

## Quiz Case

# Pancreatic head mass: To Whipple or not to Whipple

Adriana Hogeboom, MD<sup>1</sup>, Enrique Revilla Sánchez, MD<sup>1</sup>, Carolina Ibarrola, MD<sup>1</sup>, Ana Pérez-Campos, MD<sup>1</sup>

<sup>1</sup>Department of Pathology, 12 de Octubre University Hospital, Madrid, Spain.



The patient was a 57-year-old female with a 3.8 cm, solid, lobulated, and ill-defined pancreatic head lesion suspected to represent a primary pancreatic malignancy. An endoscopic ultrasound (EUS) was performed and EUS-guided fine needle aspiration (FNA) of the pancreatic mass was obtained with rapid on-site evaluation (ROSE). The direct smears showed the following [Figure 1].

### \*Corresponding author:

Adriana Hogeboom,  
Department of Pathology, 12  
de Octubre University Hospital,  
Madrid, Spain.

[ahogeboom@alumni.unav.es](mailto:ahogeboom@alumni.unav.es)

Received: 06 February 2023

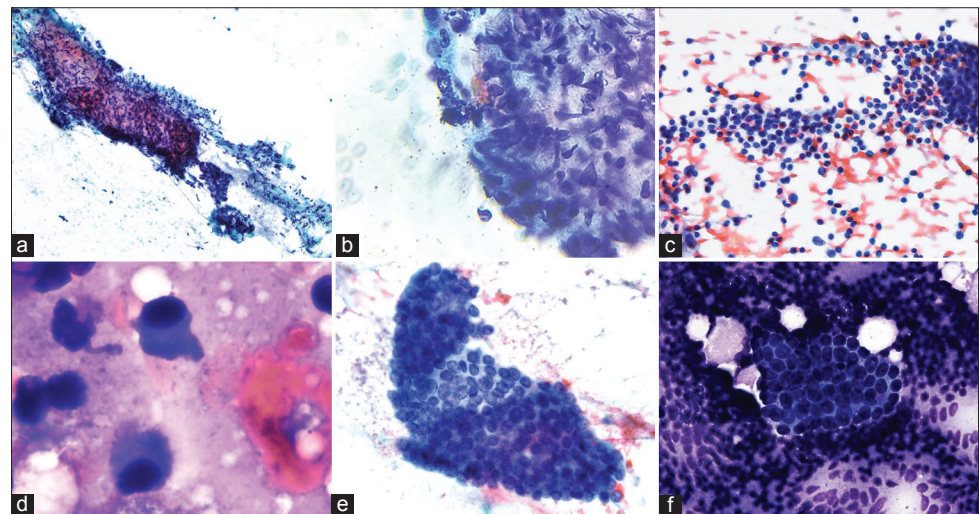
Accepted: 29 April 2023

Published: 01 September 2023

DOI

[10.25259/Cytojournal\\_12\\_2023](https://doi.org/10.25259/Cytojournal_12_2023)

Quick Response Code:



**Figure 1:** (a) and (b) Fragments of fibrous tissue with dense mononuclear cell infiltrate (Papanicolaou stain,  $\times 20$  and  $\times 100$ , respectively). (c) and (d) Dispersed background lymphomononuclear cells and high-power view of plasma cells. Lymphocytic counts of 27/60X field were identified. Plasma cells were less numerous (8/60X field). (Papanicolaou,  $\times 20$  and  $\times 100$ , respectively). (e) and (f) Ductal epithelium with slight nuclear enlargement and disorganization, consistent with mild atypia (Papanicolaou,  $\times 40$  and DiffQuik,  $\times 40$ , respectively).

## QUESTION 1

What is your interpretation?

- Negative for malignancy; mucinous cyst debris of uncertain etiology
- Positive (for malignancy); malignant glandular and squamous cells consistent with adenosquamous carcinoma
- Suspicious (for malignancy); rare markedly atypical epithelial cells suspicious for adenocarcinoma accompanied by fragments of desmoplastic stroma
- Atypical; cellular stromal elements with mononuclear cells and mild ductal epithelial atypia.

## ANSWER TO QUESTION NUMBER 1

The correct cytologic interpretation is: D. Atypical; cellular stromal elements with mononuclear cells and mild ductal epithelial atypia.

The FNA showed numerous fragments of fibrous tissue with a dense lymphomononuclear cell infiltrate present both within the stromal fragments and in the background. Lymphocytic counts of 27/60X field were identified. Plasma cells were less numerous (8/60X field). Immunocytochemical staining for immunoglobulin G4 (IgG4) performed on air-dried smears was non-contributory. Groups of ductal epithelium with mild nuclear atypia were noted. Material was not available for cell block. The case was signed out as, "Atypical; mild ductal epithelial atypia and chronic fibroinflammatory changes."

