

Case Report

A rare collision tumor of paraganglioma and intravascular large B-cell lymphoma: a case report and literature review

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Abstract: Intravascular large B-cell lymphoma (IVLBCL) is a rare and aggressive subtype of extranodal diffuse large B-cell lymphoma. It is characterized by the selective proliferation of lymphoma cells within the lumina of small blood vessels. Collision tumors involving IVLBCL are exceedingly rare, and no cases involving paraganglioma as a collision component have been reported to date. We report the case of an 80-year-old man who presented with nonspecific gastrointestinal symptoms and intermittent fever. Imaging studies suggested biliary and intra-abdominal malignancies. Surgical resection revealed a mesenteric mass. Histopathological examination demonstrated features consistent with paraganglioma. Notably, numerous atypical lymphoid cells were identified within the lumina of small vessels in the tumor. Immunohistochemical analysis showed positivity for CD20, CD19, PAX5, MUM1, and BCL2, supporting a diagnosis of IVLBCL. Epstein-Barr virus-encoded RNA (EBER) in situ hybridization was negative. Systemic involvement was excluded based on clinical evaluation and imaging findings. The final diagnosis was IVLBCL in collision with paraganglioma. Given the patient's advanced age and poor performance status, intensive chemotherapy was considered unsuitable, and targeted therapy with 'Surufatinib' was initiated. During follow-up, no recurrence of the primary tumor was observed. However, the patient subsequently developed duodenal adenocarcinoma and received appropriate treatment. The patient died approximately two years after the initial diagnosis. To the best of our knowledge, based on a systematic literature search in PubMed up to April 2026, this is the first reported case of a collision tumor composed of paraganglioma and IVLBCL. This case underscores the diagnostic challenges of IVLBCL due to its nonspecific presentation and its potential to be overlooked when coexisting with other tumors. Careful histopathological evaluation, particularly of intravascular components, is essential for accurate diagnosis. Increased awareness may facilitate early detection and improve patient outcomes.

Keywords: Intravascular large B-cell lymphoma, paraganglioma, collision tumor, case report, immunohistochemistry

Introduction

IVLBCL is a rare aggressive extranodal diffuse large B-cell lymphoma characterized by selective intravascular proliferation of lymphoma cells within small-to-medium blood vessels, especially capillaries and post-capillary venules. It typically affects the elderly, presenting with unexplained fever, neuropsychiatric symptoms, and hypoxemia, often involving the nervous system, skin, bone marrow, and lungs, with rare lymph node involvement. The intra-

vascular growth mechanism remains unclear, with poor prognosis and limited treatment. It is clinically divided into European (CNS and skin) and Asian (hemophagocytic syndrome, bone marrow involvement, multi-organ infiltration) subtypes [1-5].

Paraganglioma is a neuroendocrine tumor originating from nerve tissue, with adrenal pheochromocytomas constituting the majority. These tumors have high hereditary components with susceptibility gene mutations, presenting cate-

choline-related symptoms, endocrine abnormalities, and local compression [6].

IVLBCL is mainly treated with chemotherapy, targeted therapy for intolerant patients; paragangliomas are primarily managed by surgical resection, with targeted therapy for advanced cases. Collision tumors involving IVLBCL are extremely rare, with only about 15 cases reported globally involving meningiomas, renal tumors, and gastrointestinal stromal tumors. No previous IVLBCL-paraganglioma collision cases have been found [7, 8].

This case involved an 80-year-old male with non-specific gastrointestinal symptoms and intermittent fever. Initial imaging suggested biliary and intra-abdominal malignancies, focusing diagnosis on paraganglioma and risking overlooking IVLBCL. A third primary tumor (duodenal adenocarcinoma) developed during the disease course, presenting an extremely complex tumorigenic background. The coexistence mechanism remains unclear, and epidemiological, clinicopathological characteristics and optimal treatment strategies need further clarification.

Given the extreme rarity and non-specific manifestations of IVLBCL posing diagnostic challenges, this report fills literature gaps, supplements clinical evidence, improves clinician awareness of IVLBCL and solid tumor coexistence, reduces missed or misdiagnosis risk, and provides valuable insights for clinical diagnosis, treatment, and long-term follow-up of similar rare cases [1, 9].

