ACG CASE REPORTS JOURNAL

CASE REPORT | PANCREAS

Unicentric Castleman Disease Coexisting With Type 2 Autoimmune Pancreatitis: A Case Report Mimicking Pancreatic Cancer and Near-Whipple Surgery

Joel Gabin Konlack Mekontso, MD[1], Akil Olliverrie, MD[1], Jingwei Ren, OMS-4[2], Veronika Stefanishina, MD[1], Syed Karim, DO[3], Shahbaz Khan, MD[1], Thomas McIntyre, MD[1], and Mohammad Choudhry, MD[1]

[1]*NYC Health + Hospitals South Brooklyn Health, Brooklyn, NY*
[2]*Touro University College of Osteopathic Medicine, Harlem, NY*
[3]*NYU Langone Health, Brooklyn, NY*

ABSTRACT

This case describes a 46-year-old man presenting with epigastric pain, weight loss, and obstructive jaundice, initially misdiagnosed as pancreatic cancer due to a pancreatic head mass compressing the common bile duct. Intraoperative biopsies during an aborted Whipple procedure revealed coexisting autoimmune pancreatitis and Castleman disease. This case highlights the diagnostic challenges of Castleman disease, its potential association with autoimmune pancreatitis, and the critical role of histological analysis in differentiating it from malignancy.

KEYWORDS: unicentric Castleman disease; autoimmune pancreatitis; pancreatic head cancer; IgG-4–related disease; diagnostic and therapeutic challenge

INTRODUCTION

Unicentric Castleman Disease (UCD) is a rare lymphoproliferative disorder typically confined to a single lymph node region, often presenting with an indolent course. Its nonspecific symptoms and potential involvement of various organs often mimic malignancies or infections, posing significant diagnostic challenges. We present a unique case of UCD coexisting with autoimmune pancreatitis (AIP), manifesting as a pancreatic head mass, highlighting the complexity of diagnosis and management in such scenarios. This paper adheres to the Case Report (CARE) guidelines.[1]

CASE REPORT

A 46-year-old man with no prior medical history presented to the emergency department with 2 weeks of persistent sharp epigastric pain, poor appetite, 5-pound weight loss, and 3 days of jaundice. He denied pruritus, pale stools, dark urine, or fever. He was a nonsmoker and nondrinker, with no family history of malignancy. On examination, he was vitally stable with scleral icterus and epigastric tenderness but no lymphadenopathy or Courvoisier sign.

Initial labs revealed elevated transaminases, alkaline phosphatase, total and direct bilirubin with normal lipase, and liver synthetic function (Table 1). Viral studies (including Herpes 8 polymerase chain reaction), serum immunoglobulin G4 (IgG4) levels, and tumor markers were largely unremarkable, except for a mildly elevated cancer antigen 19-9 at 54. The differential diagnoses considered were those of an extrahepatic bile duct obstruction, with a particular focus on malignant, inflammatory, and infectious causes. Within 24 hours, abdominal ultrasonography followed by a computed tomography scan and magnetic resonance cholangiopancreatography identified a 3.2 × 3.0-cm pancreatic head mass causing common bile duct (CBD) obstruction and intrahepatic ductal dilatation (Figure 1). Endoscopic ultrasound was recommended by radiology for further characterization of the pancreatic mass, but it was unavailable. Endoscopic retrograde cholangiopancreatography confirmed external CBD compression

ACG Case Rep J 2025;12:e01635. doi:10.14309/crj.0000000000001635. Published online: March 3, 2025

Correspondence: Joel Gabin Konlack Mekontso, MD (konlackj@nychhc.org).

Table 1. Changes in liver chemistry over time

Laboratory tests	Admission	Day 1	Day 5	At discharge	After 4 weeks on prednisone	Normal range
Albumin (g/dL)	4.1	3.8	4.3	3.3	4.4	3.5–5.2
Aspartate aminotransferase (U/L)	383	377	171	49	22	< = 50
Alanine aminotransferase (U/L)	723	687	609	138	49	< = 50
Alkaline phosphatase (U/L)	756	692	608	264	113	40–129
Total bilirubin (mg/dL)	4.9	5.8	2.4	1.1	0.4	0.2–1.2
Direct bilirubin (mg/dL)	3.6	4.6	—	—	—	0.0–0.3
International normalized ratio	1.0	—	—	1.2	—	0.9–1.1
Ethanol (mg/dL)	< 10	—	—	—	—	< = 10
Carcinoembryonic antigen (ng/mL)	—	2.5	—	—	—	0.0–3.8
α-fetoprotein (ng/mL)	—	3.3	—	—	—	< = 8.3
Cancer antigen 19-9 (U/mL)	—	54	—	—	—	< = 35
IgG (mg/dL)	—	—	1,190	—	—	610–1,660
IgG subset 4 (mg/dL)	—	—	56.5	—	—	1.0–123.0

