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

Aaysha Kapila1, Jack Ghably1 and Guha Krishnaswamy2*

1Department of Internal Medicine, East Tennessee State University, Johnson City, TN, USA
2James H Quillen VA Medical Center, Johnson City, TN, USA

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 (LSPS) 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 pancreatic cancer and patients experience frequent relapses despite treatment. Very soon, patients diagnosed with AIP were being reported with extra-pancreatic manifestations such as biliary, retroperitoneal, renal, and salivary gland disease. Similar pathologic features were found in affected organs, and type 1 AIP began to be recognized as the pancreatic manifestation of a systemic autoimmune syndrome now known as IgG4-related disease [5].

The exact pathogenic mechanisms behind type 1 AIP remain unclear. Although some mechanisms have been proposed, no genetic markers have been confirmed as susceptibility factors and no specific antibodies have been identified. It has been observed that T helper 2 (Th2) cells predominate over T helper 1 (Th1) cells predominate over T helper 2 (Th2) cells in the peripheral blood while Th2 cells dominate over Th1 within the involved organs, and circulating levels of regulatory T cells (T-reg) are increased while Th1 cytokines are decreased. This has led some researchers to suggest a multiphasic mechanism by which cytokines produced by Th1 cells induce naïve T-reg cells are decreased. This has led some researchers to suggest a multiphasic mechanism by which cytokines produced by Th1 cells induce the maturation and proliferation of local B cells. During this phase, the overproduction of IL-10 leads to expansion of IgG4-producing plasma cells and the elevated levels of transforming growth factor beta induce fibrosis [6]. As Th2 and Th-reg cells are known to contribute to pathogenesis of allergic disorders, this would explain the elevated serum IgE and peripheral eosinophilia often observed in these patients [6].

Both types of AIP are known to respond quickly to systemic glucocorticoid therapy. 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.
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.

References