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Alimentary Tract

Autoimmune pancreatitis and inflammatory bowel disease: Case series and review of the literature

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ABSTRACT

Background: An association between autoimmune pancreatitis (AIP) and inflammatory bowel disease (IBD) has been documented, but its clinical significance remains unclear.
Aims: Characterize the particular phenotypes of IBD and AIP in patients with both diseases (IBD-AIP).
Methods: Retrospective study of patients with IBD-AIP followed at our IBD referral centre and literature search to identify previous reports of IBD-AIP patients.
Results: We found 5 cases of IBD-AIP in our records and 5 prior studies reporting 47 additional IBD-AIP patients. A combined analysis showed that most IBD-AIP patients were young males with ulcerative colitis, usually extensive, and that in all Crohn's disease cases, the colon was involved. IBD severity was heterogeneous across studies, ranging from mild disease to severe disease requiring colectomy. The most frequent type of AIP was idiopathic duct-centric pancreatitis (type 2) and it most often occurred after the diagnosis of IBD. AIP presentation and treatment were similar to those in the general population.
Conclusions: AIP occurs rarely with IBD; in the other way around, up to 1/3 of AIP patients, especially type 2, may have concomitant IBD. IBD-AIP patients are usually males presenting extensive colitis. More data are needed on the impact of AIP, if any, in IBD course.

1. Introduction

Inflammatory bowel disease (IBD) is a systemic disorder that often affects organs outside the gastrointestinal tract. Extra-intestinal manifestations (EIMs) are present in 6–47% of IBD patients [1,2] and are occasionally even more debilitating than the intestinal disease itself. Some EIMs may parallel the intestinal activity, while others run an independent course of bowel disease [1,3]. Furthermore, certain EIMs seem to be associated with particular forms or phenotypes of IBD. For instance, patients with primary sclerosing cholangitis (PSC) and IBD more frequently have extensive colonic involvement, quiescent or mild disease activity, and predominantly right-sided distribution when compared to IBD patients without PSC [4].

Autoimmune pancreatitis (AIP) is a benign fibroinflammatory disease of the pancreas first reported in 1961. It acquired the name, "autoimmune", later in 1995, because it was associated with hypergammaglobulinemia, was accompanied by autoantibodies and responded dramatically to corticosteroids (CS) [5]. On imaging, the pancreatic inflammatory process is classically seen as a sausage-shaped pancreas with an irregular narrowing of the pancreatic duct [6].

Two types of AIP were subsequently recognized according to clinical profile, histopathological pattern and natural history; namely, type 1 AIP or lymphoplasmacytic sclerosing pancreatitis (LPSP) and type 2 AIP or idiopathic duct-centric pancreatitis (IDCP) [5]. Box 1 summarizes the typical features of each type of AIP. Type 1 AIP occurs more often in elderly men, who present with painless jaundice, and it is the pancreatic manifestation of IgG4-systemic related disease. For this reason it is common to find in type 1 AIP patients an increase in IgG4 serum levels, and extrapancreatic symptoms due to the involvement of other organs (OOI) [7]. In type 2 AIP, by contrast, patients are younger, there is no gender predominance and the most common presentation is acute pancreatitis (AP). Type 2 is a disease limited to the pancreas [6]; however it is notable that 15–30% of patients have concomitant IBD, most often ulcerative colitis (UC) [5,8–12]. This high prevalence is in striking contrast to the 0.4% prevalence of UC in the general population [13]. These observations suggest a possible association between IBD and

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Box 1: Comparison between the clinical profiles of type 1 and type 2 autoimmune pancreatitis.

	Type 1 AIP (lymphoplasmacytic sclerosing pancreatitis)	Type 2 AIP (idiopathic duct-centric pancreatitis)
Demographics	7th decade of life 3:1 male predominance	5th decade of life Equal gender distribution
Clinical presentation	Painless jaundice	AP and abdominal pain Painless jaundice
Association with IBD	Rare	May be present in up to 1/3 of patients
Pancreatic imaging	Diffuse pancreatic parenchymal enlargement with delayed enhancement Long or multiple strictures of the main pancreatic duct	
IgG4 elevation	Increased in 2/3 of patients	Usually normal
Pancreatic histology	Periductal lymphoplasmacytic infiltration Obliterative phlebitis Storiform fibrosis Increased IgG4 positive cells (>10 per HPF)	Granuylocytic infiltration of duct wall Absent or scant IgG4 positive cells (0–10 per HPF)
Involvement of other organs	Proximal biliary tree, salivary glands, kidney and retroperitoneal fibrosis	No
Response to steroids	Excellent	
Recurrence	Common	Rare

AP, acute pancreatitis; HPF, high power field.

AIP, and several authors have proposed that AIP may be an EIM of IBD [14–18].

