum gamma globulin, IgG, or IgG4, or the presence of autoantibodies, such as antinuclear antibodies and rheumatoid factor; and 3) marked interlobular fibrosis and prominent infiltration of lymphocytes and plasma cells in the periductal area, occasionally with lymphoid follicles in the pancreas. The diagnosis of AIP is established when criterion 1 and criterion 2 or 3 or both are fulfilled and after malignant diseases, such as pancreatic or biliary cancers, have been excluded. Our patient fulfilled criteria 1 and 2 and responded well to corticosteroid therapy. Resolution or marked improvement of pancreatic and extrapancreatic lesions with steroid therapy is a specific finding not seen in other pancreatic diseases. Therefore, response to a steroid therapy has been included as a diagnostic criterion for AIP in guidelines proposed by the Mayo Clinic⁹ and by the Korean Society of Pancreatobiliary Diseases¹⁰. Considering the difficulty of performing biopsies in children, a trial of steroid therapy may be justified so that the chance to diagnose AIP is not missed in children with pancreatitis of unknown cause.

A recent study by Kamisawa et al⁶ of AIP in young patients found clinical features differing from those in middle-aged or elderly patients. The group of 6 adult patients (3 men and 3 women) younger than 40 years (range: 28 to 37 years) was compared with a group of 58 patients (46 men and 12 women) older than 40 years in whom AIP was diagnosed in the same period. They found that young patients were more likely to have abdominal pain as an initial symptom (100% vs. 43%; p<0.05) and were more likely to show serum amylase elevations (83% vs. 40%; p<0.05). Although the difference was not statistically significant, obstructive jaundice was detected in only 1 young patient (17%) but was detected in 59% of middle-aged or elderly patients. Our patient shared clinical features with the younger adults with AIP.

Elevation of serum IgG4, which is the most sensitive marker of AIP, was not observed in our case. However, the absence of elevated serum IgG4 might be another feature of AIP in young patients. Three of 4 reported cases in children and adolescents did not show elevated serum IgG4 levels¹¹⁻¹⁴, as was seen in a German series of 4 cases of AIP in young patients¹⁵. Because the mechanism of AIP remains obscure and AIP may consist of heterogeneous subtypes, AIP in young patients or that occurring as acute pancreatitis might be another subtype.

Considering that a substantial percentage of cases of chronic pancreatitis remain idiopathic, it is quite natural to assume that some of these cases might actually be AIP. In fact, a French prospective study that intended to identify autoimmune stigmata in 60 consecutive adult patients with idiopathic chronic pancreatitis found 10 patients with autoimmune diseases¹⁶. A combination of clinical and biochemical autoimmune variables were used to identify 24 patients (40%) with at least 1 autoimmune marker or disease. Another group from Poland investigated a series of 41 consecutive cases of asymptomatic chronic pancreatitis in patients younger than 18 years and found that 4 patients had an autoimmune disease and that 17 patients (41.5%) had at least 1 autoimmune marker¹⁷. Although the effectiveness of steroid treatment has not been confirmed in these patients, the assessment of autoimmune causes is clearly needed to determine the cause of pancreatitis in children and adolescents.

Given the positive response and good long-term prognosis of this condition when treated with corticosteroids¹⁸, AIP should always be considered in the differential diagnosis of pancreatitis in children and adolescents.

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