Type 1 autoimmune pancreatitis: relapse with liver abscess

Pancreatite autoimune tipo 1: recidiva com abscesso hepático

Gustavo Mesquita de Oliveira[1], Lia de Freitas Araújo Alves[1], Paloma Lucena Cabral[1], Ana Luiza Viana Pequeno[1], Clóvis Rêgo Coelho[2], Rodrigo Vieira Costa Lima[3]

ABSTRACT

Type 1 autoimmune pancreatitis is a cause of chronic pancreatitis related to the systemic disease known as IgG4-related Sclerosing Disease. Case report: We report the case of a 64-year-old male patient who presented recurrent epigastric pain radiating to the back, associated with jaundice, xerostomia, nausea, and vomiting, since 2014, diagnosed two years later with an unresectable pancreatic adenocarcinoma. The diagnosis was questioned after a few follow-up months without clinical deterioration when it was suggested the possibility of type 1 autoimmune pancreatitis in its pseudotumoral form. The patient was then treated with glucocorticoids, obtaining significant clinical improvement. After two years of follow-up, he returned asymptomatic with images suggestive of sclerosing cholangitis and a large liver abscess. Importance of the issue: The present case denotes the difficulty found in this diagnosis due to clinical and radiological resemblances with pancreatic adenocarcinoma. Besides that, it presents a seldom described disease complication, the liver abscess.

Keywords: Immunoglobulin G; Autoimmune Diseases; Pancreatitis; Cholangitis, Sclerosing; Liver Abscess.

RESUMO

A pancreatite autoimune tipo 1 é uma causa de pancreatite crônica relacionada à doença sistêmica conhecida como Doença Esclerosante relacionada à IgG4. Relato do caso: Relatamos o caso de um paciente do sexo masculino, 64 anos, que apresentou quadros recorrentes de dor epigástrica com irradiação para as costas, associada com icterícia, xerostomia, náuseas e vômitos desde 2014, diagnosticado após 2 anos com adenocarcinoma pancreático irressecável. O diagnóstico foi questionado após alguns meses de acompanhamento sem deterioração clínica, quando aventaram a possibilidade de forma pseudotumoral da pancreatite autoimune tipo 1. Realizou tratamento com glicocorticoides, obtendo melhora clínica importante. Após dois anos de acompanhamento, retorna assintomático com imagens sugestivas de colangite esclerosante e volumoso abscesso hepático. Importância do problema: O presente caso denota uma dificuldade encontrada no diagnóstico dessa entidade devido a semelhanças clínico-radiológicas com o adenocarcinoma pancreático. Além disso, apresenta uma complicação pouco descrita da doença, o abscesso hepático.

Palavras-chave: Imunoglobulina G; Doenças Autoimunes; Pancreatite; Colangite Esclerosante; Abscesso Hepático.

1. Faculdade de Medicina, Universidade Federal do Ceará (UFC), Fortaleza (CE), Brasil.
2. Serviço de Radiologia do Hospital Universitário Walter Cantídio (HUWC), Fortaleza (CE), Brasil.
3. Serviço de Gastroenterologia do HUWC, Fortaleza (CE), Brasil.

✉ Gustavo Mesquita de Oliveira. Rua Capitão Francisco Pedro, 1290 - Rodolfo Teófilo. CEP: 60430-372. Fortaleza (CE), Brasil. gustavo.moliveira75@gmail.com | Recebido em: 11/08/2019 | Aprovado em: 23/01/2020

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INTRODUCTION

IgG4-related disease (IgG4-RD), also known as IgG4-related Sclerosing Disease, is a recently defined entity characterized by serum elevated levels of IgG4, lymphoplasmacytic infiltrate and an immune-mediated fibroinflammatory process in the organs affected. This is a systemic disease associated with pancreatic impairment recognized as Type 1 Autoimmune Pancreatitis (AIP), a rare form of chronic pancreatitis. This article reports a case of a patient with AIP who recurred with a liver abscess associated with sclerosing cholangitis.

