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Case Report

Autoimmune Hepatitis-Autoimmune Pancreatitis Association: A Case Report

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Abstract

Introduction: Autoimmune diseases are the consequence of an immune response against the organism itself, abnormally considered as foreign. We report the clinical case of a patient with an association of two entities: auto-immune pancreatitis and auto-immune hepatitis.

Observation: Mr A.H, 56 years old, with no notable pathological history. He presented in consultation for cholestatic jaundice with intermittent epigastralgia aggravated by meals. Clinical examination revealed conjunctival jaundice with no other abnormalities. The biological work-up revealed cytolysis: ASAT 112, ALAT 30, cholestasis: GGT 745, PAL 838, BT 9. Lipasemia > 3 times the normal value. Abdominal ultrasound returned without abnormality. CT scan (Figure 2) showed a diffuse sausage-like hypertrophy of the pancreas with disappearance of the lobular aspect with a hyporehauled peri-glandular halo without a clearly detectable mass, suggesting a probably autoimmune pancreatitis. The liver was normal, no dilatation of the bile ducts was found. viral serologies (HAV, HCV, HBV) were negative. The serum IgG >1.1 times the upper normal value, the anti-smooth muscle Ac > 1/80. Anatomopathological study of the liver biopsy was compatible with autoimmune hepatitis (Figure 1). The diagnosis of autoimmune hepatitis was retained (diagnostic score = 7) and autoimmune pancreatitis. The patient was put on corticosteroid therapy + azathioprine with good evolution, he was kept under regular follow up.

Conclusion: The diagnosis of AIP and AIH is based on multiples criteria's and arguments, and the association of these two entities is not usual. However, this association can be evoked in a known patient with autoimmune pancreatitis, who presents symptoms or biological abnormalities suspecting an autoimmune hepatitis.

Keywords: *Autoimmune Hepatitis; Autoimmune Pancreatitis*

Introduction

Autoimmune diseases are the consequence of an immune response against the organism itself, abnormally considered as foreign. They are characterized by an inflammatory state and cellular and tissue damage that can be severe. Autoimmune pancreatitis (AIP) and autoimmune hepatitis (AIH) are examples of autoimmune damage to the digestive tract. However, their association remains rare.

We report the clinical case of a patient with an association of these two entities.

Observation

Mr A.H, 56 years old, with no notable pathological history. He presented in consultation for cholestatic jaundice with intermittent epigastralgia aggravated by meals. Clinical examination revealed conjunctival jaundice with no other abnormalities. The biological work-up revealed cytolysis: ASAT 112, ALAT 30, cholestasis: GGT 745, PAL 838, BT 9. Lipasemia > 3 times the normal value. Abdominal ultrasound returned without abnormality. CT scan (Figure 2) showed a diffuse sausage-like hypertrophy of the pancreas with disappearance of the lobular aspect with a hyporehauled peri-glandular halo without a clearly detectable mass, suggesting a probably autoimmune pancreatitis. The liver was normal, no dilatation of the bile ducts was found. viral serologies (HAV, HCV, HBV) were negative. The serum IgG > 1.1 times the upper normal value, the anti-smooth muscle Ac > 1/80. Anatomopathological study of the liver biopsy was compatible with autoimmune hepatitis (Figure 1). The diagnosis of autoimmune hepatitis was retained (diagnostic score = 7) and autoimmune pancreatitis. The patient was put on corticosteroid therapy + azathioprine with good evolution, he was kept under regular follow up.

