Autoimmune Pancreatitis-What is Known, What Needs to be Known

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Introduction

Autoimmune Pancreatitis (AIP) is an emerging clinical entity found in 4.6-6 percent of patients with chronic pancreatitis [1]. It was first reported as an idiopathic chronic pancreatitis associated with hypergammaglobulinemia by Sarles et al. [2], with the term AIP being first used by Yoshida et al. [3]. In 2003, Notohara and coworkers described two types of AIP: Lymphoplasmacytic Sclerosing Pancreatitis (LSP) termed “type 1 AIP” and idiopathic duct-centric chronic pancreatitis with Granulocyte Epithelial Lesion (GEL) termed “type 2 AIP” [1] (Table 1).

It is the histopathological findings observed on pancreatic biopsies that seem to separate AIP into two discrete disease entities. In type 1 AIP there is abundant infiltration of Immunoglobulin G4 (IgG4) positive plasma with CD4+ and CD8+ lymphocytes. Storiform fibrosis (fibrosis in a swirling pattern) around main and interlobular ducts that spares the duct epithelium and lumen is a typical feature. Similar infiltration is observed near the pancreatic veins leading to obliterative phlebitis [4]. This type of AIP often presents in men in the 5-6th decade of life as painless jaundice mimicking acute pancreatitis, and has a low relapse rate. Histologically, there is neutrophilic infiltration and granulocytic lesions observed further in disease course and in more severe presentations [7].

Type 2 AIP is considered to be a solely pancreatic disease predominantly seen in younger Caucasian patients with no sex predilection. It usually presents as obstructive jaundice with abdominal pain mimicking acute pancreatitis, and has a low relapse rate. Histologically, there is neutrophilic infiltration and granulocytic lesions that damage the duct epithelium itself, but no obliterative phlebitis or IgG4-positive plasma cells. It tends to be associated with inflammatory bowel disease, but no other extra-pancreatic manifestations have been observed with this type of AIP [6].

Both types of AIP are known to respond quickly to systemic steroids [8] and these agents can be used for both initial attacks and first or second relapses. However, further relapses (as is typical of type 1 AIP), can be treated with immunomodulator drugs such as azathioprine, mycophenolate mofetil [9,10] or cyclophosphamide. In patients intolerant to steroids or immunomodulatory therapy, Rituximab, the B cell depleting monoclonal antibody against CD-20 [11], has demonstrated efficacy.

AIP is evidenced as a diffusely enlarged pancreas demonstrating a sausage–like appearance on computed tomography (Figure 1). MRI of our patient with AIP type 1 demonstrates diffuse swelling of pancreatic body and tail which resolved with a 2 month course of steroids (Figure 1A and 1B).

Diagnostic Criteria for AIP

There have been several criteria proposed for diagnosis of AIP.

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Received November 23, 2013; Accepted November 26, 2013; Published December 03, 2013

Citation: Kapila A, Ghably J, Krishnaswamy G (2013) Autoimmune Pancreatitis-What is Known, What Needs to be Known. Pancreat Disord Ther 3: e130. doi:10.4172/2165-7092.1000e130

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in the process of evolution, as is the disease. Further investigations are needed to determine the exact pathophysiology of this condition. Hopefully with deeper insight into the origins of the disease and studies performed on larger pools of diagnosed patients, more exact diagnostic criteria can be developed and more comprehensive treatment protocols can be recommended.

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| Feature                      | Type 1 AIP                          | Type 2 AIP                          |
|------------------------------|-------------------------------------|-------------------------------------|
| Demographic Factors          |                                     |                                     |
| Age                          | Elderly                             | Young adult-middle age              |
| Sex                          | Male=Female                         | Male=Female                         |
| Clinical Factors             |                                     |                                     |
| Presentation                 | Painless obstructive jaundice       | Painless jaundice or acute pancreatitis |
| Serum IgG4                   | Elevated                            | Normal                              |
| Extra-Pancreatic             | Various other organ involvement     | Inflammatory bowel disease          |
| Response to steroids         | Excellent                           | Excellent                           |
| Recurrence                   | Common                              | Rare                                |
| Pathologic features          |                                     |                                     |
| Infiltrating cells/Lymphocytes and IgG+plasma cells/Neutrophil | | |
| Fibrosis                     | Storiform pattern                   | None                                |
| Obliterative phlebitis/Common | Sparing                             | Destruction and obliteration        |

AIP-Autoimmune Pancreatitis

Table 1: Differences between 2 subtypes of AIP.

The first diagnostic criteria was proposed by The Japanese Pancreas Society in 2000, and subsequently revised in 2006 and 2011. Another criteria that had been proposed is the HISORt-(Histology, Imaging, Serology, Other organ involvement and Response to glucocorticoids) by Mayo clinic in 2006. Another diagnostic approach was taken by the International Consensus Diagnostic Criteria (ICDC) proposed in 2011 [12]. ICDC uses five features to diagnose AIP: Pancreatic imaging, serology, other organ involvement, histology and immunostaining and optional criteria for steroid responsiveness [13]. Each feature is characterized as level 1 or 2 depending on the diagnostic reliability. The ICDC criteria had 98.4% sensitivity and 100% specificity whereas the Japanese Pancreas Society Classification had 84.4% sensitivity and 100% specificity for diagnosis of AIP [13].

Still Unfolding

As this is a relatively rare condition that has only become identified in recent decades, there is still much that needs to be learned. The role of IgG, as a bystander or as a participant is still controversial. No clear genetic markers or antibodies can be identified as markers of the disease. Different diagnostic criteria are proposed but they are still...