CASE REPORT

A 64-year-old male patient, with a history of frequent alcohol use since the age of 12, was admitted to a tertiary referral hospital in July 2016 reporting severe epigastric pain radiating to the back, associated with jaundice, xerostomia, nausea, and vomiting, since the middle of 2014. He also reported weight loss of about 16 kilograms (kg) in this period (standard weight 64 kg) despite a well-preserved appetite. There was no evidence of fever, steatorrhea, change in bowel habits, gastrointestinal bleeding, ascites, lymphadenopathy or hepatosplenomegaly.

A computed tomography (CT) scan of the abdomen was performed which revealed pancreatic parenchymal alteration, more evidently seen in the region of the head (Image 1). In that tertiary center, the surgical treatment was then indicated since the initial diagnostic hypothesis was pancreatic adenocarcinoma. Due to the intraoperative definition of the unresectable lesion, biliodigestive derivation and gastrojejunal bypass were performed. The anatomopathological result was negative for neoplastic cells and the material was compatible with fibro-neutrophilic exudate. Levels of CA 19.9 and CEA were normal in the outpatient follow-up. Due to these findings, the patient was referred to the Gastroenterology Department of the Walter Cantídio University Hospital for further investigation.

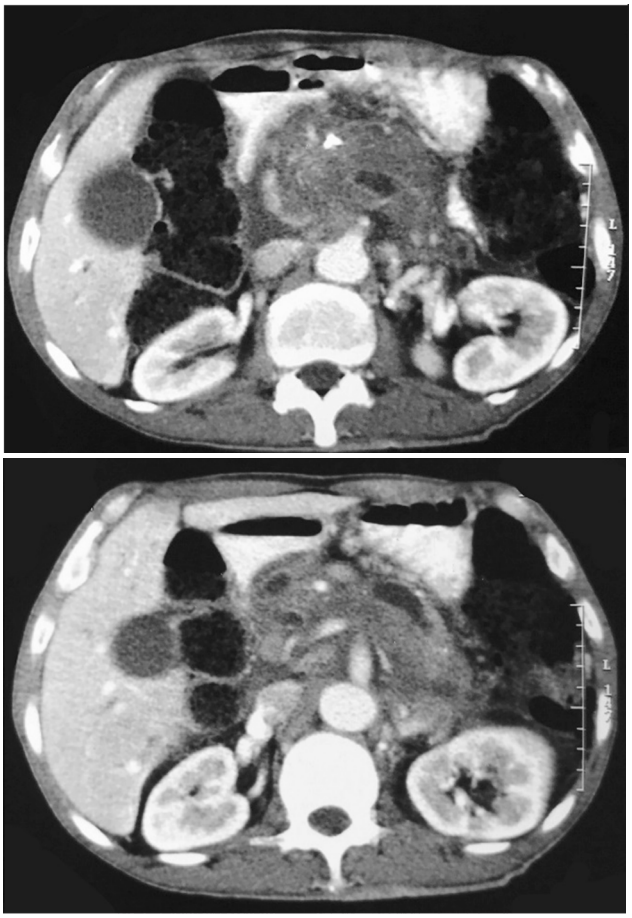

Image 1: A computed tomography (CT) scan revealed an expansive and infiltrative formation in the head of the pancreas with a cystic component. It also showed pancreatic calculi, irregular dilatation of the main pancreatic duct, and splenic and superior mesenteric vein thrombosis.

