



Contents lists available at ScienceDirect

## International Journal of Surgery Case Reports

journal homepage: [www.casereports.com](http://www.casereports.com)

## A rare case of IgG4-related systemic disease manifesting with pancreatic head mass mimicking borderline resectable cancer



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## ARTICLE INFO

## Article history:

Received 8 October 2014

Accepted 6 November 2014

Available online 11 November 2014

## Keywords:

IgG4-related disease

Autoimmune pancreatitis

Pancreatic cancer

## ABSTRACT

**INTRODUCTION:** Autoimmune pancreatitis (AIP) is a rare pancreatic disorder among chronic pancreatitis that can mimic pancreatic cancer (PC). Patients with type 1 AIP usually present obstructive jaundice associated with high level of IgG4 in serum and a pancreatic mass at radiological imaging; these disorders may be associated with other organs lesions presenting the same histopathological features, and in these cases AIP should be considered a pancreatic localization of an IgG4-related systemic disease.

**PRESENTATION OF CASE:** We report the case of a young man with initial suspect of PC to be treated with surgery, and final diagnosis of AIP in the context of an IgG4-related systemic disease.

**DISCUSSION:** Because of its similar features, several algorithms have been proposed for AIP diagnosis, based on combination of clinical/serological and radiological criteria. However, histology represents the only way to obtain definitive diagnosis, even if sometimes it is difficult to obtain biological samples.

**CONCLUSION:** IgG4-related systemic disease must be taken into account among differential diagnosis during the workup for PC, in order to avoid unnecessary surgery.

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### 1. Introduction

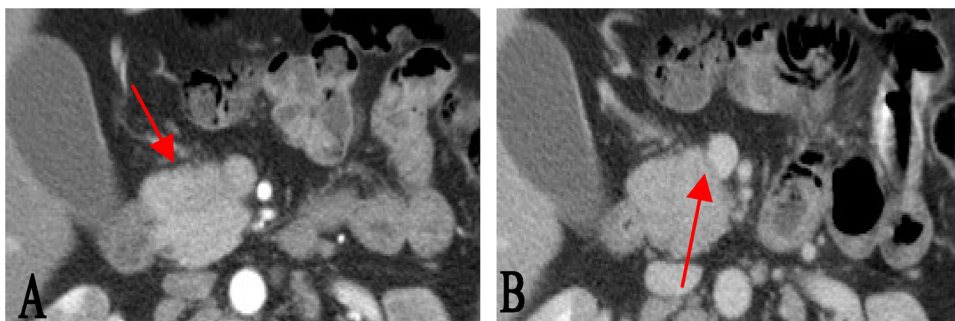
Autoimmune pancreatitis (AIP) is a rare pancreatic disorder that in recent years is drawing the attention of many clinicians because of the differential diagnosis with pancreatic cancer (PC). It comprehends two different varieties: type 1 or lymphoplasmocytic sclerosing pancreatitis, and type 2 or idiopathic duct-centric pancreatitis. The first is characterized by infiltration of a high number of IgG4 positive plasma cells (IgG4-related), while the second by neutrophilic infiltration in pancreatic duct epithelium (IgG4 not-related).<sup>1</sup> Type 1 is more frequent than type 2 and it occurs usually in adult men. Pathogenesis is not completely known but immunological mechanisms seem to be implicated. Patients with AIP may present obstructive jaundice associated with high level of IgG4 in serum and a pancreatic mass at radiological imaging. They can also show other organs involvement (IgG4-related systemic disease), and typically the response to steroid treatment is good.<sup>1</sup> AIP shares some clinical and radiological features with PC: many cases of diffuse type of AIP can be correctly diagnosed on the basis

of the various diagnostic algorithms proposed, but mass-forming AIP is very similar to PC and it may be really difficult to distinguish between the two entities. We report the case of a young man with initial suspect of PC to be treated with surgery, and final diagnosis of AIP in the context of an IgG4-related systemic disease.

