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CASE REPORT

Primary extranodal jejunal diffuse large B cell lymphoma as a diagnostic challenge for intractable emesis: a case report and review of literature

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ABSTRACT

Introduction: The gastrointestinal tract is the most common extranodal site for non-Hodgkin's lymphoma, with the most common being diffuse large B cell lymphoma. Unlike the stomach or the ileum, the jejunum is a rare site for primary extranodal lymphomas, given the scarcity of lymphoid tissue. Due to its location, inflammation in the jejunum may not be visualized on routine imaging or endoscopy, making jejunal lymphoma difficult to diagnose.
Case Description: We present a case of a 90-year-old male with 1 week of intractable emesis, initially thought to be due to viral gastroenteritis. His symptoms never improved and he underwent serial CT imagings in addition to esophagogastroduodenoscopy. A stomach biopsy and a diagnostic paracentesis did not reveal any malignant cells, but a CT enterography revealed significant jejunal inflammation with obstruction. After a month of hospitalization, a jejunal biopsy was obtained, which showed proliferation of neoplastic B cells. He was ultimately diagnosed with primary jejunal diffuse large B cell lymphoma.
Discussion: Chemotherapy and surgical resection are typically the definitive treatment for extranodal lymphoma. Clinicians, however, must carefully consider the patient's functional and nutritional statuses before offering such interventions. This case was a diagnostic challenge and demonstrated a rare GI malignancy's convoluted mimicking nature.

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KEYWORDS
Non-Hodgkin's lymphoma; extranodal diffuse large B cell lymphoma; gastrointestinal lymphoma

1. Background

Diffuse large B cell lymphoma (DLBCL), the most common subtype of non-Hodgkin's lymphoma (NHL), can either be primary nodal disease or solely extranodal [1]. Among the extranodal sites of non-Hodgkin's lymphoma, the gastrointestinal (GI) tract is the most common site [2]. Within the GI tract, the stomach is the most common site for primary malignant lymphoma followed by the small intestine [2,3]. Contrary to the ileum, the jejunum has less lymphoid tissue and is a particularly rare site for primary DLBCL [4]. The clinical presentation of DLBCL of the jejunum is often insidious and nonspecific with fever, weight loss, fatigue, anorexia, abdominal pain, nausea, and vomiting [5,6]. Unlike primary gastric NHL, which can be managed with or without surgery as there is no significant difference in survival, primary intestinal NHL has a higher overall mortality. Hence, surgery with postoperative chemotherapy and/or radiation is preferred [6–8]. A handful of cases of primary jejunal DLBCL have been reported in the literature, all of which had resulted in surgical intervention and histopathological diagnosis of DLBCL [9–11]. This disease is often misdiagnosed initially due to its nonspecific presentation and similarities in presentation to other diseases. We present a case of a 90-year-old male who presented with intractable vomiting, which was eventually diagnosed as primary jejunal DLBCL, to demonstrate the diagnostic challenge of this disease.

2. Case presentation

A fully functional 90-year-old Hispanic male presented to the emergency department with 1 day of nausea and vomiting. He had non-radiating, periumbilical and upper abdominal pain with non-bilious, non-bloody emesis. He has no blood or coffee-ground material in his vomitus. He denied any diarrhea or constipation. He had been unable to tolerate oral intake of any amount or consistency. These symptoms occurred acutely without any notable inciting factors. He denied subjective fevers, night sweats, or subjective weight loss, but had a recorded five pounds weight loss over 1 month. He had a good appetite prior to the onset of his symptoms, but he had been unable to eat or drink due to nausea and vomiting.

The patient has a past medical history of coronary artery disease, hypertension, hyperlipidemia, aortic regurgitation, mitral regurgitation, hypothyroidism, asthma, and pre-diabetes. He has a family history of