The patient was admitted to the Gastroenterology Unit, where it was suggested the diagnostic hypothesis of Autoimmune Pancreatitis type 1, IgG4-related, due to the possibility of a pseudotumoral presentation of this disease and the incompatibility of the clinical course of pancreatic adenocarcinoma in this case. According to this, serum IgG4 concentration was dosed with a result of 254 mg/dL (Normal range: 8-140 mg/dL) and it was started prednisone in therapeutic dosage. During the follow-up, slow glucocorticoid weaning was then performed. It was prescribed pancreatic enzymes, calcium, and D vitamin. Empirical treatment with antiparasitic drugs was performed due to the high prevalence of parasitosis in our region and due to the immunosu-

ppressive therapy. Bone densitometry was required. An immunohistochemical analysis of the intraoperative fragment was performed. In November 2016, the patient presented for the first time high fasting glucose levels with the hypothesis of Endocrine Pancreatic Insufficiency worsened by glucocorticoid use. He was admitted in December of the same year due to difficulties in glycemic control.

During hospitalization, the insulin regimen was adjusted and the corticoid dosage was decreased. A new abdominal CT scan was performed, which revealed maintenance of diffuse involvement pattern of the pancreas, suggestive of chronic pancreatitis. Also, contrast-enhanced tomography of the salivary glands has demonstrated highly suggestive findings of Sclerosing Sialadenitis related to IgG4 Disease. However, the immunohistochemical analysis of the intraoperative fragment of the July 2016 pancreatic biopsy was performed and revealed the absence of IgG4. Nevertheless, it was described that the sample contained scarce material, recommending a new sample for histological revaluation.

After discharge from the hospital, the patient maintained an outpatient follow-up every 4 months, and the corticosteroid weaning was performed progressively. He remained asymptomatic with periodic follow-up and prednisone was discontinued after about a year and a half of the beginning of corticotherapy. In October 2018, the patient presented with new tomographic imaging (Image 2) that confirmed therapeutic response. However, it was observed an asymptomatic hepatic abscess, which motivated a new hospitalization for further evaluation.

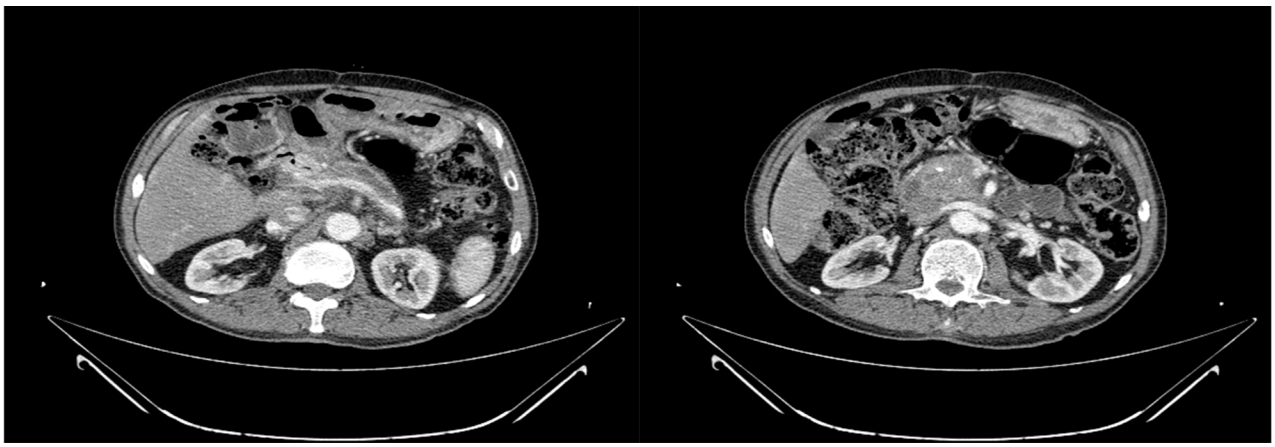

Image 2: A computed tomography (CT) scan that showed a volumetric reduction of the pancreatic head with splenic vein recanalization.

Abdominal Magnetic Resonance Imaging (MRI) and Magnetic Resonance Cholangiopancreatography were performed (Images 3 and 4) and a massive hepatic abscess was observed. There were also described areas of discontinuous narrowing of the intrahepatic bile ducts suggestive of sclerosing cholangitis. During hospitalization, he denied fever, weight loss, jaundice, loss of appetite or abdominal pain. The abscess was successfully treated with percutaneous drainage and antimicrobial therapy (ciprofloxacin and metronidazole) for six weeks. At the time of presenting this case report, he remained asymptomatic with no hepatic collection observed in control ultrasonography and is using azathioprine as maintenance therapy, with good tolerance and no drug-related side effects.