Case report

An 80-year-old man presented to our hospital. In February 2022, the patient developed abdominal discomfort without an obvious precipitating factor, manifested as abdominal distension and decreased appetite. Symptoms were accompanied by acid reflux and heartburn, fatigue, and intermittent fever, with a maximum temperature of 39°C. He also had chills without rigors, and no abdominal pain, diarrhea, nausea, or vomiting to greasy food. There were no symptoms such as cough, sputum production, dizziness, or headache. He sought medical attention at a local hospital and underwent gastroscopy. The results showed mild esophagitis and mild erythematous gastritis in

the antrum. Biopsy pathology indicated chronic mucosal inflammation with intestinal metaplasia of the glands in the cardia. Liver function tests showed no significant abnormalities, and empirical anti-gastritis treatment was ineffective. Upon recommendation from a primary care physician, he was referred to our hospital for further diagnosis and treatment.

The patient had no significant past medical history. Physical examination revealed a 3-kg weight loss. The relevant laboratory tests were carried out in the Clinical Laboratory of the hospital. Serum CA19-9 levels were elevated. After admission, further examinations were completed. Imaging via ultrasound and CT revealed pancreatic enlargement or indistinct peripancreatic regions with suspected pancreatic necrosis. Laboratory tests suggested elevated bilirubin and transaminase levels (**Figure 1A-D**). Ultrasound demonstrated dilation of intrahepatic and extrahepatic bile ducts, hypoechoic lesions in the distal extrahepatic bile duct, and sludge-like gallstones with sediment in the gallbladder. MRCP suggested a high likelihood of cholangiocarcinoma in the distal common bile duct and intra-abdominal malignancy in the left mid-lower abdomen. No evidence of metastasis was identified on imaging. After consultation with multidisciplinary team, the department of Hepatobiliary Surgery suggested surgical resection was recommended, and the patient was transferred to the Department of Hepatobiliary Surgery.

On May 20, 2022, the patient underwent cholecystectomy, biliary-enteric anastomosis, abdominal tumor resection, and adhesiolysis. During laparotomy, severe adhesions were found among the small intestine, colon, spleen, and stomach. After adhesiolysis, the common bile duct was exposed, and a firm mass was palpable at its distal end. A tumor measuring approximately 5×6 cm was observed in the mesentery at the splenic flexure of the left colon. Then the tumor and gallbladder were completely resected, followed by biliary-enteric anastomosis and closure of the abdomen in layers.

After the operation, the tumor was sent to the Pathology Department for postoperative pathological examination. Gross examination showed a gray-red tumor measuring 8.5×8×5 cm after fixation in formalin for 24 hours. The cut surface was gray-red and gray-yellow, solid, and of