At week 4 of treatment, additional workup was performed, including serum lactate dehydrogenase, ferritin, fibrinogen, antinuclear antibody, a complete immunoglobulin panel, serum protein electrophoresis with immunofixation, as well as testing for HIV, Hepatitis B surface antigen, Hepatitis B core antibody, and human herpesvirus-8 polymerase chain reaction. All results were unremarkable.

(Figure 2), and a stent was placed. Cytology showed inflammatory debris only. Suspecting pancreatic malignancy, a Whipple procedure was planned but aborted intraoperatively due to portal vein involvement. He was discharged on postoperative day 3. Histological analysis of excisional biopsies from the periportal lymph nodes revealed findings consistent with mixed cell type Castleman disease (Figures 3 and 4) and excluded malignancy. Biopsies of the pancreatic mass (Figures 5 and 6) were suggestive of Type 2 AIP. Immunohistochemistry also identified polyclonal IgG heavy chains, with specific detection of IgG4-positive plasma cells (IgG4/IgG $<$ 5%) using the MRQ-44 marker. This transformed the prognosis from malignancy to a treatable inflammatory disorder.

Three weeks after the initial presentation, the patient was started on prednisone at a dose of 0.6 mg/kg/d, totaling 40 mg divided into 2 daily doses, for 6 weeks to treat AIP. Five weeks later, the oncology tumor board reviewed the case and endorsed continuing steroid therapy. The patient responded well to treatment, with no adverse effects. Liver enzymes normalized by week 4 (Table 1), and the pancreatic mass decreased in size to 2.4 $\times$ 1.8 cm by week 7. A follow-up endoscopic retrograde cholangiopancreatography showed a patent CBD, leading to stent removal. Steroids were subsequently tapered by 5 mg weekly, and the patient remained symptom-free during this period. However, 2 weeks after completing the taper, he developed abdominal pain and intermittent bloody diarrhea. Further evaluation with esophagogastroduodenoscopy and colonoscopy revealed diffuse inflammation of the cecum and rectosigmoid colon, raising suspicion of ulcerative colitis.

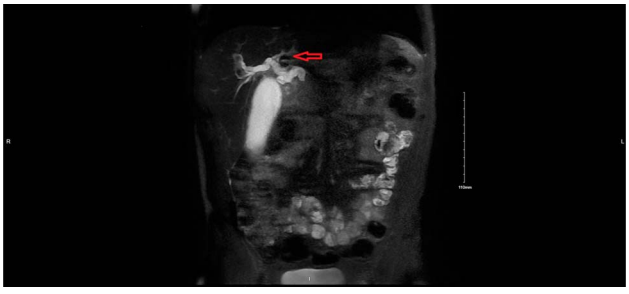

Figure 1. Magnetic resonance cholangiopancreatography showing tortuosity of the biliary tree and a short segment stricture of the distal common bile duct (red arrow).

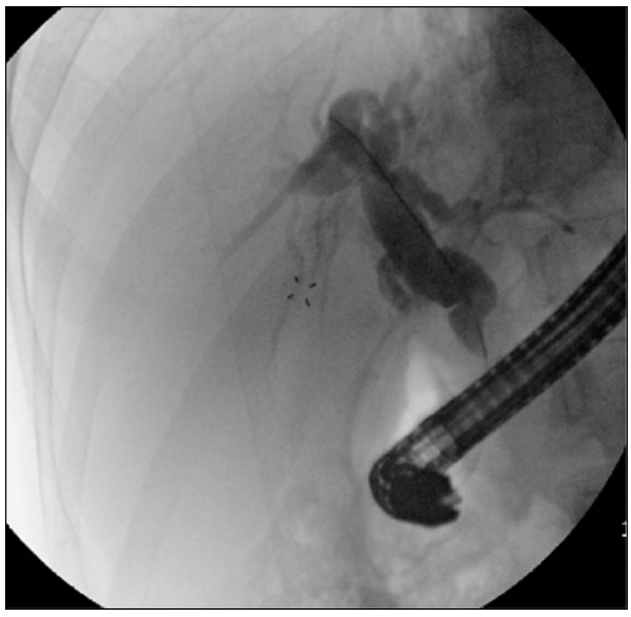

Figure 2. Endoscopic retrograde cholangiopancreatography demonstrating abrupt cutoff of the common bile duct and ductal dilation by externally compressing mass.

