Case report

IgG4 disease revealed by a type 1 autoimmune pancreatitis : a case report

ABSTRACT

Aim: to describe clinical, paraclinical and evolutive features of an IgG4 disease
Presentation of case: The patient was a male, 51 years old, seen in consultation for epigastric pain of sudden onset six days before admission, with transfixing irradiation, evolving intermittently in a febrile context. On admission, the patient was a subicterus. The evolution during hospitalization was marked by the sudden onset three days later of bilateral inflammatory polyarthritis of the knees and ankles. Biological examination revealed diabetes mellitus; lipasemia was elevated to 122U/l. There was a disturbance of the renal balance (urea=1.38 g/l and creatinine level at 35 mg/l); and a significant increase of plasma IgG4 at 2.380 g/l. The abdominal ultrasound showed a globally hypertrophic pancreatic gland, of heterogeneous structure, without focal lesions or necrosis; without biliary lithiasis. An abdominal CT scan showed, after injection of contrast medium, a global hypertrophy of the pancreas with a corporal-caudal predominance, giving a classic "sausage" appearance; associated with a lack of enhancement of the pancreatic parenchyma and an absence of dilatation of the Wirsung canal. The diagnosis of type 1 autoimmune pancreatitis was therefore retained, subject to histological examination, in view of the imaging appearance correlated with the serology, the joint involvement and the favourable evolution under corticosteroids
Conclusion: Autoimmune pancreatitis is a rare disease of recent discovery, with a predominance in elderly and male subjects. The diagnosis must be evoked in front of a pancreatic pain associated with articular manifestations, or in case of absence of obvious etiology of a pancreatitis.

Keywords: pancreas, pancreatitis, autoimmune, IgG4

1. INTRODUCTION

IgG4 disease is a systemic disorder characterized by an increase in serum immunoglobulin G subclass 4, associated with a lymphoplasmatic infiltrate of the various affected organs [1]. The organs frequently affected are: the pancreas, bile ducts, salivary glands, kidneys, aorta and lymph nodes [1-3]. Pancreatic involvement (type 1 autoimmune pancreatitis) is characterized by jaundice, altered general condition, abdominal pain, pancreatic mass and diabetes due to pancreatic insufficiency [4]. Because of its clinical and paraclinical symptomatology, the major challenge in the diagnosis of autoimmune pancreatitis lies in the differential with pancreatic or biliary cancer [5]. The prevalence and incidence of autoimmune pancreatitis in the general population are not known [6]. This is related to the fact that it is a rare disease of recent description. The majority of cases in the West are diagnosed on resection specimens for suspected pancreatic adenocarcinoma [7]. The revised criteria for clinical diagnosis of autoimmune pancreatitis (according to the Japan

Pancreatic Society) include three arguments: morphological, biological and histological. The morphological argument is the demonstration of pancreatic hypertrophy associated with narrowing of the main pancreatic duct. The biological argument is the demonstration of autoantibodies or the increase of the serum level of immunoglobulin G4. The histological argument is the presence of fibrosis with infiltration of lymphoplasmacytic cells. The diagnosis of autoimmune pancreatitis is made when there is a morphological argument (major criterion) associated with a biological or histological argument (minor criteria) [8].

2. PRESENTATION OF CASE

The patient was a male, 51 years old, seen in consultation for epigastric pain of sudden onset six days before admission, with transfixing irradiation, evolving intermittently in a febrile context. The patient was neither an alcoholic nor a smoker and had no known personal (diabetes, lithiasis) or family pathological history. On admission, the patient was found to have an altered general condition, a subicterus, and a normal-sized abdomen with diffuse tenderness, without any palpated mass or peritoneal irritation syndrome. The evolution during hospitalization was marked by the sudden onset three days later of bilateral inflammatory polyarthritis of the knees and ankles, associated with absolute functional impotence.

Biological examination revealed diabetes mellitus: fasting venous glycaemia at 6.40 g/l, qualitative glucosuria at four crosses, qualitative acetonuria at one cross, with glycated haemoglobin at 7.9%. Lipasemia was elevated to 122U/l. There was a disturbance of the renal balance (urea=1.38 g/l and creatinine level at 35 mg/l); and a significant increase of plasma IgG4 at 2.380 g/l.