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thyroid disease, but he does not have a family history of cancers. He denies tobacco, alcohol, or recreational drug use. On presentation, his vital signs were within normal limits. On examination, he appeared lean and comfortable without evidence of distress or diaphoresis. He was alert and oriented to person, time, and place. His heart and lung exams were unremarkable. He had a soft abdomen with normoactive bowel sounds and mild tenderness to palpation of his periumbilical region and bilateral upper quadrants of his abdomen. He has no rebound tenderness and no guarding. His lower extremities had 2+ pitting edema to the mid-calves. Laboratory testing revealed no significant abnormalities on basic metabolic panel, complete blood count, and thyroid function panel. His CT of the abdomen and pelvis with intravenous contrast showed a mild ileus with diffuse wall thickening, edema and mucosal thickening of small bowel loops and colon concerning for enterocolitis, significant diverticulosis, and moderate ascites. He was started on intravenous piperacillin-tazobactam and metronidazole with some improvement in symptoms, and he was able to tolerate oral intake with decreased emesis. He was discharged on oral ciprofloxacin and metronidazole, but returned to the hospital the same day and was readmitted hours later for recurrent symptoms.

The patient was started on several antiemetics, including scheduled ondansetron and prochlorperazine with as needed metoclopramide, trimethobenzamide, and promethazine for symptomatic control. Despite that, he was still unable to tolerate any oral intake and continued to have nausea and vomiting of clear-yellow fluid and feeding materials without hematemesis and coffee-ground contents. Gastroenterology consultation was obtained on hospital day three. It was thought that he most likely had viral gastroenteritis. The team therefore discontinued antibiotics and monitored him clinically.

By hospital day 5, the patient showed no improvement, and a repeat CT of the abdomen and pelvis with intravenous contrast was performed, which showed persistent gastric antral wall thickening and narrowed lumen suspicious for gastric malignancy, diffuse omental infiltration, and concerns for linitis plastica (Figure 1). He subsequently underwent esophagogastroduodenoscopy (EGD), which showed severe reflux esophagitis from recurrent emesis, a 2-cm hiatal hernia, delayed gastric emptying, extrinsic compression on lesser curvature of stomach, and white nummular lesions in the gastric antrum. Biopsy of the stomach was performed, which later showed no malignant cells. Serial abdominal x-ray found no obstruction.

The patient's hospital course was complicated by intermittent, self-limiting fevers, and his vomiting progressed to copious bilious emesis. Blood culture, urinalysis, and chest x-ray showed no source of infection. An abdominal ultrasound showed no biliary obstruction or cirrhosis but again demonstrated ascites. Due to his fever and ascites, paracentesis was performed to evaluate for spontaneous bacterial peritonitis. His ascites fluid analysis was unremarkable for infection, with a serum-ascites albumin gradient of 0.4 g/dL and total protein of ascitic fluid of 3.2 g/dL, which was concerning for either tuberculosis or peritoneal carcinomatosis. His ascites fluid, however, did not show any organisms on acid-fast bacilli smear and culture and had no malignant cells on cytological analysis. His clinical status continued to decline, with ongoing emesis and inability to have oral intake. A nasogastric tube was placed for enteral feeding, which was intermittently held due to ongoing emesis that occurred shortly after being on enteral feeds. CT enterography demonstrates progressive dilatation of the second and third duodenal segments with transition to a nondilated, thick-walled

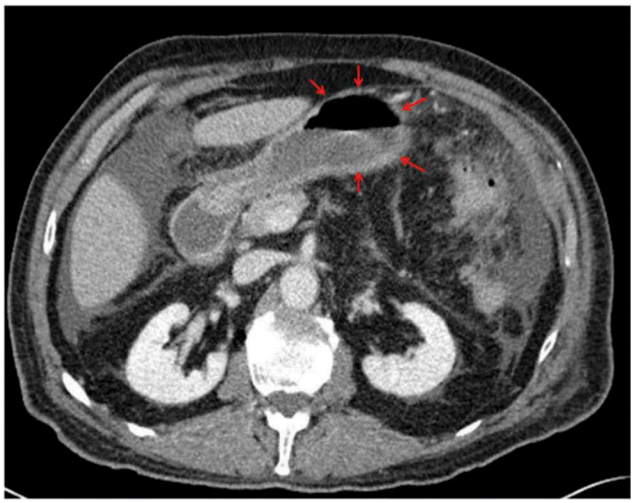

Figure 1. Computed tomography of the abdomen and pelvis with intravenous contrast displaying gastric antral wall thickening (arrows), diffuse omental infiltration, and linitis plastica.

distal fourth duodenal and jejunal segments suspicious for possible primary bowel malignancy. Along with the multifocal liver lesions, moderate ascites, and distinctive reticular infiltration of the omentum also seen on CT, this was highly suggestive of enteropathic non-Hodgkin's lymphoma (Figure 2). Given the rapid progression over a period of 3 weeks, however, these findings were thought to be more consistent with an infectious or inflammatory process rather than an aggressive neoplastic process with metastasis.