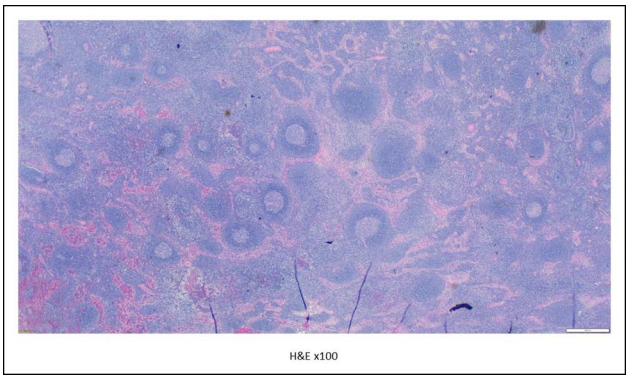

Figure 3. Lymph node biopsy showing thickened mantle zones with lymphocytes arranged in layers (onion skin appearance), extensive vascular proliferation and perivascular hyalinization in the interfollicular areas. Hematoxylin eosin stain, magnitude ×100.

Histological analysis confirmed the diagnosis, showing colonic mucosa with moderate acute colitis, cryptitis, and crypt abscesses. The patient was started on mesalamine 1,600 mg 3 times daily and achieved complete symptom resolution by his last follow-up, approximately 8 months after the initial presentation.

DISCUSSION

Castleman Disease (CD), also referred to as angiofollicular lymph node hyperplasia or giant lymph node hyperplasia, is a rare and typically benign lymphoproliferative disorder. It commonly presents as a solitary mass within lymph nodes or visceral organs, characterized by progressive enlargement. CD is divided into UCD, which involves a single lymph node or region, and multicentric CD (MCD), which affects multiple lymph node stations.[2,3] While UCD generally follows an indolent course, MCD can have a more aggressive and systemic presentation.[2] Histologically, CD exhibits a spectrum of findings, ranging from hyperplastic germinal centers with plasmacytosis (plasma cell histopathology) to atrophic germinal centers with hypervascularity (hypervascular histopathology), with a mixed histopathological pattern lying between these extremes.[2,3]

The annual incidence of CD in the United States is estimated to be 4,300–5,200 cases.[2] UCD, which most commonly manifests in the fourth decade of life, shows no significant gender or racial predilection. Frequently affected sites include the abdomen (34.4%), chest (33.6%), and head and neck (22%), with less common involvement of the axilla and pelvis.[1]

Emerging evidence suggests that UCD is a clonal neoplastic process originating from follicular dendritic cells. Recent genetic studies have identified somatic mutations in platelet-derived growth factor receptor beta in approximately 20% of UCD cases, supporting this theory. These mutations in stromal cells provide a proliferative and survival advantage, as demonstrated in vitro. In contrast, the etiology of MCD remains less well understood.[2] Some cases are linked to human herpesvirus-8 infection and subsequent viral interleukin-6 (vIL-6) production, a hypothesis supported by the efficacy of anti–IL-6 therapies in certain patients.

Autoimmune conditions are most commonly associated with MCD. The coexistence of CD and AIP is exceptionally rare and is typically observed in patients with HIV and human herpesvirus-8 positivity, which was not the case for our patient.[4,5] The proposed pathophysiological mechanism involves an inflammatory cascade triggered by the presentation of *Helicobacter pylori* antigens exhibiting molecular mimicry with pancreatic self-antigens. This process activates antigen-presenting cells, leading to a humoral immune response in which regulatory T cells stimulate IL-6—also implicated in CD pathogenesis—and subsequently drive IgG4 production.[4,6] This hypothesis seems plausible in our case, as gastric biopsies revealed the presence of *Helicobacter pylori*. In addition, this rare pathology may be linked to other autoimmune conditions, such as ulcerative colitis, as observed in our case. While steroid-induced colitis was considered given the timing of the abdominal pain and bloody diarrhea, the rectosigmoid colon