### 2. Case report

A 46-years old man was admitted in a peripheral hospital for jaundice associated with progressive asthenia and weight loss. Laboratory tests showed elevated bilirubin (6, 9 mg/dl) and hepatic enzymes (AST/ALT 107/176 U/L, GGT 760 U/L). CA 19-9 was negative. CT scan showed a mass in pancreatic head (diameter 42 mm × 28 mm) (Fig. 1A), with mild Wirsung and bile ducts dilatation and suspected encasement of superior mesenteric vein (Fig. 1B); both kidneys presented increased size. At that time patient was transferred to our institution for surgical treatment. A pancreatic EUS-FNA was performed: EUS evidenced a pancreatic head mass (diameter 45 mm), with doubt of encasement of the mesenteric vein; Wirsung and common bile duct were enlarged; multiple pericaval and peripancreatic lymphnodes were present. Pathologists did not found carcinoma cells but they were not able to perform a definitive diagnosis. Histopathological assessment was

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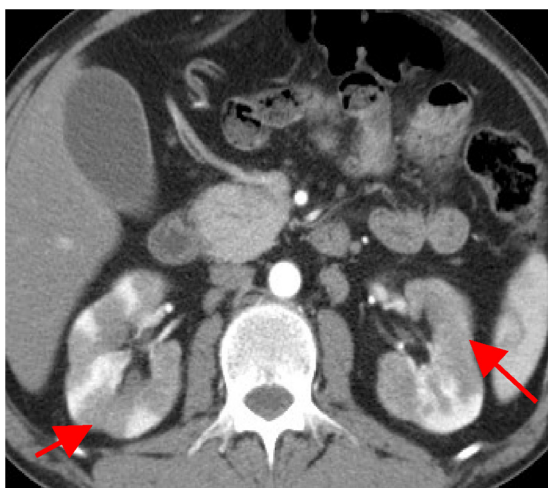
**Fig. 1.** First CT scan. Arterial phase (A): pancreatic head with low-density mass measuring 42 mm × 28 mm. Portal phase (B): suspected involvement of the superior mesenteric vein.

performed, but IgG positive plasmacells were few, and it was not possible to evaluate the IgG4 percentage. A second CT scan showed diffuse head pancreatic enlargement and atrophy of the tail with a Wirsung segmental dilatation. Both kidneys presented abnormal parenchyma with pseudonodular images (Fig. 2). Other investigations were performed: serum Ig level, C3–C4 and auto-antibodies resulted normal, but serum IgG4 level was 180 mg/dl (ref. 30–90 mg/dl). Patient underwent kidney biopsy, that showed interstitial nephritis IgG4-related. After starting with steroid treatment, patient clinical conditions and laboratory tests improved. One month later, CT scan showed normalization of the kidneys with reduction of the pancreatic lesion (Fig. 3) and of the peripancreatic lymphnodes. Bilirubin and hepatic enzymes were normal. Six month later, CT scan did not evidence pancreatic lesions.

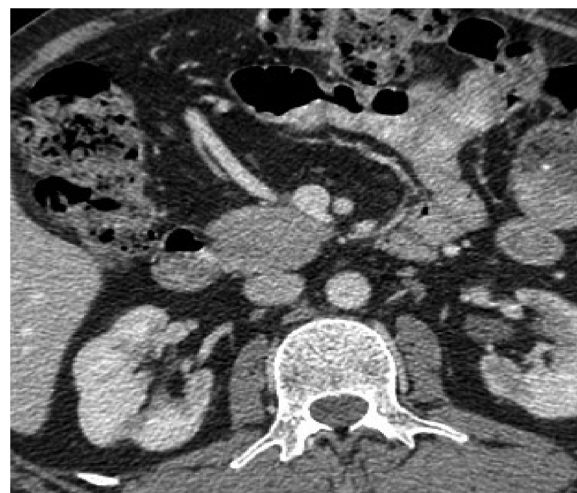
### 3. Discussion

The case proposed demonstrated how clinical and radiological presentation of AIP can be similar to that of PC. Thus, AIP should be considered among differential diagnosis of PC in order to avoid unnecessary pancreatic resections; some studies reported that 2–5% of pancreatic lesions resected with suspect of PC turned out to be AIP at histological analysis.<sup>2,3</sup> Consequently, it should be very important to do a correct diagnosis of AIP before surgery. In 2011 the International Association of Pancreatology proposed the International Consensus Diagnostic Criteria (ICDC) for AIP.<sup>4</sup> Presenting all cardinal features of AIP, ICDC evidenced elements to differentiate AIP from PC. First, clinical presentation of AIP can be acute, with obstructive jaundice by a pancreatic mass, or chronic