The abdominal ultrasound performed on admission showed a globally hypertrophic pancreatic gland, of heterogeneous structure, without focal lesions or necrosis; without biliary lithiasis. An abdominal CT scan showed, after injection of contrast medium, a global hypertrophy of the pancreas with a corporal-caudal predominance, giving a classic "sausage" appearance; associated with a lack of enhancement of the pancreatic parenchyma and an absence of dilatation of the Wirsung canal. (Figure 1)

The radiographic work-up showed: global joint pinching, hypertrophy of the tibial spines and calcification of the quadricipital tendon insertions with fluid effusion in both knees. In both ankles: pinching of the tibio-talar joint with calcaneal tendon calcifications.

The patient was treated with level 2 analgesics, regular insulin and corticosteroid therapy with 40 mg of methylprednisolone/day. The clinical evolution was made fifteen days after the beginning of the treatment towards a complete improvement of the symptomatology (icterus, fever, abdominal pains, arthralgias). The evolution of the biological assessment showed a negativation of glucosuria and ketonuria; normalization of venous glycemia, lipasemia and liver function tests. The control abdominal ultrasound showed a partial regression of the pancreatic hypertrophy. At the end of the 30 days of hospitalization, the patient was discharged with an insulin protocol and a diabetic diet. The corticosteroid dose was gradually reduced in 10mg increments every 14 days.

The diagnosis of type 1 autoimmune pancreatitis was therefore retained, subject to histological examination, in view of the imaging appearance correlated with the serology, the joint involvement and the favourable evolution under corticosteroids, in accordance with the recommendations of the International Pancreatology Association.

3. DISCUSSION

Autoimmune pancreatitis is a rare pathology of recent description [7]. We report in this study the first case described in the department of Hepato-Gastro-Enterology. Nevertheless, we believe that it is a pathology of underestimated diagnosis.

The case we report is that of a 51 year old male patient with no previous pathological history. Chari et al in the United States also reported a predominance of male patients (83%) and patients over 50 years of age (mean: 63+/-18 years) [9].

The symptoms of autoimmune pancreatitis are not specific. The most common clinical presentation is painless jaundice caused by a mass in the head of the pancreas. This symptomatology is similar to that of our patient. The extrahepatic manifestations were renal involvement and inflammatory polyarthritis. Rheumatoid factor assay was not performed; however, elevation of this factor has been reported in 25% to 29% of patients with autoimmune pancreatitis [4, 11]. Our patient did not present any lymph node or lymphatic involvement as described in some series [12].

The biological work-up showed diabetes mellitus with proteinuria and acetonuria. This finding confirms the data in the literature according to which autoimmune pancreatitis is often associated with pancreatic insufficiency [4] leading to the development of diabetes mellitus [13] in more than 80% of cases.

Serum IgG4 levels measured by nephelometry showed a specific increase. IgG4 is the best marker of autoimmune pancreatitis [14]. Its sensitivity is between 52% and 95%, and its specificity between 81% and 89% [15]. We made the diagnosis of autoimmune pancreatitis on the basis of a significant increase in serum IgG4 associated with global hypertrophy of the pancreatic gland; in accordance with international recommendations [8, 16]. No histological analysis was performed.

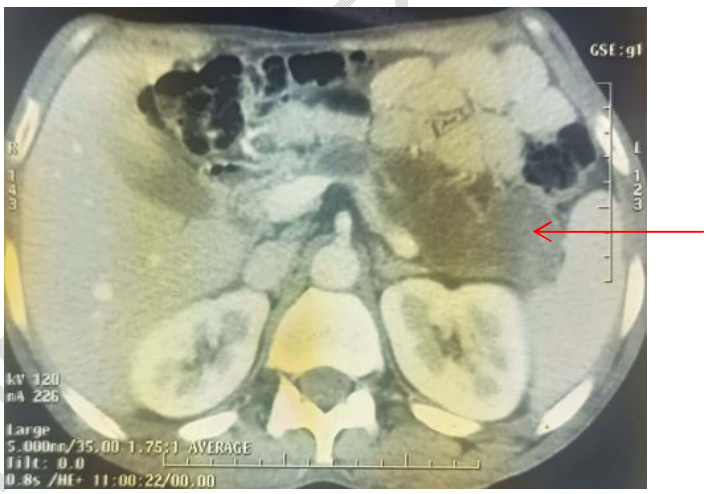

Fig. 1. abdominal CT scan showing hypertrophy of the pancreas with lack of enhancement after injection of contrast medium (red arrow)