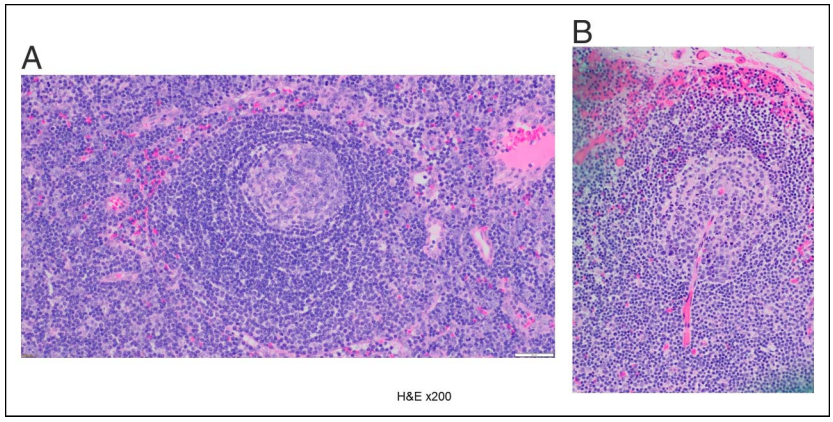

Figure 4. Lymph node biopsy showing (A) a thickened mantle zone with lymphocytes arranged in layers, (B) an atretic germinal center traversed by a sclerotic penetrating vessel and hyalinization (lollipop follicle). Hematoxylin eosin stain, magnitude ×200.

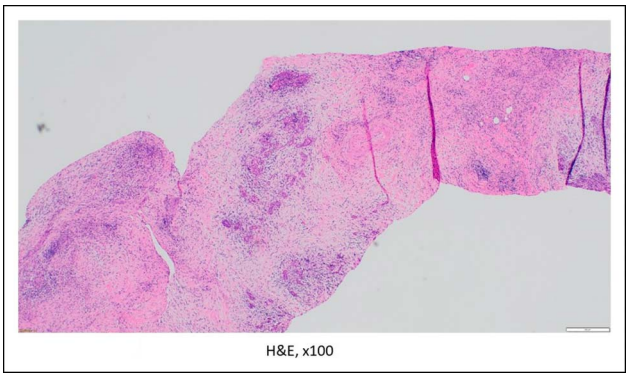

Figure 5. Pancreatic biopsy showing acinar and periductal lymphoplasmacytic inflammatory infiltrate. Lobular fibrosis is also present. Hematoxylin eosin stain, magnitude ×100.

involvement, typical histological findings, and the patient's positive response to mesalamine made this diagnosis less probable.

UCD can be incidentally detected in imaging studies as a solitary enlarged lymph node.[3] It may also present with nonspecific symptoms or as a solitary, progressively enlarging mass causing organ compression, as observed in our case. Due to its rarity and varied clinical presentations, diagnosis can be challenging. Differential diagnoses include lymphoma and in cases involving the pancreas, neuroendocrine tumors, or paragangliomas.[3,7,8] A definitive diagnosis is made through histopathological examination, which reveals the characteristic features of CD.[3]

The treatment of UCD primarily involves surgical resection, regardless of histopathologic subtype, as in our case, with prednisone used for managing AIP.[3,9,10] Complete surgical excision is often curative, leading to the resolution of both symptoms and laboratory abnormalities.[3] In unresectable cases, alternative therapies such as radiation therapy, embolization, or targeted treatments with rituximab (anti-CD20 antibody), siltuximab (anti–IL-6 monoclonal antibody), and tocilizumab (IL-6 receptor antagonist) are viable options.[3] The prognosis for UCD after complete surgical resection is excellent, with 10-year survival rates exceeding 95% in some cohorts.[10]

In conclusion, this case illustrates the complexity of diagnosing and managing UCD, particularly when coexisting with AIP. The diagnostic overlap with malignancies and other rare conditions highlights the critical role of comprehensive histopathological evaluation. This case also suggests a potential association between UCD and AIP, pointing to shared immunological pathways that warrant further investigation. Complete surgical resection remains the cornerstone of UCD treatment, offering an excellent prognosis when achieved. Continued research is essential to better understand the interplay between these conditions and to optimize both diagnostic and therapeutic strategies.

DISCLOSURES

Author contributions: All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work. Concept and design: JG Konlack Mekontso, A. Olliverrie, J. Ren, V. Stefanishina, S. Karim, S. Khan, T. McIntyre, and M. Choudhry. Acquisition, analysis, or interpretation of data: JG Konlack Mekontso, A. Olliverrie, J. Ren, V. Stefanishina, S. Karim, S. Khan, T. McIntyre, and M. Choudhry. Drafting of the manuscript: JG Konlack Mekontso, A. Olliverrie, J. Ren, V. Stefanishina, and S. Karim. Critical review of the manuscript for important intellectual content: JG Konlack Mekontso, A. Olliverrie, J. Ren, V. Stefanishina, S. Karim, S. Khan, T. McIntyre, and M. Choudhry. Supervisor and article guarantor: M. Choudhry.