with symptoms of chronic pancreatitis (pain, diarrhea, diabetes).<sup>4</sup> In AIP jaundice can sometimes float (as in our patient) or even spontaneously attenuate, while in PC jaundice progresses steadily.<sup>5</sup> In 50–70% of cases AIP is associated with other organs lesions (retroperitoneal fibrosis, interstitial nephritis, sclerosing cholangitis) with the same histopathological features; these disorders are known as IgG4-related disease. Extrapancreatic alterations can occur also in absence of pancreas involvement.<sup>6,7</sup> Our patient showed the association of AIP and interstitial nephritis as manifestation of IgG4-related systemic disease. As regards serology, a marked elevation of serum IgG4 (>2 times upper normal limit) is suggestive of type 1 AIP, but false positive elevation can occur also in PC.<sup>4</sup> Radiological findings are different in AIP and PC; abdominal CT/RMN generally show in AIP a diffuse enlargement of the pancreas associated with a typical capsule-like rim and delayed contrast enhancement; on the other hand patients with PC commonly present a mass that takes poor contrast enhancement in pancreatic phase and distal pancreas atrophy.<sup>4,8</sup> Our patient presented atypical radiological pattern of AIP, such as a low-density mass of the pancreatic head, a distal pancreas atrophy and a Wirsung dilatation; in these cases differential diagnosis between the two disorders is more difficult. A peculiar feature of AIP is the response to steroid treatment; however, corticosteroid diagnostic therapy is not generally recommended, and it should only be performed in carefully selected patients after obtaining negative results from a work-up for pancreatic cancer, including EUS-FNA. Finally, histology can give definitive diagnosis of AIP since histopathological pattern is diagnostic for type 1 AIP; typical features are: elevated plasma cells and lymphocytes infiltration, high



**Fig. 2.** Second CT scan: both kidneys present abnormal parenchyma with pseudonodular images and incremented volume.



**Fig. 3.** CT scan one month after starting steroid therapy: kidneys morphological normalization and reduction of the pancreatic lesion (33 mm × 23 mm).

number (>10 cells per HPF) of IgG4 positive plasma cells, storiform fibrosis, venulitis.<sup>4</sup> Reported accuracy and sensitivity of EUS-FNA for diagnosis of pancreatic neoplasm ranges from 75 to 79% to 92%.<sup>9</sup> According to Eloubeidi in case of difficult differential diagnosis between AIP and PC, EUS-FNA should be recommended during the diagnostic workup.<sup>10</sup> However, definitive diagnosis of AIP by EUS-FNA may be difficult, because of the small sample obtained; in our experience EUS-FNA was not diagnostic, and we performed the right diagnosis only after the renal biopsy.

#### 4. Conclusion

AIP can mimic PC, and it could be the pancreatic localization of an IgG4-related systemic disease. For patients presenting with obstructive jaundice and a pancreatic mass, AIP should be considered as a differential diagnosis to avoid unnecessary surgery. Probable diagnosis of AIP may be currently obtained based on careful consideration of a combination of clinical/serological and radiological criteria, eventually extended to other organs involved. Definitive diagnosis of mass-forming AIP is possible only with histological examination; the role of histology is crucial, even if sometimes it is difficult to obtain adequate biopsy material.

#### Conflict of interest

Nothing to declare.

#### Funding

Nothing to declare.

#### Ethical approval

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

#### Author contributions

All authors contributed equally and extensively to this work by discussing the results and implications and commenting on the manuscript at all stages. A. Franchello and S. Silvestri designed the study and they wrote the manuscript in association with F. Gonella. A. Franchello also supervised the paper along with D. Campra. The other authors collected data and reviewed literature articles.

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