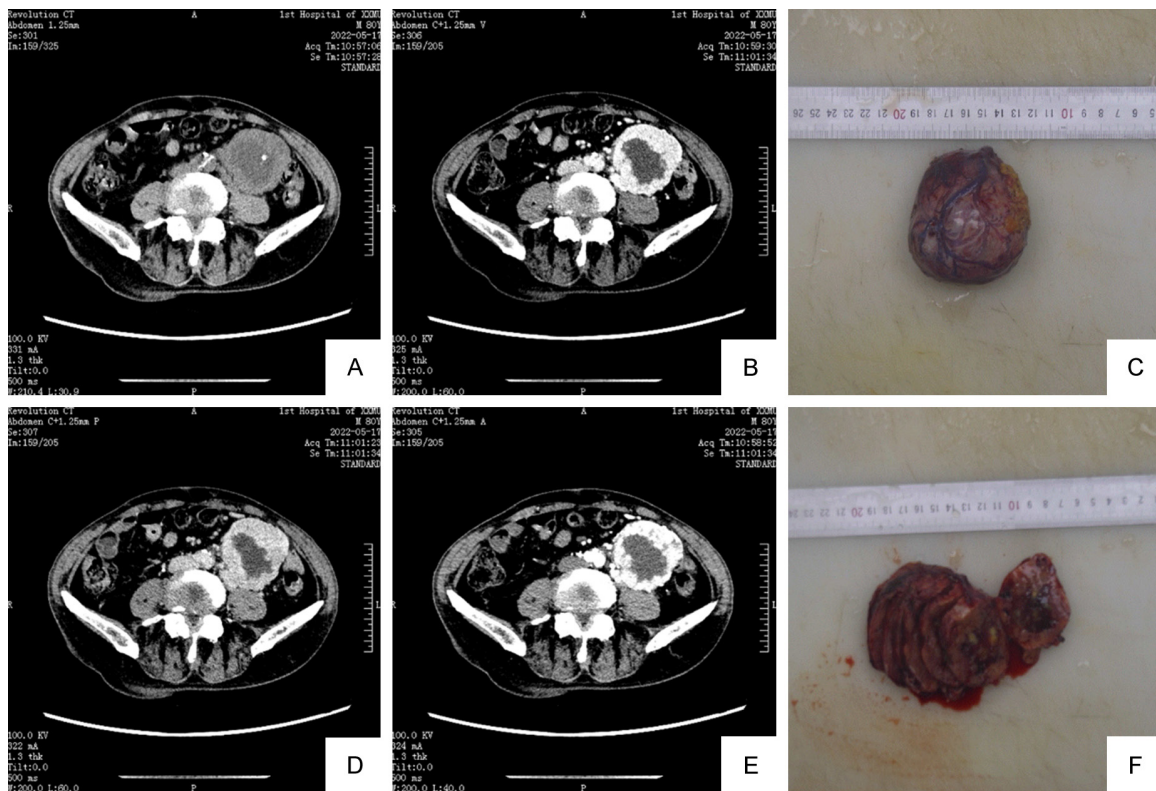


Figure 1. Radiological image and macroscopic appearance of the solid tumor. A. Plain Scan. B. Venous Phase. C. Arterial Phase. D. Lag Phase. E, F. Macroscopic tumor exam revealed a grayish-red, 8.5×8×5 cm mass with a medium, encapsulated texture; cut surface showed grayish-white areas, partly solid and microcystic, with focal hemorrhage.

medium consistency, with an intact capsule (**Figure 1E, 1F**). Microscopically, the tumor showed that capsule was intact and intratumoral vessels were dilated and congested. Partial stromal edema and minor erythrocyte extravasation were observed. Tumor cells were predominantly oval with granular basophilic cytoplasm (**Figure 2A**). Occasional pigment-containing or chromaffin-like cells were seen, with a solid growth pattern. Mitotic figures were fewer than 5 per high-power field. No definite tumor necrosis, neural invasion, or vascular invasion was identified. Then we performed immunohistochemical detection on the tumor. The result showed Ki-67 positivity was observed in approximately 5% of tumor cells (**Figure 3G**). All results indicate the tumor had the proliferation of this tumor is probably not that active.

In addition to the main tumor component, abnormal vascular dilation was noted. Numerous atypical cells were present within the vascular lumen, morphologically distinct from the main tumor cells (**Figure 3A**). These cells were oval or

round, with clear nuclear membranes, coarse chromatin, and prominent nucleoli. These cells were more than twice the size of normal lymphocytes. Tumor cells selectively proliferated within small- to medium-sized vascular lumina, especially capillaries. Immunohistochemistry showed that the main tumor cells expressed Syn (**Figure 2B**), CgA (**Figure 2C**), and Vimentin. ERG, CD34 (**Figure 3E**), and SMA were used to label blood vessels. Intravascular atypical cells expressed LCA, Bcl-6 (**Figure 3B**), CD19, CD20, Cyclin D1, MUM-1, and PAX-5. In situ hybridization showed EBER negativity. The immunohistochemical marker Bcl-6 (**Figure 3B**), CD10 (**Figure 3C**), CD30 (**Figure 3D**) and CD45 (**Figure 3F**) were not expressed. Systemic involvement was excluded based on follow-up, imaging, and clinical findings involving vessels.

Based on clinical presentation, intraoperative findings, gross examination, and immunohistochemistry, the final diagnosis was paraganglioma with intravascular large B-cell lymphoma. The clinical diagnosis also included malignant

