

## PANCREAS NEWS

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### Autoimmune Pancreatitis: An Autonomous Disease or a Single Entity in a Complex Puzzle of a Multi-Organ Disorder?

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Autoimmune pancreatitis is a relatively uncommon, non-alcohol-related form of chronic pancreatitis which has received increasing attention in recent years. In fact, autoimmune pancreatitis represents a "hot topic" in pancreatology, as witnessed by the many reports and extensive recently published reviews [1, 2, 3, 4, 5, 6]. The first report of the disease which dates back to 1961 documented patients who suffered from chronic inflammatory sclerosis of the pancreas associated with hypergammaglobulinemia [7], even if the possibility of an autoimmune mechanism in the pathogenesis of chronic pancreatitis had been already stressed in 1959 [8]. After three decades of single case reports of only limited series of patients with non-alcoholic chronic pancreatitis predominantly associated with chronic inflammatory bowel diseases or sclerosing cholangitis, in 1991, Kawaguchi *et al.* [9] gave the first detailed description of this special type of pancreatitis and called it "lymphoplasmacytic sclerosing pancreatitis". In 1995, Yoshida *et al.*, reporting a relatively large series from Japan, coined the term autoimmune pancreatitis [10]. Autoimmune pancreatitis is currently recognized as a distinct clinical entity worldwide, identified as a chronic inflammatory condition of the pancreas in which an autoimmune mechanism is involved [6, 11]. High serum IgG4 concentrations have been identified as its distinguishing characteristic and as a marker of autoimmunity as well as of disease activity [12]. The presence of concomitant disorders in other organs together with autoimmune pancreatitis was mainly intended as the proof that the spectrum disease of the pancreas was comparable to that of the bile ducts, liver, colon or salivary glands [13].

Recently, Kamisawa *et al.* [14] have proposed a novel clinicopathological entity, named "IgG4-related sclerosing disease" (IgG4-RSC) which was based on the histological and immunohistochemical examination of various organs of patients affected by autoimmune pancreatitis. This systemic disease may present different clinical manifestations related to the frequent involvement not only of the pancreas (autoimmune pancreatitis), but also of the bile duct (sclerosing cholangitis, cholecystitis), the salivary gland (sialoadenitis), the retroperitoneum (fibrosis), the kidney (tubulointerstitial nephritis), the lung (interstitial pneumonia), the prostate (prostatitis) and the lymphnodes (lymphadenopathy). Extensive IgG4-positive plasma-cells and T-lymphocyte infiltration of various organs constitutes a common characteristics of this disease. Most of the affected patients present autoimmune pancreatitis at the moment of diagnosis, but pancreatic involvement can be absent [15]; in general, more than two organs are affected, but it is possible to find it in only one of them. The disease occurs more frequently in older men and responds well to corticosteroid treatment. Beginning with the analysis of Japanese patients with IgG4-related disorders, Masaoki *et al.* [16] have very recently proposed an extension of the IgG4-RSC syndromic complex into a new clinical entity characterized by hyper-IgG4 gammaglobulinemia and IgG4-positive plasma-cell infiltration into the tissue, this being considered an expression of a lymphoproliferative disease ("IgG4-positive multiorgan lymphoproliferative syndrome"; IgG4+MOLPS). In addition to the pathologies considered within the IgG4-RSC group, this syndrome also includes Mikulicz's disease, Küttner's tumors, inflammatory pseudotumors (of the lung, liver, and breast), mediastinal fibrosis and autoimmune hypophysitis. IgG4+MOLPS should be differentiated from Sjögren's syndrome, which presents a similar organ distribution but different clinical-epidemiological-histopathological features and a different autoantibody pattern. Other rare conditions such as multicentric Castelman's disease and idiopathic plasmacytic lymphadenopathy should also be considered in differential diagnosis.

**Key words** Autoimmune Diseases; Biological Markers; Diagnosis, Differential; Epidemiology

**Abbreviations** IgG4+MOLPS: IgG4-positive multiorgan lymphoproliferative syndrome; IgG4-RSC: IgG4-related sclerosing disease

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These recent papers, based on solid epidemiological, clinical and histopathological features, raise strongly doubts as to autoimmune pancreatitis being considered an autonomous entity and support its classification as a single entity within a multiorgan syndromic complex. At the moment, this working hypothesis may be considered well-grounded only in Eastern populations; studies from Western countries are necessary to confirm this fascinating scenario.

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