Repeat esophagogastroduodenoscopy with push enteroscopy showed Grade D esophagitis, gastritis, and jejunal inflammation with edema and erythema (Figure 3). The obtained biopsy from this procedure demonstrated a transition from normal jejunal mucosa to pathologically-involved and distorted mucosa, which was characterized by diffuse infiltrate of large neoplastic cells with highly irregular nuclei, moderate amount of cytoplasm, and centroblastic morphology. Immunohistochemistry identified sheets of B cells expressing CD45, CD20, CD79a, and BCL6 (subset), but not CD10, MUM1, CD138, cyclin D1, and cytokeratin AE1/AE3. This therefore affirmed the diagnosis of DLBCL, specifically the germinal center B cell type based on the Hans algorithm. The proliferation index (Ki-67) was approximately 90% (Figure 4).

Due to the patient's continued emesis, he developed a fever and was found to have aspiration pneumonia on chest x-ray. He was treated with a 7-day course of ampicillin-sulbactam and was started on partial parenteral nutrition. Palliative care and hematology/oncology consultation services were involved in his care. After a discussion with the patient and his family, it was decided that due to his poor nutritional status and deconditioned state, he would not pursue aggressive therapies such as surgery or chemotherapy.

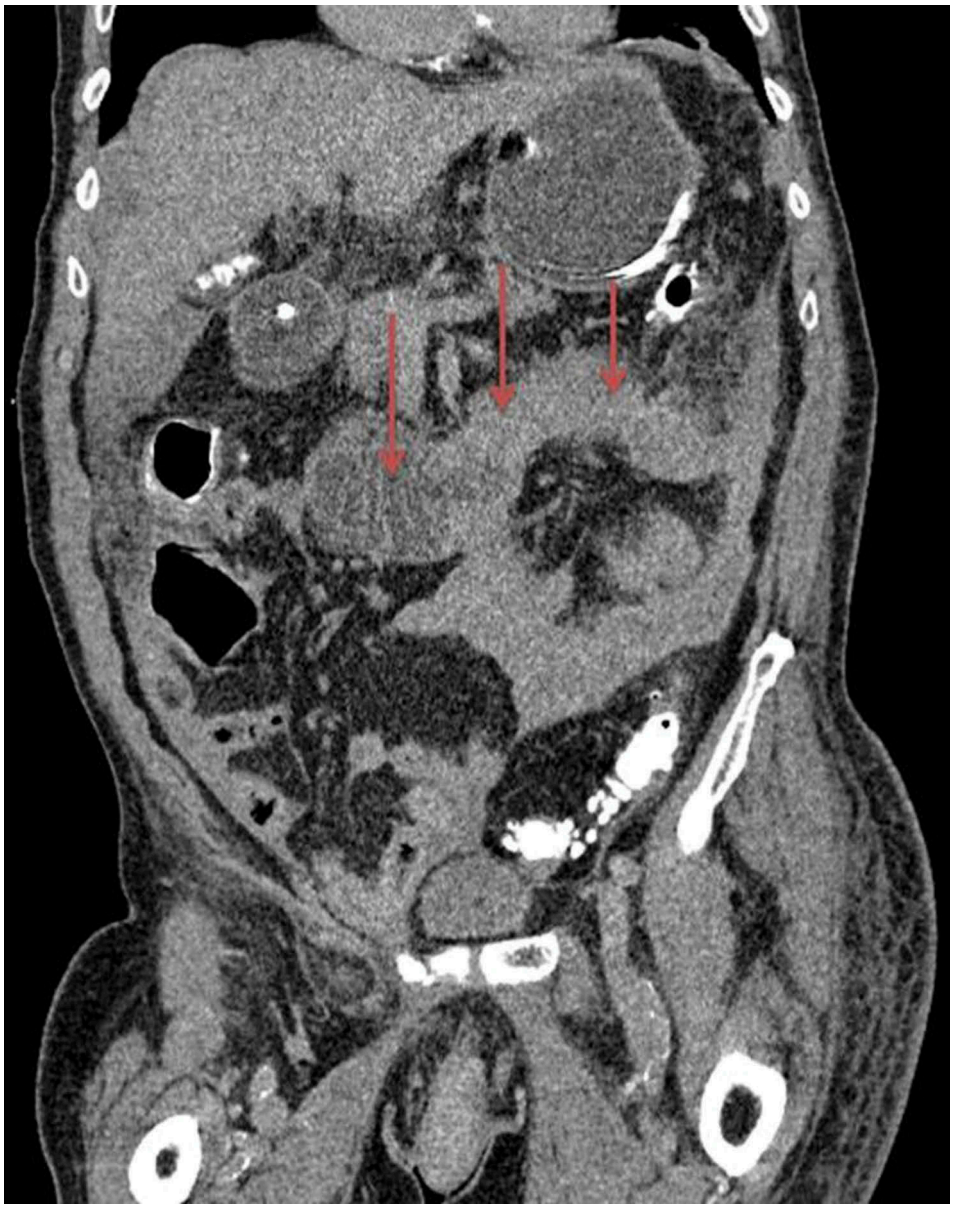

Figure 2. Computed tomography enterography showing jejunal inflammation with edema.

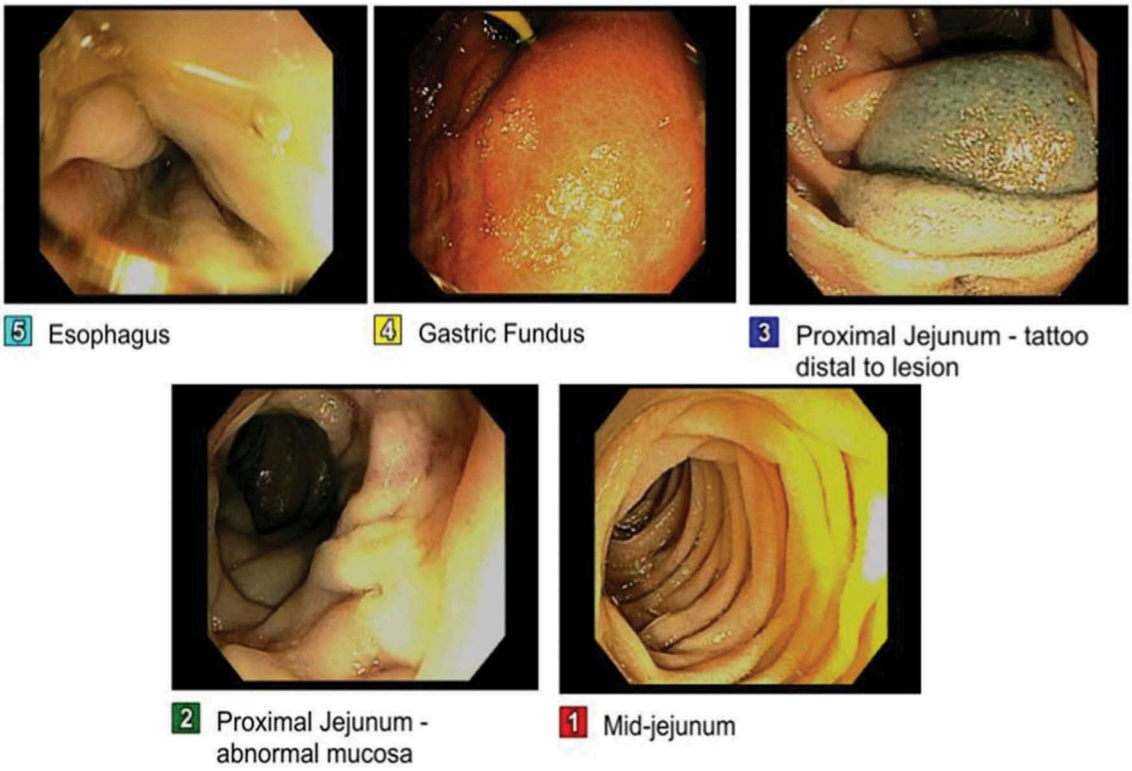

Figure 3. Direct visualization of the GI tract by push enteroscopy, showing abnormal proximal jejunal mucosa and swelling.

