

When Pathology Marries Clinics: the Honolulu Consensus Document and the Guidelines of the International Association of Pancreatology on Autoimmune Pancreatitis

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Autoimmune pancreatitis has been extensively described in reports from the Far East, Europe and the USA. The diagnosis was based on the presence of four main criteria related to histological findings, radiological features, other organ involvement, and clinical and instrumental response to steroid therapy [1, 2, 3, 4, 5, 6]. As defined in these terms, the diagnostic approach and general management of autoimmune pancreatitis seems to be quite “linear” but the subject presents a lot a controversial aspects, namely, concerning histopathology (microscopic and macroscopic) as well as clinical findings.

Large series of patients observed in Japan have been identified as affected by autoimmune pancreatitis based on distinct clinical features, without the need for histology to confirm this diagnosis. On the contrary, detailed descriptions of at least two histopathological patterns (i.e. lymphoplasmacytic sclerosing pancreatitis without granulocytic epithelial lesions and idiopathic duct-centric pancreatitis with granulocytic epithelial lesions) have been reported in Europe and the USA to define the presence of autoimmune pancreatitis, independently from the clinical phenotypes. In particular, the presence of granulocytic epithelial lesions associated with idiopathic duct-centric pancreatitis is considered a hallmark of autoimmune pancreatitis in Europe while lymphoplasmacytic sclerosing pancreatitis represents the basis for the diagnosis in the USA. Accordingly, the identification of two types of autoimmune pancreatitis has been proposed: type 1 autoimmune pancreatitis (histopathological pattern of lymphoplasmacytic sclerosing pancreatitis) and type 2 autoimmune

pancreatitis (pattern of idiopathic duct-centric pancreatitis). Differences in serology and clinical presentation between these two forms are also described. Type 1 autoimmune pancreatitis presents high levels of serum IgG4 levels and nonspecific autoantibodies, prevalence of male gender, more advanced age, frequent involvement of other organs (salivary glands, biliary tract, kidney, lung, retroperitoneum) and possible relapse of the disease after steroid treatment. On the contrary, type 2 autoimmune pancreatitis does not have definite serologic autoimmune markers, the affected patients are younger without any gender difference, only the colon may be involved (ulcerative colitis) and relapse after steroids is infrequent. In Japan, only type 1 autoimmune pancreatitis is considered an autoimmune disorder with the identification of a distinct clinicopathological entity, called “IgG4-related sclerosing disease” [7]. In addition, this entity was recently considered a partial expression of a lymphoproliferative disease called “IgG4 positive multiorgan lymphoproliferative syndrome”, a more complex, multiorgan disorder with the possible inclusion of Mikulicz’s disease, Küttner tumors, inflammatory pseudotumors (of the lung, liver, and breast), mediastinal fibrosis and autoimmune hypophysitis [8]. The subject is even more complicated by the fact that autoimmune pancreatitis may be macroscopically focal or diffuse [9]. Focal autoimmune pancreatitis is characterized by segmental involvement of the parenchyma with the possibility of a low-density mass being present at imaging. The Italian proposal for the diagnosis of autoimmune pancreatitis, which is different from that suggested in Japan and the USA, is based on the instrumental distinction between the focal and the diffuse forms of the disease [10]. In the case of focal autoimmune pancreatitis, particularly in the presence of a low-density pancreatic mass, the clinical challenge is to exclude pancreatic cancer and correctly diagnose the autoimmune pancreatitis whereas diffuse autoimmune pancreatitis may be confused with acute

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pancreatitis or with cholangiocarcinoma when jaundice secondary to a common bile duct stricture is present. Recently, a group of international experts proposed a consensus document [11] with the aim of overcoming controversy on the histopathology and clinics of autoimmune pancreatitis. In summary, the main statements of this article are: a) autoimmune pancreatitis has unique histopathological features which allow it to be differentiated from other forms of chronic pancreatitis; b) there are definite histologic criteria for lymphoplasmacytic sclerosing pancreatitis and idiopathic duct-centric pancreatitis; c) the two histopathologically distinct types of autoimmune pancreatitis are associated with distinct clinical profiles; d) the clinical phenotypes associated with the histopathological patterns of lymphoplasmacytic sclerosing pancreatitis and idiopathic duct-centric pancreatitis should be referred to as type 1 and type 2 autoimmune pancreatitis, respectively. Starting from this consensus document, the same group of experts has more recently published a comprehensive article [12] which represents the guidelines of the International Association of Pancreatology on autoimmune pancreatitis. The distinction of autoimmune pancreatitis into types was confirmed but the diagnosis of type 1 and type 2 autoimmune pancreatitis was categorized as definite or probable in relation to the diagnostic reliability of each of the five cardinal features of autoimmune pancreatitis, namely, imaging of the pancreatic parenchyma and duct, serology, other organ involvement, pancreatic histology, and an optional criterion of response to steroid therapy. In addition, a new category was identified (autoimmune pancreatitis not otherwise specified) for some cases in which the distinction between the two subtypes of autoimmune pancreatitis was not possible. These articles are a praiseworthy and successful attempt of promoting worldwide recognition and optimal management of autoimmune pancreatitis in clinical practice.

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