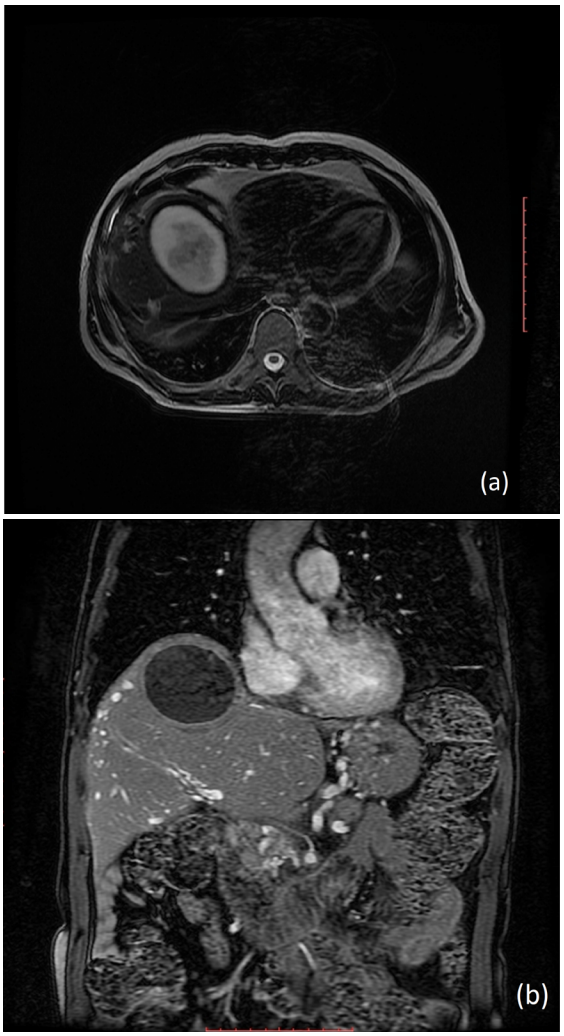

Image 3: Abscess in the VIII liver segment measuring 8.2 x 6.0 x 5.2 cm shown in (a) axial T2-weighted and (b) Fat-saturated post gadolinium coronal T1-weighted Abdominal MRI.

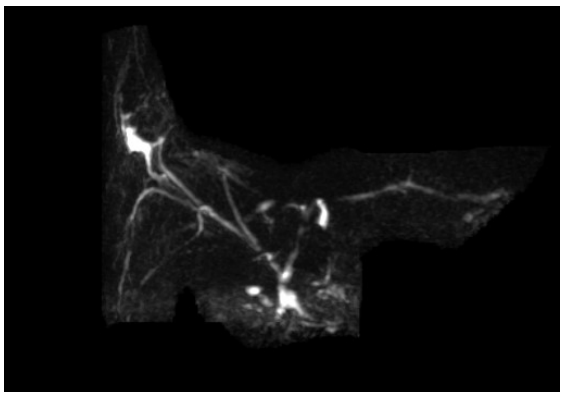

Image 4: Magnetic Resonance Cholangiopancreatography that revealed discontinuous narrowing of the intrahepatic bile ducts, with predominantly central involvement.