The patient received a peripherally inserted central catheter for total parenteral nutrition on hospital day 24 and was discharged the following day for home hospice. He did not receive any follow-up after discharge and eventually expired.

3. Discussion

The acuity of intractable emesis and the nonspecific symptoms of abdominal pain and decreased oral intake without any radiographic evidence of obstruction, as in this case, presented itself as a diagnostic challenge. The cause was initially attributed to gastroenteritis with post-infectious gastroparesis; however, the prolonged hospitalization with lack of symptomatic improvement suggested an alternate underlying cause. Although several factors including his age, radiographic findings of linitis plastica and ascites were highly suggestive of a malignant process, extensive workup did not directly point to a specific diagnosis. The initial CT of the abdomen and pelvis with intravenous contrast commented on mild ileus and diffuse wall thickening and mesenteric edema and abdominal pelvic ascites, but it did not reveal any obstructive masses or enlarged lymph nodes. These findings reassured the clinician and led to an initial diagnosis of gastroenteritis.

Repeat CT imaging, however, reported antral wall thickening, linitis plastic, and diffuse omental infiltration, which was concerning for gastric malignancy. Subsequent EGD did not show any esophageal or duodenal obstructions. Although extrinsic compression of the stomach was observed, there were no masses identified on imaging. Furthermore, both the stomach biopsy and cytological analysis of ascitic fluid did not reveal any malignant cells, which may have provided false reassurance. Persistent symptoms without any improvements prompted a CT enterography. CT enterography, compared to routine CT abdomen and pelvis, uses thinner sectioning and enteric contrast to display the small bowel in its entirety and includes assessment for entire bowel wall thickness along with surrounding mesenteric and perienteric fat. This ultimately revealed the jejunum as the site of obstruction.

Given the discrete location of the DLBCL in the jejunum, which was not easily accessible by endoscopy or visualized on routine imaging, there was a delay to obtaining a biopsy and a final diagnosis. Repeat endoscopy, CT scans, and refractory symptoms despite gastric decompression with nasogastric tube were suggestive of a distal obstructive process beyond the proximal part of the small intestine. The resultant delay in diagnosis led to ongoing malnutrition in this patient, and he eventually required parenteral nutrition. Only after visualization of the distal part of the small intestine with EGD with push enteroscopy was the lesion visualized, biopsied, and confirmed pathologically to be DLBCL. Like the described case, many cases of DLBCL of the jejunum are convoluted and often present only after symptoms and complications have developed [9–12].