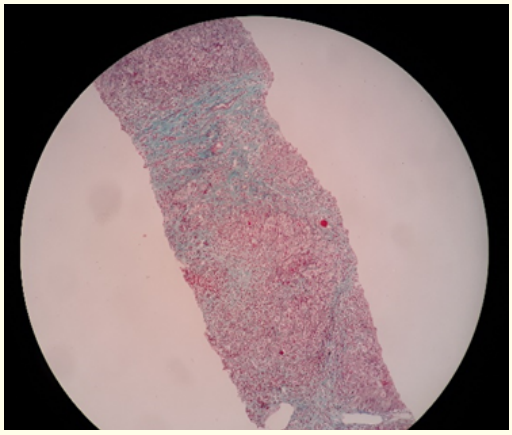

Figure 1: *Liver biopsy showing autoimmune hepatitis.*

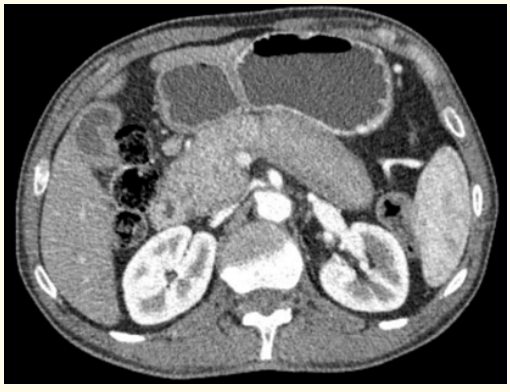

Figure 2: *CT scan showing autoimmune pancreatitis.*

Discussion

Autoimmune pancreatitis

Autoimmune pancreatitis (AIP) is a particular and rare form of chronic pancreatitis (less than 6% of cases) whose incidence is recently increasing [1]. The diagnosis is based on clinical, biological, radiological and histological criteria [2].

Taking into account its clinical, biological, morphological and histological manifestations, we can distinguish 2 types of autoimmune pancreatitis: Type 1 with IgG4 which is often associated with other organ involvement. It is also called lymphoplasmacytic pancreatitis. And Type 2, otherwise known as chronic idiopathic autoimmune pancreatitis, which is not associated with autoimmune involvement of other organs. The IgG4 level is usually normal in type 2 [3,4].

Inflammation in autoimmune pancreatitis may involve the entire pancreas, but when it is focal, the head of the pancreas is most frequently affected.

Histologically, periductal and inter-lobular infiltration of the pancreatic tissue by plasma cells is responsible for the elevation of plasma IgG4 levels. Inflammation will progress to fibrosis, irregular ductal strictures and atrophy of the acini [5-7].

Clinically, autoimmune pancreatitis is revealed by symptoms of an acute edematous pancreatitis with acute pancreatic-like pain, nausea and vomiting, and even sepsis in the most severe forms.

Abdominal CT shows infiltration of the pancreas with loss of lobulations in the affected areas. In rare cases, the size of the pancreas remains normal, and pancreatic atrophy is not common either. A minimal heterogeneous appearance of the peri-pancreatic fat, similar to acute edematous pancreatitis, may also be seen. The hypodense appearance surrounding the pancreas (Halo sign) is found in 15 - 80% of patients. [4,6-9].

Studies have been done regarding the contribution of IgG4 in autoimmune pancreatitis. A study by Lee., *et al*. shows that a cut-off value of 135 mg/dl has a specificity of 95% and a sensitivity of 97% in the differential diagnosis of autoimmune pancreatitis and pancreatic cancer. The study also highlights a correlation between IgG4 levels and disease activity [6,7,10].

The most frequently affected organs in association with type 1 pancreatitis are the lacrimal glands, kidneys and salivary glands. Other extra-pancreatic IgG4 disorders may be encountered: thyroiditis, interstitial lung disease, cervical and mediastinal adenopathy, cholecystitis and cholangitis [3,6,11,12].

Corticotherapy allows a complete and permanent clinical, biological and radiological remission. The ductal stenoses regress and the glands resume their endocrine and exocrine activity [6,10-12].

Autoimmune hepatitis

Described by Waldenström and Kunkel in the 1950s, this entity initially inherited a varied nomenclature, including chronic active hepatitis, cirrhosis of young women, and plasma cell hepatitis [13]. The current name of autoimmune hepatitis was adopted in 1992 [14]. It is a chronic inflammatory disease that can occur at any age, in both sexes and of all ethnic origins, but is more likely to affect women (F: M ratio of 3.6: 1). Its prevalence is estimated at 10-17/100,000 in Europe [15]. In order to explain the pathogenesis of autoimmune hepatitis, a genetic predisposition is implied, including major histocompatibility complex (HLA) genes. For example, for type 1 AIH, in North America and Europe, HLA-DR3 and HLA-DR4 alleles would be a susceptibility factor. An immune response to an environmental trigger constituted

by an external pathogen, a drug or a toxin, could erroneously target structurally similar internal components (molecular mimicry). This breakdown in immune tolerance would then lead to an innate and acquired immune response that would be self-sustaining [16].