DISCUSSION

AIP is a rare disorder characterized by lymphoplasmacytic infiltrate and fibrosis in the pancreas and a very good response to steroids[1]. It predominantly affects men during the seventh decade of life, as seen in our patient[2]. Patients most commonly present with painless obstructive jaundice, but a variety of manifestations have been described: abdominal pain, weight loss, pancreatic mass, recurrent pancreatitis, pancreatic duct stricture and symptoms related to systemic diseases[3]. It can be divided into two types, each one with its diagnostic criteria[4]. Type 1, the most common[2], is histologically characterized by periductal plasma and lymphocytes infiltrate, "storiform" fibrosis, obliterative phlebitis, and great infiltration by IgG4+ plasma cells (>10 cells per higher-power field)[1,4]. This histologic description is called Lymphoplasmacytic sclerosing pancreatitis (LPSP) or AIP without granulocyte epithelial lesions (GEL). It is considered a pancreatic manifestation of IgG4-related disease (elevated serum IgG4 levels are seen in more than 90% of patients)[5], so there are many extrapancreatic symptoms. On the other hand, type 2 is typically characterized by GEL and is not associated with high levels of IgG4 and usually affects younger patients[6].

Several diagnostic criteria for AIP were proposed from various countries between 2002 and 2009. These diagnostic criteria varied reflecting the differences in the diagnostic approach and patient population (proportion of type 1 and type 2 AIP). The International Consensus Diagnostic Criteria (ICDC) for AIP[1] were designed to make diagnostic evaluation less rigid and acknowledge the two AIP subtypes. It is a complex criteria based on the five cardinal features of AIP: (1) imaging features of pancreatic parenchyma (CT, MRI) and pancreatic duct (endoscopic retrograde cholangiopancreatography or magnetic resonance cholangiopancreatography), (2) serology (IgG4, IgG, and antinuclear antibody), (3) other organ involvement, (4) histopathology of the pancreas, and (5) response to steroid therapy.

Another widespread diagnostic criteria is the one suggested by the Mayo Clinic, which similarly emphasizes five important categories:

1. Histology: LPSP or lymphoplasmacytic infiltrate with storiform fibrosis showing abundant IgG4-positive cells.
2. Typical pancreatic imaging: diffusely enlarged gland with delayed enhancement; diffusely irregular, attenuated main pancreatic duct.
3. Serology: elevated serum IgG4 level (normal 8–140 mg/dL).
4. Other organ involvement: hilar/intrahepatic biliary strictures, persistent distal biliary stricture, parotid/lacrimal gland involvement, mediastinal lymphadenopathy, retroperitoneal fibrosis.
5. Response to steroid treatment.

These categories are then combined to form three distinct diagnostic groups: Group A (diagnostic pancreatic histology), Group B (typical imaging + serology), and Group C (response to steroids)[7]. Following these criteria, our patient met the diagnostic of AIP according to his response to steroids, associated with elevated serum IgG4.

It is important to highlight that our patient did not present the typical histological findings, with his biopsy showing only fibro-neutrophilic exudate and negative immunohistochemistry for IgG-4 MRQ-44 and polyclonal IgG. Zhang L. et al (2007) investigated the role of IgG4 staining in the diagnosis of autoimmune pancreatitis, analyzing 29 cases of AIP. There was moderate to marked staining in 21 of 29 cases, with only one case presenting no IgG4-positive plasma cell infiltration. That study found that there were increased numbers of pancreatic IgG4-positive plasma cells in AIP compared to chronic alcoholic pancreatitis and pancreatic ductal adenocarcinoma. However, in our case, the results of the biopsy and its IgG4 staining should be questioned, considering that the sample contained scarce material[8].

One of the obstacles to obtaining the diagnosis was the resemblance of the imaging of the AIP with pancreatic adenocarcinoma. AIP can be divided into two forms: diffuse or localized. The focal form of AIP, also called pseudotumoral form, can present as a pancreatic mass and therefore can mimic an adenocarcinoma. The distinction between these two entities is important since the treatment approach and prognosis are quite different. Obstructive jaundice, weight loss, and abdominal pain are clinical features of both. Some findings in MRI and Diffusion-Weighted MRI are more frequently seen in AIP, thus can help to distinguish it from cancer: similar or high signal intensity on portal phase and 3- and 20-minute delayed phase images, homogeneous enhancement, no peripancreatic fat infiltration, no internal cystic or necrotic portion, capsule-like rim, no upstream pancreatitis, no vascular invasion, and duct penetrating sign[9,10]. Serologically, elevated levels of IgG4 favors the diagnosis of AIP. While the patient had a cystic component on CT, 2-year presentation moves away from the hypothesis of cancer.