4. CONCLUSION

Autoimmune pancreatitis is a rare disease of recent discovery, with a predominance in elderly and male subjects. The diagnosis must be evoked in front of a pancreatic pain associated with articular manifestations, or in case of absence of obvious etiology of a pancreatitis. This diagnosis is defined by recommandations of International Association of Pancreatology

CONSENT

All authors declare that 'written informed consent was obtained from the patient for publication of this case report and accompanying images.

REFERENCES

1. Kamisawa T. IgG4-positive plasma cells specially infiltrate various organs in autoimmune pancreatitis. Pancreas 2004; 29: 167–168.

2. Deshpande V, Chicano S, Finkelberg D, Selig M, Mino-Kenudson M, Brugge W. autoimmune pancreatitis: a systemic immune complex mediated disease. Am J Surg Pathol 2006; 30: 1537–1545.

3. Stone JH, Khosroshahi A, Deshpande V, Stone J. IgG4-related systemic disease accounts for a significant proportion of thoracic lymphoplasmacytic aortitis cases. Arthritis Care Res 2010; 62: 316–322.

4. Vonlaufen A, Frossard J-L. Pancréatite autoimmune. Rev Med Suisse 2010; 6: 1662–6.

5. Kamisawa T, Notohara K, Shimosegawa T. Two clinocopathologic subtypes of autoimmune pancreatitis:LPSP and IDCP. 2010; 139: 22–5.

6. Zamboni G, Luttges J, Capelli P. Histopathological features of diagnostic and clinical relevance in autoimmune pancreatitis: A study on 53 resection specimens and 9 biopsy specimens. Virchows Archs 2004; 445: 552–63.

7. Pearson RK, Longnecker DS, Chari ST. Controversies in clinical pancreatology: Autoimmune pancreatitis: Does it exist? Pancreas 2003; 2: 1–13.

8. Shimosegawa T, Chari ST, Frulloni L, Kamisawa T, Kawa S, Mino-Kenudson M, et al. International consensus diagnostic criteria for autoimmune pancreatitis: guidelines of the International Association of Pancreatology. Pancreas 2011; 40: 352–358.

9. Chari ST, Smyrk TC, Levy MJ, Topazian MD, Takahashi N, Zhang L, et al. Diagnosis of autoimmune pancreatitis: The Mayo Clinic experience. Clin Gastroenterol Hepatol 2006; 4: 1010–16.

10. Takayama M, Hamano H, Ochi Y. Recurrent attacks of autoimmune pancreatitis result in pancreatic stone formation. Am J Gastroenterol 2004; 99: 932–7.

11. Okazaki K, Uchida K, Ohana M, Nakase H, Uose S, Inai M. Autoimmune-related pancreatitis is associated with autoantibodies and a Th1/Th2-type cellular immune response. Gastroenterol 2000; 118: 573–581.

12. Pickart T, Mayerle J, Lerch M. Autoimmune pancreatitis. Nat Clin Pr Gastroenterol Hepatol 2007; 4: 14–23.

13. Nishimori I, Tamakoshi A, Kawa S. Influence of steroid therapy on the course of diabetes mellitus in patients with autoimmune pancreatitis: Findings from a nation wide survey in Japan. Pancreas 2006; 32: 244–8.

14. Oseini A, Chaiteerakij R, Shire A, Ghazale A, Kaiya J, Moser C, et al. Utility of serum Immunoglobulin G4 in distinguishing Immunoglobulin G4-associated cholangitis from cholangiocarcinoma. Hepatology 2011; 54: 940–948.

15. Hamano H, Kawa S, Horiuchi A, Unno H, Furuya N, Akamatsu T, et al. High serum IgG4 concentrations in patients with sclerosing pancreatitis. N Engl J Med 2001; 344: 732–8.

16. Okazaki K, Kawa S, Kamisawa T, Naruse S, Tanaka S, Nishimori I, et al. Clinical diagnostic criteria of autoimmune pancreatitis: revised proposal. J Gastroenterol 2006; 41: 626–31.