## ADDITIONAL DETAILS, FOLLOW-UP AND BRIEF DISCUSSION

The patient denied alcohol consumption but had a remote history of tobacco use. Prior to detection of the lesion, she had visited the emergency room on two occasions over a 3-month period due to epigastric pain accompanied by weight loss and anorexia. She eventually underwent cephalic duodenopancreatectomy. Macroscopic examination of the specimen revealed an ill-defined, tan, 4 cm lesion within the pancreatic head. Histologic sections of the lesion [Figure 2] showed dense lymphoplasmacytic infiltrates with perineural accentuation, storiform fibrosis, and acinar atrophy. Non-obliterative lymphoplasmacytic phlebitis and non-necrotizing

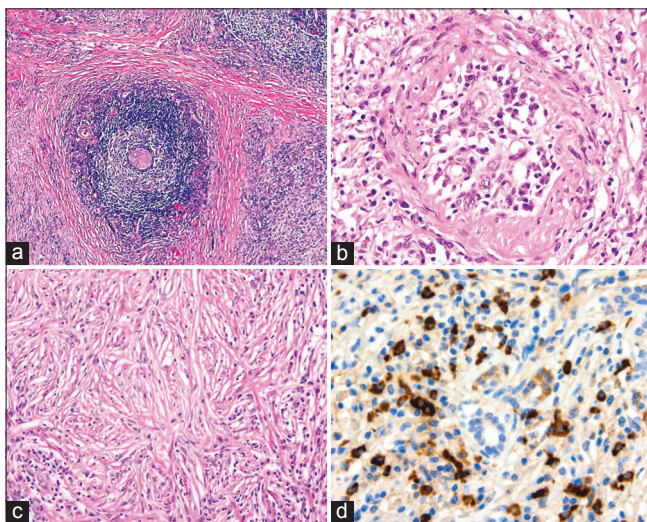
obliterative arteritis were observed. Immunohistochemistry revealed over 50 IgG4-positive plasma cells per high power field and an IgG4 to IgG ratio of over 50%. These findings proved histologically highly suggestive of IgG4-related autoimmune pancreatitis (AIP).

The patient's serum IgG4 level preoperatively was 85 mg/dL and postoperatively rose to 122 mg/dL. Both values were insufficient to meet the serological diagnostic criterion of 136 mg/dL for IgG4-related disease.<sup>[1]</sup> However, clinical follow-up was significant for persistent enlargement of abdominal lymph nodes as well as elevated alkaline phosphatase and gamma-glutamyl transferase, presumed to represent IgG4-related lymphadenopathy and cholangiopathy. Prednisone and methotrexate therapy were initiated with subsequent resolution of lymphadenopathy and normalization of liver enzymes. The patient is asymptomatic 2 years after surgery.

It is important to be aware of mass-forming inflammatory lesions of the pancreas such as AIP which may clinically and radiologically simulate pancreatic malignancy sometimes leading to unnecessary surgical resection. Although EUS guided FNA (EUS-FNA) is often a useful adjunct in the diagnosis of pancreatic lesions, allowing for correct classification of many cases, the preoperative diagnosis of AIP based on EUS-FNA is challenging, and no widely accepted cytologic criteria have been reported.<sup>[2,3]</sup> Furthermore, benign features suggestive of AIP do not rule out false negative results induced by sampling error.<sup>[4]</sup>

## ADDITIONAL QUIZ QUESTIONS

- Q2. All of the following are suggestive of Type 1 AIP over Type 2 AIP, EXCEPT:
- Systemic disease
  - Frequent relapses
  - Swift response to immunosuppression
  - Inflammatory bowel disease (IBD).
- Q3. All are pathological characteristics of Type 1 AIP, EXCEPT:
- Lymphoplasmacytic inflammation with storiform fibrosis
  - Preferential involvement of pancreatic tail
  - IgG4+/IgG+ plasma cell ratio of >40%
  - Obliterative phlebitis.
- Q4. Which of the following is true regarding the cytomorphologic findings of Type 1 AIP:
- Fragments of cellular fibrous stroma are common
  - Ductal epithelial atypia precludes diagnosis of AIP
  - Cytologic findings are highly specific and alone are sufficient for a definitive diagnosis
  - On FNA, AIP is indistinguishable from chronic pancreatitis, NOS.



