JOP. J Pancreas (Online) 2005; 6(6):609-611.

PANCREAS NEWS

Diagnosis of Autoimmune Pancreatitis: Clinical and Histological Assessment

Raffaele Pezzilli, Lorenzo Fantini

Department of Internal Medicine, Sant'Orsola-Malpighi Hospital. Bologna, Italy

Autoimmune pancreatitis has received increased attention from clinical and basic researchers in the last few years because it is a field of chronic benign pancreatic diseases in which notable advances have been made. The number of cases of this disease which have been diagnosed has increased in the past few years [1, 2]. Recently, a new paper has been published by French authors whose efforts were addressed towards evaluating the presence of autoimmune pancreatitis in patients with so-called "idiopathic" pancreatitis [3]. The aim of this study was to identify autoimmune stigmata in the three forms of idiopathic chronic pancreatitis: pseudotumoral, duct-destructive and classic chronic pancreatitis. All patients who underwent exploration for idiopathic chronic pancreatitis were enrolled in the study. The data recorded were examination by an internal medicine specialist, autoantibody and immunoglobulin screening, and pancreatic duct imaging. The authors included 60 patients: 11 had pseudotumoral chronic pancreatitis, 27 had duct-destructive disease, and the remaining 22 had an classic chronic pancreatitis. There were no significant differences among the three types with regard to sex ratio, age, frequency of episodes of acute pancreatitis, or obstructive jaundice. Pancreatic calcifications were seen only in 81% of the cases with the classic form of chronic pancreatitis. Autoimmune disease was present in ten patients and was associated with ulcerative colitis in five patients, primary sclerosing cholangitis in two patients, and Sjögren's syndrome, Hashimoto's thyroiditis and Graves' disease in one patient each. Autoimmune diseases were present in 36% of the patients with pseudotumoral form, in 19% of those with duct-destructive form and in 5% only of those with the classic form. IG4 levels were increased in 2 of 6 in the pseudotumoral, 1 of 9 in the duct-destructive, and in none of the 12 patients in the classic group. Combining clinical and biochemical autoimmune parameters, 40% of the patients had at least 1 autoimmune marker of the disease. What importance do the results of this study indicate? Clinical or biochemical autoimmune stigmata are present in 40% of European patients with idiopathic chronic pancreatitis and, in these patients, we need to search for the presence of an autoimmune mechanism which sustains chronic benign disease.

From a therapeutic point of view, steroids are a well-known efficacious treatment of autoimmune pancreatitis, as demonstrated by a recent paper from Japan [4] which demonstrated, in two cases of autoimmune pancreatitis, the regression not only of the inflammatory infiltration but also of pancreatic fibrosis after a short course of oral steroid therapy. Furthermore, long term steroid treatment [5] has been demonstrated to be a good therapeutic approach in 21 patients having autoimmune pancreatitis with a rate of

19% of clinical recurrence of the disease. Other therapeutic strategies have appeared in recent years such as treatment with ursodeoxycholic acid [6]. However, we need to define the histological pattern of the disease in order to cure it. In fact, from a pathological point of view autoimmune pancreatitis is characterized by diffuse or focal pancreatic swelling with a narrowing of the pancreatic duct and/or common bile duct. The histological hallmark of this type of pancreatitis is lymphoplasmacytic infiltration, especially concentrated on the pancreatic ducts [7, 8, 9]. At present, we also have the possibility of classifying the various pathological aspects of autoimmune pancreatitis, such as the Mayo Clinic classification [10] which identified two histologic groups: lymphoplasmacytic sclerosing pancreatitis and idiopathic duct-centric chronic pancreatitis. The latter classification comes from Europe [11]. These authors found that granulocytic epithelial lesions predominantly occur in a subset of patients who are younger, more commonly have ulcerative colitis and Crohn's disease, and seem to have fewer recurrences than patients without granulocytic epithelial lesions. Another important finding of this paper is that pancreatic biopsy material is helpful in establishing the diagnosis of autoimmune pancreatitis. In line with this previous paper is the paper from the U.S. [12]. In this paper, the authors identified 16 patients with autoimmune pancreatitis, initially evaluated by EUS-guided FNAB, eleven of whom subsequently underwent a pancreaticoduodenectomy. They compared this group of patients to a cohort of EUS-guided aspirates from 16 patients with ductal carcinoma of the pancreas and 19 patients with chronic pancreatitis. In all 51 cases, they semiquantitatively evaluated presence and atypia of ductal cells, presence and cellularity of stromal fragments, and inflammatory cells, type and distribution. Fifty percent of the autoimmune cases presented as obstructive jaundice. EUS and CT scan showed mass lesions in 10 and 6 cases, respectively. There were three false-positive cytologic diagnoses, an adenocarcinoma, a solid-pseudopapillary tumor and a mucinous neoplasm. Ductal epithelium was inconspicuous and was seen in 6 cases. The FNAB samples showed background lymphocytes in three autoimmune cases and this feature was absent in the control cohort. Stromal fragments with embedded lymphocytes were seen in 37.5% of autoimmune cases, in only 12.5% of the patients with adenocarcinoma and in none of those with pancreatitis. The cellularity of stromal fragments was significantly higher in autoimmune pancreatitis than in the control group. The main finding of this study is that the presence of stromal fragments of high cellularity with a lymphoid infiltrate in conjunction with clinical and radiological findings could potentially both establish the diagnosis of autoimmune pancreatitis and exclude the presence of a carcinoma, thus preventing pancreatic resection and rendering a specific medical treatment of patients with autoimmune disease possible.