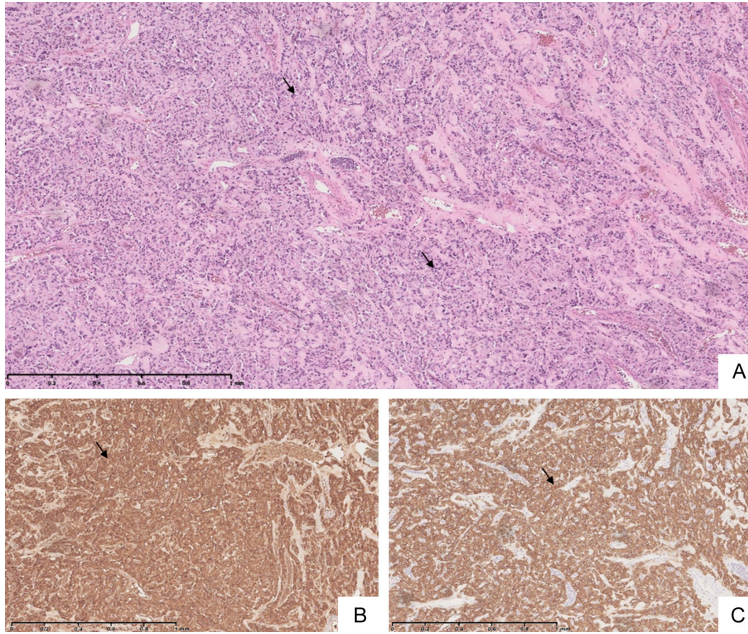


Figure 2. Histopathological features of paraganglioma component. (A) The diffuse, sheet-like clusters of solid tumor cells within the neoplasm typically exhibit irregular polygonal shapes, with cell volumes slightly larger than normal. The cytoplasm is abundant, granular, and sometimes relatively vacuolated, with indistinct cell boundaries (10 $\times$). And it's Immunohistochemical stains for (B) Syn, (C) CgA (4 $\times$). The arrows point positive cells, which are paraganglioma cells.

biliary tumor, gallstones, liver abscess, bilateral renal abscesses, and upper gastrointestinal inflammation.

On July 7, 2022, the patient was admitted to the oncology department for post-operative chemotherapy. The admission diagnosis given by the Oncology Department was the postoperative abdominal paraganglioma with intra-vascular large B-cell lymphoma, EBER(-). A high likelihood of distal common bile duct cholangiocarcinoma was also considered. Other diagnoses included postoperative acute cholecystitis with abscess and gallstones. Subsequently, relevant postoperative auxiliary examinations were completed for the patient to comprehensively assess the patient's postoperative condition. Preoperative magnetic resonance cholangiopancreatography (MRCP) revealed a lesion in the distal common bile duct that was highly suggestive of cholangiocarcinoma. Nevertheless, definitive neoplastic tissue from this anatomical region was not obtained intraoperatively; consequently, postoperative pathological examination failed to validate the diagnosis of cholangiocarcinoma. Therefore, this diagno-

sis was established solely on the basis of imaging manifestations. During the postoperative treatment with 'Surufatinib' capsules, serial follow-up imaging examinations demonstrated no evident disease progression or metastatic lesions, whereas the biliary abnormalities remained stable or exhibited partial improvement. Accordingly, the lesion was ultimately regarded as a suspected yet unconfirmed malignant biliary lesion, with a high probability of distal common bile duct carcinoma. Based on history, symptoms, pathology, and imaging, chemotherapy combined with targeted and immunotherapy was recommended.

Considering the patient's advanced age and poor tolerance, and after discussion with family members, 'Surufatinib' capsules were administered for anti-angiogenic and immu-

nomodulatory therapy. After the treatment plan was settled down, the patient was discharged with instructions and came back to hospital regularly for chemotherapy returned regularly for follow-up.

In December of the same year, the patient developed abdominal distension and returned for outpatient evaluation. Imaging showed no evidence of recurrence or metastasis. In view of the results of the imaging examination, the doctor maintained the original treatment plan that oral 'Surufatinib' capsules 150 mg once daily and instructed the patient to go home for continued observation. But in April 2024, the patient was readmitted due to intermittent abdominal distension for 10 days. The blood tests including routine blood count, fasting glucose, lipid profile, renal function, and tumor markers showed mild abnormalities were consistent with age and medical history. Pelvic CT revealed new bilateral pleural effusion, perihepatic and esophageal fluid, increased pelvic effusion, and thickening of the gastric antrum to descending duodenum wall. After consultation with gastroenterologists, acid suppression

