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Autoimmune Pancreatitis in Hungary: A Multicenter Nationwide Study

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Key Words

Autoimmune pancreatitis · Granulocytic epithelial lesion · Idiopathic duct centric pancreatitis · IgG4 · Lymphoplasmacytic sclerosing pancreatitis · Steroid therapy

Abstract

Background: To date, most cases of autoimmune pancreatitis (AIP) have been reported from Japan. The aim of the present study was to assess the clinical features and management of AIP cases in Hungary. ***Methods:*** The demographics, clinical presentation, laboratory and imaging findings, extrapancreatic involvement, treatment response and recurrence were evaluated in the first 17 patients diagnosed with AIP in Hungary. ***Results:*** The mean age at presentation was 42.7 years (range: 16–74); 47% of the patients were women. New-onset mild abdominal pain (76%), weight loss (41%) and jaundice (41%) were the most common symptoms, with inflammatory bowel disease being the most frequent (36%) extrapancreatic manifestation. Diffuse pancreatic swelling was seen in 7 patients (41%) and a focal pancreatic mass in 8 (47%). Endoscopic retrograde cholangiopancreatography revealed pancreatic duct strictures in all study patients. The serum IgG4 level at presentation was elevated in 62% of the 8 patients in whom it was measured. All the percutaneous core biopsies (5 patients) and surgical specimens (2 patients), and 2 of the 4 biopsies of the papilla of Vater revealed the typical characteristic findings of AIP: a diffuse lymphoplasmacytic infiltration, marked interstitial fibrosis and obliterative phlebitis. Immunostaining indicated IgG4-positive plasma cells in 62% of the 8 patients in whom it was performed. Granulocytic epithelial lesions (GEL) were present in 3 patients. The patients without GELs were older (mean age 59 years), while those with GEL were younger (mean age 34 years), and 2 of 3 were female and had ulcerative colitis. A complete response to steroid treatment was achieved in all 15 patients. Because of the suspicion of a pancreatic tumor, 2 patients with focal AIP underwent partial pancreatectomy. One patient relapsed, but responded to azathioprine. ***Conclusions:*** This first Hungarian series has confirmed several previously reported findings on AIP. AIP with GEL was relatively frequent among our patients: these patients tended to be younger than in earlier studies and displayed a female preponderance with a high coincidence of ulcerative colitis. Performance of a percutaneous biopsy is strongly recommended. The response to immunosuppressive therapy was excellent.

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Introduction

Autoimmune pancreatitis (AIP) is a special type of chronic pancreatitis (CP), which displays clinical, serological, radiological and in particular histological features that are clearly distinct from other types of CP, such as alcoholic, hereditary and paraduodenal CP. The characteristics of the disease have been described in detail in excellent reviews [1–5]. Most cases of AIP have been reported from Japan. Although AIP is currently more often recognized in Europe [6–10], the number of European clinical reports to date is low and no study is available from central Eastern Europe.

AIP predominantly affects males over the age of 50 years. Recent studies demonstrated that two distinct histological patterns of AIP exist [9–11]. The histological pattern in type-1 AIP, referred to as lymphoplasmacytic sclerosing pancreatitis (LPSP), is characterized by a periductal lymphoplasmacytic infiltration, storiform fibrosis, obliterative phlebitis and IgG4-positive plasma cells. LPSP corresponds to the Japanese description of AIP [12] and is thought to be the pancreatic manifestation of an IgG4-associated systemic disease [13]. IgG4-related systemic diseases may involve the biliary tree, salivary glands, retroperitoneum, stomach, lymph nodes and kidneys. An extrapancreatic manifestation is seen in about 40–50% of the cases. The histopathological pattern in type-2 AIP is known as idiopathic duct centric CP (IDCP) or granulocyte epithelial lesion (GEL)-positive pancreatitis, which resembles the European description of duct-destructive CP [9, 14].

The aim of the present prospective multicenter study was to assess the clinical features, laboratory and imaging findings, extrapancreatic involvement, treatment response and recurrence of AIP cases in Hungary.

Patients and Methods

Between May 1, 2008, and October 30, 2010, patients diagnosed with AIP in Hungarian Gastroenterological Centers were enrolled in our study. The diagnosis of type-1 AIP was established according to the HISORt criteria [15], while type-2 AIP was distinguished on the basis of the presence of the histological criterion GEL [9, 11]. Patient data were retrieved from medical documentation and follow-up data and were collected prospectively. All the patients participated in the continuous clinical follow-up. Treatment was carried out in the course of everyday clinical practice. All the patients underwent abdominal CT. In the event of obstructive jaundice, therapeutic endoscopic retrograde cholangiopancreatography (ERCP) was performed, and a polyethylene stent was inserted into the bile duct if optimization of bile flow was necessary. Depending on the local possibilities, magnetic resonance cholangiopancreatography and/or diagnostic ERCP were performed to visualize abnormalities in the biliopancreatic region. When focal enlargement of the pancreas was detected, ultrasound-guided fine-needle aspiration or core biopsy was carried out. If the papilla of Vater was swollen, the biopsy was taken by means of duodenoscopy. The diagnosis of type-1 AIP was supported by the presence of duct centric lymphoplasmacytic infiltration, storiform fibrosis, obliterative phlebitis and >10 IgG4-positive plasma cells per high power field. IgG4 immunohistochemical staining was performed with monoclonal anti-human IgG4 antibody (Invitrogen, Carlsbad, Calif., USA). IgG4 seronegativity and the presence of GEL were diagnostic of type-2 AIP. The level of serum IgG4 was measured in the available samples (Binding Site Ltd., Birmingham, UK).

After the diagnosis of AIP had been established, the patients were treated with 30–40 mg prednisolone per day for 1–2 months. After 4 weeks, response was assessed. Response to therapy was defined as complete when a symptomatic improvement and complete resolution of the imaging abnormalities were seen. In the event of an adequate therapeutic response, the steroid dose was tapered to 5 mg/week. If a relapse occurred during the decrease in the steroid dose, the level of prednisolone was increased during the acute flare-up, and azathioprine at a dose of 1–2 mg/kg body weight per day was added for long-term immunosuppression. In patients who had undergone stent implantation in the bile duct, ERCP examination was repeated after steroid therapy; in case of improvement of the stenosis, the stent was removed.

Data were statistically evaluated using the χ^2 test. Values of $p < 0.05$ were accepted as statistically significant.

Table 1. Clinical presentation of the AIP patients

Age, years	42.7 (16–74)
Female, n	8 (47%)
Abdominal pain, n	13 (76%)
Weight loss, n	7 (41%)
Obstructive jaundice, n	7 (41%)
Diabetes mellitus, n	2 (12%)
Autoimmune disorder, n	8 (47%)

Results

AIP was diagnosed in 17 patients during the study period. At the time of establishment of the diagnosis, the median age of the patients was 42.7 years (range: 16–74); 47% of them were women (table 1). The most frequent symptoms were mild abdominal pain, a moderate weight loss and obstructive jaundice. In 5 patients (29%), inflammatory bowel disease had been diagnosed earlier, 2 patients had type-1 diabetes mellitus and another patient had sialadenitis. The serum levels of pancreatic enzymes