**Figure 2:** (a) Dense lymphoplasmacytic infiltrate with marked perineural accentuation (H&E,  $\times 4$ ). (b) Obliterative arteritis with recanalization and transmural lymphoplasmacytic inflammatory infiltrate (H&E,  $\times 20$ ). (c) Fibrosis exhibiting a storiform-pattern (H&E,  $\times 20$ ). (d) Numerous immunoglobulin G4 (IgG4)-positive plasma cells (IgG4 immunohistochemistry,  $\times 40$ ).

## ANSWERS TO ADDITIONAL QUIZ QUESTIONS AND BRIEF REVIEW OF THE TOPIC

Q2. (d); Q3. (b); Q4. (a).

Q2. (d) AIP is a pancreatobiliary-centric inflammatory disease, typically marked by corticosteroid responsiveness and classified in two groups. Type 1 AIP often affects elderly males, associates extrapancreatic manifestations of systemic IgG4-related disease (including cholangitis, sialadenitis, retroperitoneal fibrosis, or lymphadenopathy), shows frequent relapses and elevation of serum IgG4 in approximately 80% of cases.<sup>[5]</sup> In contrast, Type 2 AIP is considered to be an isolated pancreatic disorder and does not show elevation of serum IgG4. Recurrence is rare. Interestingly, Type 2 AIP is linked to inflammatory bowel disease (ulcerative colitis or Crohn's disease), seen in up to 16–30% of Type 2 AIP cases.<sup>[5,6]</sup>

Q3. (b) AIP most often involves the head of the pancreas.<sup>[7]</sup> Type 1 AIP is histologically characterized by a dense lymphoplasmacytic infiltrate, storiform fibrosis, obliterative phlebitis, and increased numbers of IgG4 positive plasma cells, typically >50/high-power field, and IgG4+/IgG+ ratio of >40%.<sup>[8]</sup> Lymphoplasmacytic arteritis and a preferentially perineural distribution of inflammation have also been described.<sup>[8,9]</sup> Type 2 AIP is histologically characterized by periductal inflammation with granulocytic epithelial lesions and relative paucity of IgG4-positive plasma cells.<sup>[10]</sup>

Q4. (a) EUS-FNA alone is widely considered to be insufficient to make a definitive diagnosis of AIP, probably at least partially due to a lack of architectural integrity.<sup>[11]</sup> In fact, International Consensus Diagnostic Criteria for AIP (2011) list core/surgical biopsy specimens as preferable for diagnosis of AIP.<sup>[12]</sup> Despite this, certain cytological findings in conjunction with clinicoradiological clues can aid in establishing a diagnosis of AIP in certain cases. A recent retrospective review of AIP FNA results found that cellularity of stromal fragments was significantly higher in AIP than in the control group.<sup>[2]</sup> Furthermore, stromal fragments with embedded lymphocytes (>30/60x) were seen in almost 40% of AIP cases versus 0% in chronic pancreatitis, NOS.<sup>[2]</sup> Other authors have found that AIP is often reported as “atypical” on FNA, probably due to ductal epithelial atypia secondary to surrounding inflammatory and fibrotic changes.<sup>[4]</sup> Performance of IgG4 immunolabeling on the cell block material and/or pre-operative identification of elevated serum IgG4 levels may provide valuable information. Unfortunately, as occurred in the present case, not all cases of Type 1 AIP demonstrate elevated serum IgG4 and cell block material was not available for evaluation.

## SUMMARY

Awareness of AIP's potential to clinically and radiologically simulate pancreatic malignancy is important to avoid unnecessary surgery.

Although AIP on FNA lacks specific cytomorphologic features, cellular stromal fragments, mild ductal epithelial atypia and prominent lymphocytic infiltrate are common findings and may support the diagnosis in the proper context.

Corticosteroid responsiveness and elevated serum IgG4 are useful clues which, in conjunction with suggestive cytomorphology, may reduce gratuitous duodenopancreatectomy.

## COMPETING INTERESTS STATEMENT BY ALL AUTHORS

The authors declare that they have no competing interests.

## AUTHORSHIP STATEMENT BY ALL AUTHORS

AH collected the details of the case, carried out literature review, and drafted the manuscript. APC conceptualized the case, and edited the manuscript. ERS and CI performed data review and review of the manuscript.

## ETHICS STATEMENT BY ALL AUTHORS

Given that this case is without identifiers, our institution does not require approval from the Institutional Review Board.

## LIST OF ABBREVIATIONS (In alphabetic order)

AIP – Autoimmune pancreatitis  
 EUS – Endoscopic ultrasound  
 FNA – Fine needle aspiration  
 GGT – Gamma-glutamyl transferase  
 IBD – Inflammatory bowel disease  
 IgG4 – Immunoglobulin G4  
 MRI – Magnetic resonance image  
 NOS – Not otherwise specified  
 PET-CT – Positron emission tomography - computed tomography  
 ROSE – Rapid on-site evaluation

## EDITORIAL/PEERREVIEW STATEMENT

To ensure the integrity and highest quality of CytoJournal publications, the review process of this manuscript was conducted under a **double-blind model** (the authors are blinded for reviewers and vice versa) through automatic online system.