Another diagnostic barrier was the overlap between AIP and alcoholic pancreatitis. The presence of heavy alcohol consumption, duct dilation, and pancreatic calcifications on CT in our patient could suggest alcohol-induced pancreatitis, although there is no peripancreatic fat necrosis and pseudocyst formation, which is often seen in alcohol etiology. Besides, the high levels of serum IgG4, good response to steroids, and extrapancreatic symptoms as sclerosing sialadenitis favors the diagnosis of AIP[11].

AIP is one of the best-studied organ manifestations of IgG4-RD. Other known organs to be affected are bile ducts, salivary glands, lacrimal glands, kidneys, retroperitoneum, and lungs. Besides AIP, the current patient presented clinical and radiological findings suggestive of Sclerosing Sialadenitis related to IgG4 Disease, which contributes to the systemic diagnosis of IgG4-RD[12]. Our patient also presented a relapse with radiological findings indicative of IgG4-related sclerosing cholangitis (IgG4-SC)[13]. IgG4-SC is the most common extrapancreatic manifestation of AIP and shares similar clinical features with Primary Sclerosing Cholangitis (PSC). While the majority of patients of PSC is diagnosed asymptomatic, the most frequent symptom reported in IgG4-SC is jaundice and clinical presentation of cholestasis, with IgG4-SC being more acute and of a shorter duration[14,15]. Tokala et al[16] proposed MRI imaging findings that favor IgG4-SC to help distinguish both conditions, which are: bile duct wall thickness greater than 2.5 mm, continuous involvement of the bile ducts, gallbladder involvement, and absence of hepatic parenchyma involvement. Moreover, IgG4-SC usually presents an increased serum IgG4 level, dense infiltration of IgG4-positive plasma cells with fibrosis in the bile duct wall,

and good response to steroids[17]. In this case, the biliary disease was relatively long, differing from the classical beaded PSC appearance.

Recurrence after corticosteroid withdrawal can occur in 53% of patients, especially in those with type 1 AIP[18]. Although there is not much evidence about long-term prognosis, regular follow-up with clinical analysis and imaging studies is strongly recommended[15].

Besides, our patient developed a pyogenic liver abscess. The main causes of bacterial liver abscesses are biliary tract diseases, such as choledocholithiasis, obstructing tumors, strictures, and congenital anomalies of the biliary tree[19,20]. This case report describes a hepatic abscess as a rare complication of IgG4-SC. According to a keyword search in PubMed, there were no other cases reported of liver abscesses as a complication of IgG4-SC. Shibata et al[21] reported a case of IgG4-related hepatic inflammatory pseudotumor evolving with a pyogenic abscess, suggesting that the evolution was due to the treatment with steroids. In our patient's case, we theorize that the narrowing of intrahepatic bile ducts associated with the patient's diabetes and steroid use led to an increased risk of developing pyogenic hepatic abscess[21,22].

CONCLUSION

AIP is a known complication of IgG4-RD, whose diagnosis should be suspected in patients with unexplained pancreatic mass and it is an important diagnostic consideration due to the consequences of a misconducted case as pancreatic adenocarcinoma, including aggressive surgical approach. It commonly presents as painless obstructive jaundice in old males and may be accompanied by other organ involvement or systemic symptoms. The confirmatory diagnosis may be difficult to establish and clinical presentation can be quite variable. Immunohistology results are not always compatible. Recently, the Mayo Clinic proposed diagnostic criteria to support it. This case report presented an AIP with a seldom reported association of IgG4-SC and pyogenic liver abscess, suggesting a correlation of these diseases.

CONFLICT OF INTEREST

The authors have no conflict of interest.

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