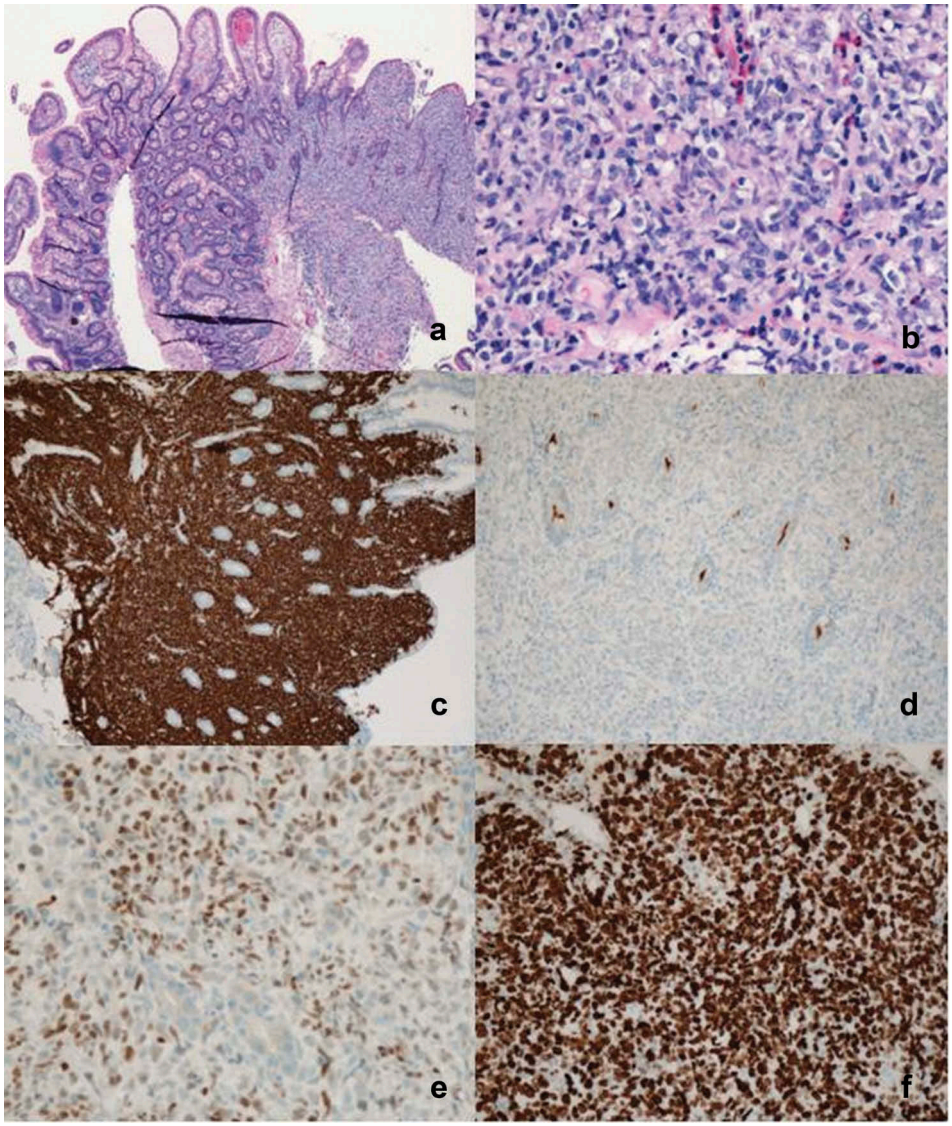

Figure 4. (a). H&E (4X) of the jejunal biopsy with transitional area from normal (left side) to abnormal with diffuse infiltrate of the lamina propria with sheets of large neoplastic cells (b). Neoplastic cells with irregular nuclei, moderate clear cytoplasm, and a centroblastic morphology (40X) (c). CD20 homogeneously stains neoplastic B cells which are negative for CD10 (d) and positive for BCL6 (e). (f). Proliferation index is very high by Ki67.

The patient did not experience any fevers or night sweats initially, which is atypical of lymphoma. Furthermore, he had multiple imaging studies that showed no enlarged masses or lymph nodes, which made the diagnosis difficult. In contrast to our case, the initial presentation of primary jejunal DLBCL can be fatal, requiring emergent surgical intervention. DLBCL of the jejunum can often mimic Crohn's disease. With multiple skip ulcers on imaging and symptoms of bowel perforation that require emergent surgical resection, the diagnosis of DLBCL can only be reached after a thorough pathological examination [10]. In younger patients, DLBCL can also present with acute B-symptoms with general malaise and perforation of the jejunum, resulting in hemodynamic instability with shock and peritonism, necessitating surgical intervention [9]. For these cases of DLBCL, the mainstay of management is immediate surgical intervention followed by R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone) combination systemic therapy with long-term surveillance [9–11,13,14]. Similar to the patient, other reported cases of DLBCL of the jejunum had multiple readmissions and extensive workup prior to reaching the final diagnosis. For patients with nonspecific symptoms and inconclusive routine imaging studies, small intestinal CT enterography should be considered first to evaluate for small bowel wall thickening and stenosis [11,15]; however, biopsy of lesional tissue, which may be obtained during surgical resection, with pathological workup remains the gold standard for diagnosis [14,16,17].

4. Conclusion

Isolated primary jejunum extranodal lymphoma is extremely rare and may be acutely debilitating. The clinical presentation of gastrointestinal DLBCL is often nonspecific, and the differential diagnosis is

broad, including infectious, autoimmune, or malignant processes. Early consultation to gastroenterology should be made if the patient does not improve with conservative management. Although definitive treatments are available, the patient's nutritional and functional states should be considered before offering chemotherapy and/or surgery.

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Contribution

All authors were involved in the patient's care. All authors approved the final manuscript. LV and HY drafted the manuscript and made the figures. AB provided the histopathological images.

Disclosure statement

No potential conflict of interest was reported by the authors.

Ethical Statement

The authors have personally communicated with family and obtained verbal consent for the publication of the manuscript.

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