## REFERENCES

1. Umehara H, Okazaki K, Kawa S, Takahashi H, Goto H, Matsui S, *et al.* The 2020 revised comprehensive diagnostic (RCD) criteria for IgG4-RD. *Mod Rheumatol* 2021;31:529-33.
2. Deshpande V, Mino-Kenudson M, Brugge WR, Pitman MB, Castillo CF, Warshaw AL, *et al.* Endoscopic ultrasound guided fine needle aspiration biopsy of autoimmune pancreatitis: Diagnostic criteria and pitfalls. *Am J Surg Pathol* 2005;29:1464-71.
3. Yoon SB, Moon SH, Song TJ, Kim JH, Kim MH. Endoscopic ultrasound-guided fine needle aspiration versus biopsy for diagnosis of autoimmune pancreatitis: Systematic review and comparative meta-analysis. *Dig Endosc* 2021;33:1024-33.
4. Holmes BJ, Hruban RH, Wolfgang CL, Ali SZ. Fine needle aspirate of autoimmune pancreatitis (lymphoplasmacytic sclerosing pancreatitis): cytomorphologic characteristics and clinical correlates. *Acta Cytol* 2012;56:228-32.
5. Shinagare S, Shinagare AB, Deshpande V. Autoimmune pancreatitis: A guide for the histopathologist. *Semin Diagn Pathol* 2012;29:197-204.
6. Tsen A, Alishahi Y, Rosenkranz L. Autoimmune pancreatitis and inflammatory bowel disease: An updated review. *J Clin Gastroenterol* 2017;51:208-14.
7. Raina A, Yadav D, Krasinskas AM, McGrath KM, Khalid A, Sanders M, *et al.* Evaluation and management of autoimmune pancreatitis: Experience at a large US center. *Am J Gastroenterol* 2009;104:2295-306.
8. Deshpande V, Zen Y, Chan JK, Yi EE, Sato Y, Yoshino T, *et al.* Consensus statement on the pathology of IgG4-related disease. *Mod Pathol* 2012;25:1181-92.
9. Farris AB 3<sup>rd</sup>, Basturk O, Adsay NV. Pancreatitis, other inflammatory lesions, and pancreatic pseudotumors. *Surg Pathol Clin* 2011;4:625-50.
10. Chari ST, Kloppel G, Zhang L, Notohara K, Lerch MM, Shimosegawa T. Histopathologic and clinical subtypes of autoimmune pancreatitis: the Honolulu consensus document. *Pancreatology* 2010;10:664-72.
11. Majumder S, Chari ST. EUS-guided FNA for diagnosing autoimmune pancreatitis: Does it enhance existing consensus criteria? *Gastrointest Endosc* 2016;84:805-7.
12. 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;40:352-8.

**How to cite this article:** Hogeboom A, Revilla Sánchez E, Ibarrola C, IbarrolaPérez-Campos A. Pancreatic head mass: To Whipple or not to Whipple. *CytoJournal* 2023;20:28.

HTML of this article is available FREE at:  
[https://dx.doi.org/10.25259/Cytojournal\\_12\\_2023](https://dx.doi.org/10.25259/Cytojournal_12_2023)

**The FIRST Open Access cytopathology journal**

Publish in *CytoJournal* and **RETAIN** your *copyright* for your intellectual property

**Become Cytopathology Foundation Member** to get all the benefits

Annual membership fee is nominal US \$ 50 (US \$ 1000 for life)

**In case of economic hardship it is free**

For details visit <https://cytojournal.com/cf-member>

PubMed indexed

**FREE** world wide open access

**Online processing** with rapid turnaround time.

**Real time** dissemination of time-sensitive technology.

Publishes as many **colored high-resolution images**

Read it, cite it, bookmark it, use RSS feed, & many----



**CYTOJOURNAL**

[www.cytojournal.com](http://www.cytojournal.com)

Peer-reviewed academic cytopathology journal





# NextGen CelBloking™ Kits

**Frustrated with your cell blocks?  
We have a better solution!**

**Nano**

## Nano NextGen CelBloking™

Cell block kit to process single scattered cell specimens and tissue fragments of **any** cellularity.



**PATENT PENDING**



**Pack #1**



**Pack #2**

**Micro**

## Micro NextGen CelBloking™

For cellular specimens (more than 1 ml concentrated specimen with Tissuecrit more than 50%)



**PATENT PENDING**



**Pack #2**