Keywords Autoimmune Diseases; Histology; Pancreatic Neoplasms; Pancreatitis; Steroids; Ultrasonography; Ursodeoxycholic Acid

Correspondence
Raffaele Pezzilli
Dipartimento di Medicina Interna
Ospedale Sant'Orsola-Malpighi
Via Massarenti, 9
40138 Bologna
Italy
Phone: +39-051.636.4148
Fax:+39-051.636.4148
E-mail: pezzilli@aosp.bo.it

References

1. Pearson RK, Longnecker DS, Chari ST, Smyrk TC, Okazaki K, Frulloni L, Cavallini G. Controversies in clinical pancreatology: autoimmune pancreatitis: does it exist? Pancreas 2003; 27:1-13. [PMID 12826899]

2. Kim KP, Kim MH, Lee SS, Seo DW, Lee SK. Autoimmune pancreatitis: it may be a worldwide entity. Gastroenterology 2004; 126:1214. [PMID 15057766]

3. Nahon Uzan K, Levy P, O'Toole D, Belmatoug N, Vullierme MP, Couvelard A, et al. Is idiopathic chronic pancreatitis an autoimmune disease? Clin Gastroenterol Hepatol 2005; 3:903-9. [PMID 16234029]

4. Song MH, Kim MH, Lee SK, Seo DW, Lee SS, Han J, et al. Regression of pancreatic fibrosis after steroid therapy in patients with autoimmune chronic pancreatitis. Pancreas 2005; 30:83-6. [PMID 15632704]

5. Wakabayashi T, Kawaura Y, Satomura Y, Watanabe H, Motoo Y, Sawabu N. Long-term prognosis of duct-narrowing chronic pancreatitis: strategy for steroid treatment. Pancreas 2005; 30:31-9. [PMID 15632697]

6. Tsubakio K, Kiriyama K, Matsushima N, Taniguchi M, Shizusawa T, Katoh T, et al. Autoimmune pancreatitis successfully treated with ursodeoxycholic acid. Intern Med 2002; 41:1142-6. [PMID 12521203]

7. Ectors N, Maillet B, Aerts R, Geboes K, Donner A, Borchard F, et al. Non-alcoholic duct destructive chronic pancreatitis. Gut 1997; 41:263-8. [PMID 9301509]

8. Klimstra DS, Conlon KC, Adsay NV. Lymphoplasmacytic sclerosing pancreatitis with pseudotumor formation. Pathol Case Rev 2001; 6:94-9.

9. Kawaguchi K, Koike M, Tsuruta K, Okamoto A, Tabata I, Fujita N. Lymphoplasmacytic sclerosing pancreatitis with cholangitis: a variant of primary sclerosing cholangitis extensively involving pancreas. Hum Pathol 1991; 22:387-95. [PMID 2050373]

10. Notohara K, Burgart LJ, Yadav D, Chari S, Smyrk TC. Idiopathic chronic pancreatitis with periductal lymphoplasmacytic infiltration: clinicopathologic features of 35 cases. Am J Surg Pathol 2003; 27:1119-27. [PMID 12883244]

11. Zamboni G, Luttges J, Capelli P, Frulloni L, Cavallini G, Pederzoli P, et al. Histopathological features of diagnostic and clinical relevance in autoimmune pancreatitis: a study on 53 resection specimens and 9 biopsy specimens. Virchows Arch 2004; 445:552-63. [PMID 15517359]

12. Deshpande V, Mino-Kenudson M, Brugge WR, Pitman MB, Castillo CF, Warshaw AL, Lauwers GY. Endoscopic ultrasound guided fine needle aspiration biopsy of autoimmune pancreatitis: diagnostic criteria and pitfalls. Am J Surg Pathol 2005; 29:1464-71. [PMID 16224213]