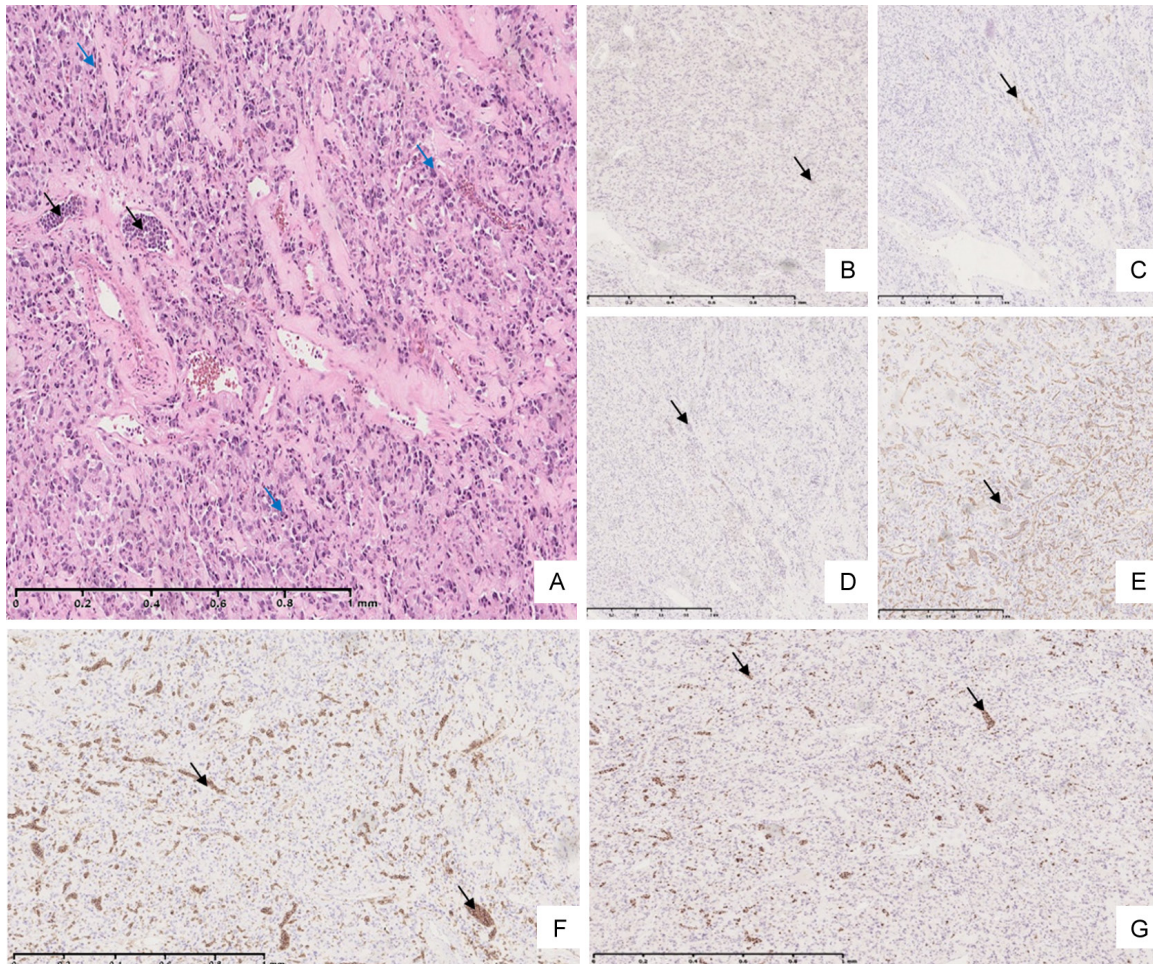


Figure 3. (A) Intravascular diffuse lymphocyte-like cells are visible (10×). Immunohistochemical stains for (B) Bcl-6. The arrows point positive cells, which are intravascular diffuse lymphocyte-like cells. (C) CD10. (D) CD30. (E) CD34. They marked the vessels together. And the arrows point the Intravascular diffuse lymphocyte-like cells, whose CD10 is positive but CD30 and CD34 was negative. (F) CD45. The positive cells with arrows pointed was intravascular diffuse lymphocyte-like cells. (G) The Intravascular diffuse lymphocyte-like cells (arrow pointed cells) with an Ki-67 expression was approximately 85% which shows an high proliferation level. Blue arrows indicate paraganglioma cells, whereas black arrows indicate intravascular lymphoma cells.

