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Autoimmune Pancreatitis and Treatment Approaches with Case Reports

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ABSTRACT

Objective: In this study, we aimed to review retrospectively the data of 10 patient who were treated and followed-up in our clinic and to review the current approaches in the diagnosis and treatment of autoimmune pancreatitis (AIP).

Material and Methods: We reviewed 10 patients retrospectively who were operated on and had the diagnosis of AIP histopathologically in the Ege University School of Medicine Department of General Surgery.

Results: Between June 2001-November 2010, 10 patients who were diagnosed as AIP were examined retrospectively. Radiologically, a pancreatic mass was found in the pancreatic head with ultrasound in 7 (70%) of 10 patients and suspicious lesions were identified in the head of the pancreas in 3 (30%) patients. All patients were operated on in our clinic with the preliminary diagnosis of pancreatic head tumor; 8 patients underwent Whipple's procedure, 1 patient underwent pylorus preserving pancreaticoduodenectomy, and in 1 patient an exploratory pancreatic biopsy (frozen section) was carried out.

Conclusion: Autoimmune pancreatitis is a disease with increasing incidence and characterized by lymphoplasmocytic cell infiltration and fibrosis. Patients with a pancreatic mass, if there is an autoimmune disease or chronic pancreatitis suspected in the detailed history, it is necessary to evaluate patients in terms of AIP serologically to protect the patients from an incoorectng diagnosis and morbidity of surgery.

Key Words: Autoimmune pancreatitis, diagnosis, treatment approaches

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Introduction

Chronic pancreatitis is an inflammatory condition that can lead to exocrine and endocrine dysfunction and permanent structural changes occur. Compared with acute pancreatitis, chronic pancreatitis is a progressive disease. Chronic pancreatitis is characterized by mononuclear cell infiltration and focal fibrosis morphologically.

Autoimmune pancreatitis was first defined by Sarles et al. (1) in 1961 as a form of chronic pancreatitis in a patient with hypergammaglobulinemia. In the following years, cases were reported with different names (lymphoplasmocytic sclerosing pancreatitis, lobulocentric AIP, ductocentric AIP), but the first definition of AIP as a form of chronic pancreatitis was made by Yoshida et al (2).

Although the frequency of occurrence has increased due to the technological advances in ultrasonography, computed tomography and magnetic resonance imaging, AIP is currently still a rare disease and is difficult to distinguish from pancreatitis and pancreatic cancer in the early period (3). Nishimori et al. (4) has reported the incidence of AIP as 8.2/1000000. The patient's presenting symptoms are; abdominal pain, anorexia and jaundice. In a subgroup of patients, AIP is determined during the investigation of other autoimmune diseases (Sjogren's, etc.). High levels of IgG4 and several other autoantibodies are detected serologically in many of the patients.

The histopathological findings of AIP are characterized by the periductal localization of predominantly CD4-positive T cells, IgG4-positive plasma cells, storiform fibrosis with acinar cell atrophy frequently resulting in the stenosis of the main pancreatic duct, and obliterative fibrosis which is called lymphoplasmacytic sclerosing pancreatitis (5). Corticosteroid therapy can be effective sometimes. However, operative procedures can be carried out with the pre-diagnosis of pancreatic cancer in some of the patients (6). In this study, we aimed to review retrospectively the 10 patients who were treated and followed-up in our clinic and examine the current approaches in the diagnosis and treatment in AIP.

Material and Methods

We reviewed 10 AIP patients who were operated in Ege University School of Medicine Department of General Surgery. Preoperative abdominal ultrasonography and computed tomography examinations were performed in all of the patients. Serum CA 19-9 levels were evaluated in 8 of 10 patients. All operations were performed with the preliminary diagnosis of pancreatic cancer.

Results

Between June 2001-November 2010, 10 patients who were diagnosed as AIP were examined retrospectively. Of the 10 patients, 7 patients were men and 3 were women. The

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mean age was 52 (30-71). Of the 10 patients, seven patients (70%) presented with jaundice, 2 (20%) with elevated serum liver enzymes and 1 (10%) with the complaint of abdominal pain. Serum IgG4 or other autoantibody levels were not examined in any of the patients because AIP was not suspected..

Radiologically, by using ultrasonography, a pancreatic mass was identified in the head of the pancreas in 7 (70%) of the 10 patients and suspicious lesions were identified in the head of the pancreas in 3 (30%) patients. Computed tomography scan revealed a mass lesion in all of the patients in the head of the pancreas and common bile duct dilatation was identified in 8 (80%) of the patients. CA 19-9 levels were analyzed in 8 patients and high levels (112-309) were determined in 5 (63%) of the patients (Table 1). Endoscopic retrograde cholangiopancreatography (ERCP) was performed in 5 of the patients. ERCP findings consistent with pancreatic head tumor were identified and a plastic stent was inserted. In 1 patient with jaundice, the second part of the duodenum could not be entered due to external compression of the duodenum and percutaneous biliary drainage was performed.