Despite this suggested association, the connection between IBD and AIP is still not widely recognized, nor is the relationship between the clinical course and features of the IBD and those of the AIP [8,11,14]. Hence, we have sought to describe the characteristics of both IBD and AIP when they occur together in the IBD-AIP syndrome.

2. Materials and methods

2.1. Case series

The study was conducted at The Mount Sinai Hospital, an IBD tertiary referral centre. We performed a search for patients with diagnosis of IBD and AIP who attended The Mount Sinai Hospital, between January 2003 and April 2015, using the Mount Sinai Crohn's and Colitis Registry. This Registry was created in 2013 to prospectively enrol IBD patients who attended Mount Sinai Hospital. In addition, patients prior to 2013 were retrospectively searched using Data Warehouse that contains all electronic medical records (EMR), since 2003 and 2010 for inpatient and outpatient diagnosis, respectively. IBD was searched using IBD related ICD-9 codes (Crohn's disease – 555.0, 555.1, 555.2, 555.9; and ulcerative colitis – 556.0, 556.1, 556.2, 556.3, 556.5, 556.6, 556.9). To identify patients with AIP we searched the Registry and Data Warehouse for pancreas related ICD-9 codes: 577.0 acute pancreatitis, 577.1 chronic pancreatitis, 577.2 cyst and pseudocyst of pancreas, 577.8 other specified diseases of pancreas and 577.9 unspecified disease of pancreas. A total of 120 patients were found to have IBD and pancreatic disorders. The EMR of each case, including clinical notes, imaging and pathology records, was reviewed for the following keywords: "auto-immune pancreatitis", "sausage pancreas", "lymphoplasmacytic infiltration", "granulocytic infiltration", "granulocyte epithelial lesions", "storiform fibrosis", "obliterative phlebitis", "IgG4 positive cells" and "IgG4".

An IBD diagnosis required the standard histological criteria in a patient with a compatible clinical history, endoscopic or surgical features and/or imaging abnormalities [19,20]. The diagnosis of AIP was based on the International consensus diagnostic criteria (ICDC) criteria, specifically, imaging, serology, histology, OOI and response to CS [21]. Additionally, other causes of pancreatitis were excluded, namely gallstones, heavy alcohol intake, medications, hypercalcemia, hypertriglyceridemia and anatomical abnormalities. Genetic testing for cystic fibrosis transmembrane conductance regulator (CFTR), serine protease inhibitor Kazal type 1 (SPINK1) or trypsinogen cationic genes (PRSS1), was not available.

A retrospective analysis of EMR was conducted to identify demographic data, clinical presentation, serological markers, histological findings, imaging features and therapy for AIP and IBD. Particularly, for IBD, we registered disease distribution, disease activity, change in disease extension and IBD-related medical and surgical therapies, hospitalizations and death. Regarding AIP, we extracted clinical presentation including OOI, complications, hospitalizations and recurrences; IgG4; imaging studies; and medical, surgical, and endoscopic treatments. AIP recurrence was defined as the recurrence of symptoms and/or radiological manifestations. Follow-up time for AIP and IBD was defined as the period between diagnosis and the last available outpatient or inpatient record.

The Mount Sinai Medical Centre Institutional Review Board approved the study protocol.

2.2. Literature review of published cases

A literature query was conducted to identify studies reporting epidemiology, phenotype and treatment of IBD and/or AIP in IBD-AIP patients. A broad PubMed/Medline search was performed from inception to 31st of July 2015 using the following keywords: autoimmune pancreatitis, type 1 autoimmune pancreatitis, lymphoplasmacytic sclerosing pancreatitis, type 2 autoimmune pancreatitis or idiopathic duct-centric pancreatitis combined with inflammatory bowel disease, Crohn's disease, ulcerative colitis or IBD. Additionally, we hand-searched the references of the most recent (≥2010) review papers published on AIP to identify additional relevant titles.

3. Results

3.1. Case series

In total, our search identified 8 IBD patients who were suspected of having AIP. Three cases were excluded because they were lost to follow-up before diagnostic investigation was completed (IgG4 serum levels, imaging showing resolution of pancreatic abnormalities after steroid therapy and/or investigation of OOI). Hence, our study population comprised 5 adult patients with IBD and a diagnosis of AIP (Tables 1 and 2). The median IBD follow-up time was 72 months, ranging from 11 to 108 months.

3.2. IBD phenotype in patients with AIP

All 5 IBD patients had UC, established by the combination of clinical, endoscopic and histological features. Four were male and the median age at IBD diagnosis was 33 years (Table 1). None of the patients had a family history of IBD or other autoimmune conditions. At presentation, UC was left-sided in 2 patients and involved the entire colon in a third case. Disease spread proximally from proctitis to pancolitis in a fourth patient. In the fifth case disease extension was not available. Two patients had PSC, diagnosed at the same time as UC. The diagnosis of PSC was based