and gastric protection therapy were recommended. With the treatment, the patient experienced symptomatic improvement. And do the Gastroscopy with biopsy at the same time, the biopsy revealed some fibrous collagen tissues covered by a small amount of squamous epithelium and their granulation tissue hyperplasia with neutrophil, lymphocyte, and plasma cell infiltration was observed. The following immunohistochemistry showed P40 (focal positive), P53 (wild type), and Ki-67 (5%). We also completed pathological biopsies of other parts. Biopsy of the lesser curvature of the cardia indicated chronic atrophic gastritis. Biopsy of the descending duodenum revealed adenocarcinoma. Biopsy of the duodenal bulb showed ch-

ronic active mucosal inflammation. Based on pathology, a diagnosis of duodenal adenocarcinoma was established. The patient was considered to have triple primary tumors. Chemotherapy was initiated for the newly diagnosed duodenal adenocarcinoma while continuing 'surufatinib' capsules. Based on the patient's condition and colorectal cancer guidelines, contraindications were excluded. The Oncology Department ultimately selected a treatment plan to address the newly-developed duodenal adenocarcinoma which was Capecitabine 1.5 g twice daily and the adjusted treatment plan started on March 30, 2024. With the new plan, the patient improved and requested discharge.

In October 2024, follow-up was conducted via telephone and the family reported that the patient had died. The families refused in-depth interviews because of the neuropsychiatric and dermatologic symptom, so further details were unavailable about the details of this patient in the final stage of life.

After feeding back the follow-up results to the relevant departments, we discussed this case again in a multidisciplinary consultation. Experts from all departments agreed that the patient's condition was extremely rare, being lymphoma with a collision tumor, and the collision tumor was a type of neuroendocrine tumor. The author then conducted a search of relevant literature. At least before March 2024, no such symptoms had been documented.

Treatment decision-making and follow-up

The Collision Tumor of PGL and IVLBCL is a rare case of dual-tumor composite lesions. The difficult point of clinical treatment is the fundamental disagreement of their biological behavior and treatment response spectrum which could drive the treatment decision into an strategic paradox [7, 9, 10].

IVLBCL is a rare subtype of aggressive B-cell non-Hodgkin lymphoma, pathologically characterized by selective proliferation of neoplastic cells confined within vascular lumens which lead to an high propensity for systemic dissemination and an aggressive clinical course. Current standard treatment mostly led to the rituximab-based immunochemotherapy regimen. Among these regimens, R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, prednisone) has been established as the cornerstone of first-line induction therapy which aims to systematic eradication of systemic micrometastases [1-5].

PGL represent neuroendocrine tumors derived from the neural crest. Its treatment highly rely to the stages. Stage R0 firstly choose the surgery to complete resection. For metastatic or unresectable cases, the treatment turns to non-chemotherapeutic modalities such as PRRT, targeted agents, local ablation and so on [6, 8].

The therapeutic windows of the two tumor entities do not overlap. IVLBCL needs a fast and prompt and intensive systemic immunochemo-

therapy. PGL tends to receive focal surgical resection or targeted intervention. When the Collision Tumor of this two components, If R-CHOP is administered first, immunosuppression may raise the risk of hemorrhage or catecholamine crisis associated with PGL; if surgery is prioritized, lymphoma treatment will be delayed, thereby providing a time window for disease dissemination. No single therapeutic regimen can simultaneously meet both treatment requirements [2, 8].

In terms of treatment planning, the attending oncologist took the patient's general condition and family factors into primary consideration. After a definitive diagnosis was established, the physician discussed treatment options with the patient without delay. Given the patient's poor baseline physical status and advanced age, the individual was unlikely to tolerate the R-CHOP regimen. In addition to the patient's advanced age, the family members also reported that the patient was unable to perform activities of daily living independently. Therefore, the family preferred the patient to receive primary treatment at home, with the therapeutic goals of slowing disease progression and preserving the patient's quality of life rather than pursuing complete cure. Consistent with the family's wishes, the patient refused hospital-based interventions including radiotherapy and chemotherapy, and favored home-based treatment to spend more time with family members at the end of life. Taking all the above circumstances into comprehensive consideration, the physician formulated an oral medication regimen, which was designed to delay disease progression, maintain the patient's quality of life to the greatest extent, and satisfy the psychological expectations of both the patient and the family.

Surufatinib targeted inhibition VEGFR, FGFR and CSF-1R pathways. It also has the function of anti-angiogenesis and immunomodulation. Many evidence has been obtained supporting its therapeutic coverage of advanced neuroendocrine neoplasms. Considering the neuroendocrine origin of PGL and patient can't tolerate the conventional cytotoxic chemotherapy, doctors finally chose the Surufatinib [8].