All patients were operated on in our clinic with the preliminary diagnosis of pancreatic head tumor; 8 patients underwent Whipple's procedure, 1 patient underwent pylorus -preserving pancreaticoduodenectomy, and in 1 patient an exploratory pancreatic biopsy (frozen section) was performed. In this patient as the frozen section revealed no malignity, no further surgical procedure was performed. In the histopathological examination, lymphoplasmacytoid cell infiltration was found only within the pancreas in 5 patients, both in pancreas and papilla in 4 of the patients and pancreas, papilla and common bile duct in 1 of the patients. In addition to lymphoplasmacytoid cell infiltration, fibrosis was observed in 5 of the patients. Excised and examined lymph nodes did not reveal any signs of malignancy and have been reported as reactive lymph nodes. The largest lymph node diameter was reported as 25 mm. There was no patient with a history of alcohol.

Discussion

Autoimmune pancreatitis is a disease which has an increasing frequency of diagnosis and is characterized by lymphoplasmacytoid cell infiltration and fibrosis. For the correct diagnosis, an expert multidisciplinary team approach is required which includes a gastroenterologist, general surgeon and pathologist. Diagnostic criteria are according to the Japanese guideline which were published in 2006; irregular wall structure in the main pancreatic duct with diffuse or segmental narrowing, diffuse or localized enlargement of the pancreas radiologically, high levels of serum gamma globulin, IgG4 or presence of rheumatoid factor or antinuclear antibody, interlobular fibrosis and periductal prominent lymphocyte and plasma cell infiltration (Table 2) (7). Serum IgG4 levels constitute 3-6% of the total level of IgG and high levels are detected in atopic dermatitis, parasitic disease and pemphigus vulgaris (6). IgG4 is not a specific marker for the diagnosis of AIP serologically (6). AIP's coincidence with other autoimmune diseases varies according to geographical regions and it has been reported that AIP is associated with other autoimmune diseases in 35-56% of Japanese patients and 16% in European patients (8).

Autoimmune pancreatitis frequently causes the appearance of a mass in the pancreas in radiological tests and it is confused with cancer of the pancreas. In case of suspicion of AIP by clinical features and detailed history of the patient, serum IgG4 and other autoantibodies levels should be obtained (9). Since pathological confirmation of autoimmune pancreatitis is difficult, corticosteroid therapy can be used as a diagnostic tool in patients whose clinical and laboratory findings are strongly suggestive of autoimmune pancreatitis. If the diagnosis of AIP could not be confirmed serologically and/or complete resolution of the pancreatic mass is not determined after steroid treatment, tissue biopsy must be obtained (9).

Cross-sectional imaging studies usually shows diffuse enlargement and ERCP reveals a long attenuated segment of the pancreatic duct in autoimmune pancreatits. However none of these findings were detected in our patients and operations were planned due to a pancreatic mass in our study. CA 19-9

Table 1. Clinical characteristics of 28 patients with autoimmune chronic pancreatitis

Sex	Age	Diabetes	CT	CEA (ng/mL)	Ca 19-9 (u/mL)	Operation
Male	67	+	PM	-	-	Whipple
Male	50	-	PM	2.6	57	Whipple
Male	35	+	PM	3.5	772	Whipple
Male	34	+	PM	4.2	14.9	IOBx
Male	55	-	PM	3.1	13.9	Whipple
Male	63	+	PM	-	39.3	Whipple
Male	53	-	PM	4.0	113	PPPD
Female	64	-	PM	3.2	154	Whipple
Female	71	-	PM	-	-	Whipple
Female	30	-	PM	1.7	392	Whipple

CT: Computed tomography, PM: Pancreatic mass, IOBx: Intraoperative biopsy, PPPD: Pylorus preserving pancreaticoduodenectomy

Table 2. Clinical diagnostic criteria of autoimmune pancreatitis (According to Japenese guideline, 2006)

A. Diffuse or segmental narrowing of the main pancreatic duct with irregular wall and diffuse or localized enlargement of the pancreas by imaging studies, such as abdominal ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI)

B. High serum γ-globulin, IgG, or IgG4, or the presence of autoantibodies, such as antinuclear antibodies and rheumatoid factor

C. Marked interlobular fibrosis and prominent infiltration of lymphocytes and plasma cells in the periductal area, occasionally with lymphoid follicles in the pancreas

Diagnosis of autoimmune pancreatitis is established when criterion 1, together with criterion 2 and/or 3, are fulfilled. However, it is necessary to exclude malignant diseases such as pancreatic or biliary cancers

level measured in 5 of 8 patients and high-value determination is interesting. IgG4 and other autoantibodies levels were not evaluated as we did not suspect the diagnosis of AIP in our patients preoperatively. The patients were diagnosed as AIP histologically. Patients were out of follow-up in the postoperative period so we cannot give any information about the follow-up period. None of our patients had steroid therapy preoperatively as AIP was not suspected preoperatively. For these reasons, patients with pancreatic mass with a detailed history of an autoimmune disease, history of alcohol consumption or chronic pancreatitis should be suspected as AIP and patients should be investigated serologically to protect the patients from being misdiagnosed as having pancreatic cancer and having the morbidity of surgery. Although the number of cases in this study is inadequate, it can be seen that AIP is often confused with pancreatic cancer and patients can be misdirected to surgery.

Conclusion

Autoimmune pancreatitis is a disease with increasing incidence and is characterized by r lymphoplasmocytic cell infiltration and fibrosis. Patients with a pancreatic mass, if suspected of an autoimmune disease or chronic pancreatitis in the detailed history, it is necessary to evaluate patients in terms of AIP serologically to protect the patients from the wrong diagnosis and morbidity of surgery.

Conflict of Interest

No conflict of interest was declared by the authors.

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