Nearly one third of patients with AIH are asymptomatic, which may contribute to late recognition of the disease, at the cirrhosis stage in 25% of cases [17]. The onset may be insidious with non-specific symptoms (asthenia, fever, nausea, vomiting). Frequently, it is a chronic elevation (3 to 6 months) of transaminases (ASAT, ALAT) that attracts the attention of the physician. More rarely, AIH may manifest as fulminant hepatitis (jaundice, transaminases 1000 IU/l) [18].

Some patients present with features of AIH and signs of cholestatic disease with increased alkaline phosphatase and/or bilirubin. Conversely, one may also have a clinic of primary biliary cirrhosis (PBC) or primary sclerosing cholangitis (PSC) with elements of AIH [19,20].

In more than a third of cases, other inflammatory diseases may be associated with AIH, such as autoimmune thyroiditis, celiac disease, ulcerative colitis, and rheumatoid arthritis. Less commonly, association with type 1 diabetes, systemic lupus erythematosus, mixed connectivitis, Sjogren's syndrome, systemic sclerosis, hemolytic anemia, idiopathic thrombocytopenic purpura, vitiligo, or autoimmune polyglandular syndrome type 1 can also be found [21,22].

The histologic appearance of AIH is that of chronic hepatitis with some characteristic signs that may aid in the diagnosis, but are not completely specific. There is no histological difference between the two types of AIH. It is most often a combination of portal and periportal inflammation (typically predominantly plasma cell) associated with an interface hepatitis.

The diagnosis is based on the criteria of the 2008 simplified diagnostic score (Table 1) [23].

Clinical feature	Points
ANA or SMA	
≥ 1:40	+1
ANA or SMA ≥ 1:80 or LKM1 ≥ 1:40 or SIA-positive	+2
Serum IgG	
> Upper limit of normal	+1
> 1.1 times upper limit of normal	+2
Histologic findings	
Compatible with AIH	+1
Typical of AIH	+2
Hepatitis viral market	
Negative	+2
Aggregate score without treatment	
Definite AIH	≥7
Probable AIH	≥6

Table 1: *Simplified diagnosis criteria of AIH.*

Treatment is based on corticosteroid therapy and azathioprine. It should be emphasized that combined treatment (corticosteroid + azathioprine) is preferable from the outset, except in cases of marked leuko thrombocytopenia (cirrhosis with hypersplenism) or in cases of uncertain diagnosis requiring trial treatment with corticosteroid alone. This allows the use of a lower dose of corticosteroids than in monotherapy while maintaining the same efficacy and thus reducing their adverse effects. If there is a good response to the initial treatment, the steroids are reduced in successive steps before being stopped, while the dosage of azathioprine is increased to 2 mg/kg/d [24,25].

Association of AIH and AIP

The combination of AIH and AIP is not common. However, the diagnosis can be made in a known patient with AIH who presents with pancreatic-like pain and/or elevated pancreatic enzymes.

There are few cases of autoimmune hepatitis-autoimmune pancreatitis association described in the literature. One case has been published of a 44-year-old female patient who presented with pancreatic-like pain, hepatomegaly and jaundice. Biological workup showed cholestasis, cytolysis, elevated lipasemia, and high levels of anti-smooth muscle, ANA, and IgG antibodies. The CT scan showed a heterogeneous inflammatory aspect of the pancreas in favor of an acute pancreatitis. Histological study of the liver parenchyma showed lobular and portal inflammation with a lymphopasmacytic infiltrate. The clinical and biological evolution of the patient was favorable under corticotherapy and azathioprine [26].

Conclusion

The diagnosis of AIP and AIH is based on multiples criteria's and arguments, and the association of these two entities is not usual. However, this association can be evoked in a known patient with autoimmune pancreatitis, who presents symptoms or biological abnormalities suspecting an autoimmune hepatitis.

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