Discussion

To the best of our knowledge, based on a systematic literature search in PubMed up to

March 2024, no previous cases describing the coexistence of IVLBCL and paraganglioma have been reported. This article reports the world's first case of intravascular large B-cell lymphoma colliding with paraganglioma [7, 9].

The present case demonstrates several distinctive features. First, it represents an extremely rare collision tumor composed of paraganglioma and IVLBCL. Unlike conventional IVLBCL cases presenting with systemic symptoms or multiorgan involvement, the lymphoma component was incidentally identified within the vascular lumina of the paraganglioma, without clear evidence of systemic disease. Second, the clinical presentation was dominated by nonspecific gastrointestinal symptoms and imaging findings suggestive of biliary malignancy, leading to an initial diagnostic focus on the solid tumor component and increasing the risk of overlooking the intravascular lymphoma component. The diagnosis was established only after careful histopathological and immunohistochemical evaluation. Third, the coexistence of three distinct neoplasms - paraganglioma, IVLBCL, and subsequent duodenal adenocarcinoma - suggests a highly complex tumorigenic background.

IVLBCL is a distinct subtype of extranodal DLBCL, characterized by selective proliferation of lymphoma cells within the lumens of small blood vessels. It typically affects elderly individuals and presents with fever of unknown origin, neuropsychiatric symptoms, and unexplained hypoxemia. IVLBCL has a poor prognosis and limited therapeutic efficacy. The mechanism underlying its intravascular growth pattern remains unclear, but it has been hypothesized to involve the lack of homing receptors and adhesion molecules, including CD29 and CD54. It commonly involves the nervous system, skin, bone marrow, and lungs, while lymph node involvement is relatively rare. Two main clinical subtypes have been identified: the European type, characterized by central nervous system and skin involvement, and the Asian type, presenting as hemophagocytic syndrome, bone marrow involvement, and extensive multi-organ infiltration. Due to its diverse and nonspecific clinical manifestations, this disease is often diagnosed only at an advanced clinical stage or during autopsy [1-5].

Owing to its variable clinical presentation, approximately half of IVLBCL cases were historically diagnosed only after autopsy, though recent data show more than half can now be diagnosed during the patient's lifetime. Collision tumors involving IVLBCL are even rarer, with approximately 15 reported cases. In 2024, Liu Jia et al. reported five cases, with ages ranging from 53 to 73 years (median 65 years) and a male-to-female ratio of 3:2. Components included meningeal tumors, renal tumors, clear cell renal cell carcinoma, and cirrhosis, all with poor prognosis. Because initial symptoms are often caused by solid tumors, diagnosis is more challenging than that of IVLBCL alone. In total, 16 IVLBCL collision tumors (including the present case) showed a median age of 73 years and a male-to-female ratio of 3:5. Components included central nervous system lesions, squamous intraepithelial neoplasia, ductal carcinoma in situ, and gastrointestinal stromal tumors. Postoperative survival ranged from 0.13 months to 28 months. Differences in age, sex ratio, tumor components, and survival indicate the need for continued research. Expanding sample size will help refine epidemiological and clinicopathological characteristics and optimize treatment strategies. The clinicopathological characteristics of the reported IVLBCL collision tumors are summarized in **Figure 4**. In this case, the solid tumor component was a paraganglioma, with complex nomenclature and diverse manifestations increasing diagnostic difficulty [2, 5].

In this case, the patient presented with gastrointestinal symptoms, leading clinicians to focus primarily on paraganglioma, and the abnormal intravascular lymphocytes were nearly overlooked [7, 9, 10].

Shared genetic mutation features may offer potential therapeutic targets. Future research may explore novel targets simultaneously affecting IVLBCL and associated paragangliomas. This case provides several important clinical implications. First, IVLBCL should be considered in the differential diagnosis when atypical lymphoid cells are identified within vascular lumina, even in the presence of an apparently unrelated solid tumor. Second, this case underscores the critical role of comprehensive pathological evaluation, including immunohis-