Acknowledgments: We would like to express our sincere appreciation to Mrs. Vera Platsky for preparing and providing the pathology slides, and to Dr. Sushant Remersu for his valuable contributions and critical insights, which have significantly enhanced the quality of this manuscript.

Financial disclosure: None to report.

Previous presentation: This work was presented as a poster at the American College of Gastroenterology's conference on October 27, 2024, in Philadelphia, PA.

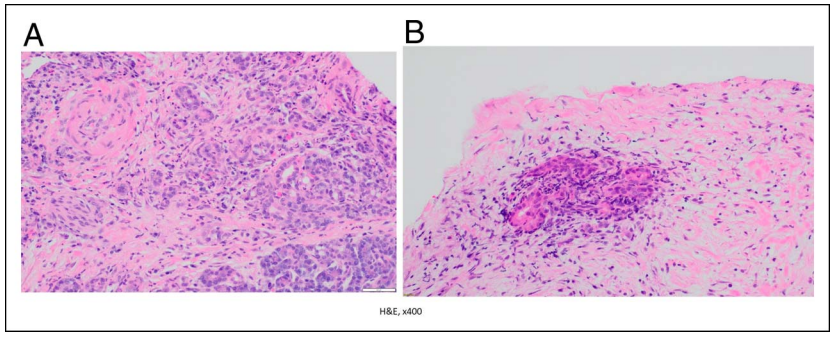

Figure 6. Pancreatic biopsy showing (A) acini with granulocytic and lymphoplasmacytic inflammatory infiltrate, (B) granulocytic epithelial lesions with parenchymal fibrosis. Hematoxylin eosin stain, magnitude ×400.

Informed consent was obtained for this case report.

Received December 24, 2024; Accepted February 4, 2025

REFERENCES

1. Riley DS, Barber MS, Kienle GS, et al. CARE guidelines for case reports: Explanation and elaboration document. *J Clin Epidemiol.* 2017;89:218–35.
2. Hoffmann C, Oksenhendler E, Littler S, Grant L, Kanhai K, Fajgenbaum DC. The clinical picture of Castleman disease: A systematic review and meta-analysis. *Blood Adv.* 2024;8(18):4924–35.
3. Dispenzieri A, Fajgenbaum DC. Overview of Castleman disease. *Blood.* 2020;135(16):1353–64.
4. Gatti-Mays ME, Kardon D, Chieu TT, Firozvi K. Autoimmune pancreatitis in the setting of multifocal Castleman disease in an HIV-negative, HHV-8-negative, 70-year-old man. *Clin Adv Hematol Oncol.* 2012;10:683–6.
5. Miwa I, Watanabe F, Maruyama Y, et al. [A case of Castleman disease (plasma cell type) in which autoimmune pancreatitis developed 6 years later]. *Nihon Shokakibyo Gakkai Zasshi.* 2007;104(2):239–44.
6. Nicoli P, Guerrasio A. Autoimmune pancreatitis, IgG4-related disease, and Castleman disease: Is there a link? *Clin Adv Hematol Oncol.* 2012;10:687–8.
7. Zhou J, Wang C, Chen Z. Hepatobiliary and pancreatic: Castleman disease of the pancreas diagnosed by endoscopic ultrasound. *J Gastroenterol Hepatol.* 2021;36(8):2036.
8. Liu SL, Luo M, Gou HX, Yang XL, He K. Castleman disease of the pancreas mimicking pancreatic malignancy on 68Ga-DOTATATE and 18F-fluorodeoxyglucose positron emission tomography/computed tomography: A case report. *World J Gastrointest Surg.* 2022;14(5):514–20.
9. Mitsos S, Stamatopoulos A, Patrini D, George RS, Lawrence DR, Panagiotopoulos N. The role of surgical resection in unicentric Castleman's disease: A systematic review. *Adv Respir Med.* 2018;86(1):36–43.
10. Talat N, Belgaumkar AP, Schulte KM. Surgery in Castleman's disease: A systematic review of 404 published cases. *Ann Surg.* 2012;255(4):677–84.