IVLBCL colliding with paraganglioma: a rare case

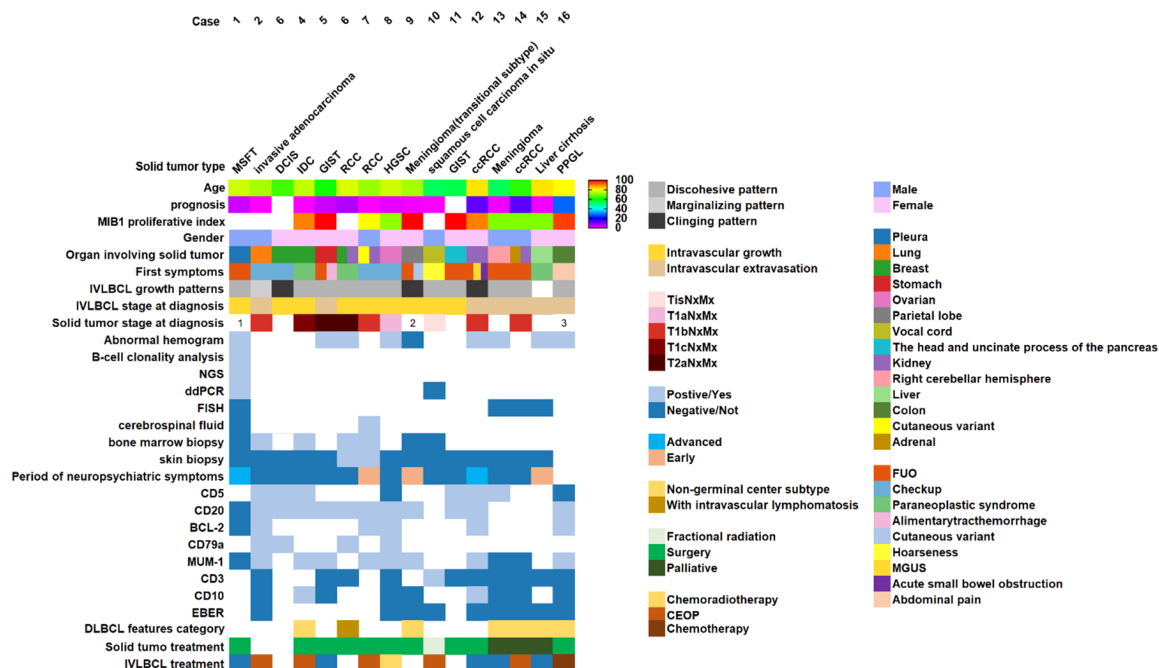


Figure 4. Clinicopathological characteristics of reported cases of intravascular large B-cell lymphoma (IVLBCL) collision tumors. The heatmap summarizes demographic data, tumor types, clinical presentations, pathological features, diagnostic approaches, and treatment strategies across all included cases. Each column represents an individual case, while rows correspond to specific clinical or pathological variables, including age, prognosis, proliferation index, organ involvement, growth patterns, staging, immunophenotype (e.g., CD markers, MUM1, BCL-2, EBER), and therapeutic modalities. Color coding indicates categorical or quantitative differences as defined in the legend, including growth patterns (discohesive, marginalizing, and intravascular), organ distribution, symptom profiles, and treatment regimens. The figure highlights the heterogeneity of IVLBCL collision tumors in terms of clinical manifestations, involved organs, and outcomes, as well as the predominance of advanced-stage disease and variable diagnostic pathways. Notably, most cases demonstrate poor prognosis and diverse solid tumor components, underscoring the diagnostic complexity and the need for improved recognition and management strategies.

tochemistry, in identifying rare composite or collision tumors. Routine evaluation of intravascular compartments may improve detection rates of occult IVLBCL. Third, the case highlights the diagnostic challenge posed by non-specific clinical manifestations. Early recognition of IVLBCL remains difficult, and clinicians should maintain a high index of suspicion, particularly in elderly patients with unexplained systemic symptoms. Finally, the occurrence of multiple primary tumors suggests the need for careful long-term surveillance and individualized management strategies.

Conclusion

In summary, we report the first documented case of a collision tumor composed of paraganglioma and intravascular large B-cell lymphoma. This case highlights the diagnostic difficulty of IVLBCL, particularly when it coexists with a solid tumor and presents with nonspecific clinical

manifestations. Careful histopathological evaluation, especially of intravascular components, is essential to avoid missed diagnosis. Furthermore, this case underscores the importance of maintaining a high index of suspicion for occult hematological malignancies in unusual tumor settings and suggests that comprehensive pathological assessment may improve early detection. The coexistence of multiple primary tumors in this patient also indicates the need for individualized management and long-term surveillance strategies. Greater awareness of such rare collision tumors may contribute to improved diagnostic accuracy and better clinical outcomes.

Disclosure of conflict of interest

None.

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