Unusual bilateral kidney and duodenal plasmablastic lymphoma presentation in an elderly patient: A case report

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Abstract. The present report described the case of a 71-year-old man who was admitted to the emergency department with a 7-day history of progressive left flank pain and tarry stool. Bedside point-of-care ultrasound of the left kidney showed lobulated ill-defined hypoechoic foci in the perirenal spaces with mild hydronephrosis. Subsequent contrast-enhanced abdominal computed tomography revealed lobulated low-density lesions in the bilateral perirenal space and paraaortic space. The patient was subsequently admitted to the internal medicine department of the hospital. Renal and duodenal biopsies were arranged, and pathology reports were consistent with the findings of plasmablastic lymphoma (PBL). This unusual presentation of flank pain and tarry stool caused by recurrent PBL highlighted that genitourinary or gastrointestinal manifestations could occur in cases of PBL recurrence. The patient received intensive chemotherapy regimens comprising a combination of etoposide, prednisone, vincristine, cyclophosphamide and doxorubicin hydrochloride for aggressive non-Hodgkin's lymphoma to achieve a good response.

Introduction

Plasmablastic lymphoma (PBL) is an uncommon but aggressive subtype of diffuse large B-cell lymphoma that is associated with acquired immunodeficiency syndrome and characterized by its association with Epstein-Barr virus (EBV) (1). PBL is diagnostically challenging and has a poor prognosis (2). PBL diagnosis through fine-needle aspiration cytology is infrequently reported, yet cytomorphologic features such as hypercellular smears with abundance of plasmablastic cells may provide an early indicator for diagnosing PBL (3). The immunophenotype of PBL is positive for the plasma cell markers CD79a, multiple myeloma 1/interferon regulatory factor 4, B lymphocyte-induced maturation protein-1, CD38 and CD138, but negative for the B-cell markers CD19, CD20 and paired box 5 (4). The intensification role of induction chemotherapy is controversial. Additionally, novel agents, such as bortezomib and lenalidomide, have shown effectiveness in relapsed cases and serve a relatively important role in frontline treatment (5,6). PBL predominantly occurs in immunosuppressed men with a solid organ transplant. Some case reports have indicated that allogeneic hematopoietic stem cell transplantation provides long-term survival opportunities for these patients (2). The present study reported an unusual case of bilateral renal and duodenal PBL.

Case report

A 71-year-old man presented to the emergency department of the Tri-Service General Hospital (Taipei, Taiwan) in July 2020 with a 7-day history of progressive left flank pain and tarry stool. Their past medical history (14 years ago) included PBL of the left nasal cavity and paranasal sinuses. The patient received radiotherapy for PBL, which metastasized to the right neck 4 years ago. Their vital signs were normal, and physical examination showed left costovertebral angle tenderness. The laboratory tests revealed a blood urea nitrogen level of 38 mg/dl, serum creatinine level of 1.4 mg/dl, lactic acid dehydrogenase of 3,090 U/l and positive fecal occult blood. Bedside point-of-care ultrasound of the left kidney revealed lobulated ill-defined hypoechoic foci in the perirenal spaces with mild hydronephrosis (Fig. 1A). Subsequent contrast-enhanced computed tomography (CT) of the abdomen demonstrated lobulated low-density lesions in the bilateral perirenal and paraaortic spaces (Fig. 1B and C). The patient was subsequently admitted to the internal medicine department.

The laboratory findings included mild anemia and the detection of monoclonal immunoglobulin (Ig)G and κ/λ-type Bence Jones protein. The patient was negative for human immunodeficiency virus (HIV) rapid point-of-care test, hepatitis B virus, hepatitis C virus and EBV viral-capsid

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antigen (EBV-VCA) IgM (<10.00 U/ml), but positive for EBV-VCA IgG (>750.00 U/ml). Renal and duodenal biopsies were arranged to rule out malignancy. The tissues were fixed by perfusion with 4% formaldehyde for at least 6 h at room temperature, paraffin-embedded at 60˚C, cut into 20-μm-thick sections. The tissue sections were rehydrated in TBS (25 mM Tris-HCl, pH 7.4, 137 mM NaCl, 2.7 mM KCl) for 5 min at room temperature. They were then incubated with the antibody in 'antibody diluent' (Dako; Agilent Technologies, Inc.) for 30 min at room temperature. Immunohistochemical staining was performed using the following antibodies: anti-CD20 (cat. no. SM3140B; 1:300; OriGene Technologies, Inc.), anti-CD79a (cat. no. TA351934; 1:300; OriGene Technologies, Inc.), anti-CD3 (cat. no. 14-0032-82; 1:100; BD Biosciences), anti-CD138 (cat. no. 36-2900; 1:500; Thermo Fisher Scientific, Inc.), anti-CD38 (cat. no MA5-14413; 1:500; Thermo Fisher Scientific, Inc.) and anti-CD10 (cat. no. TA327616; 1:60; OriGene Technologies, Inc.), placed horizontally on a thermal plate at 37˚C. The sections were then rinsed three times in TBS and subjected to the detection reaction. Briefly, the slides were incubated with HRP-conjugated DISCOVERY® Universal Secondary Antibody (cat. no. 760-4205, Ventana Medical Systems; Roche Tissue Diagnostics), and detected by the Discovery DAB Map Kit (Ventana Medical Systems; Roche Tissue Diagnostics) for 30 min at room temperature. The duodenal biopsies were positive for CD79a (Fig. 2A), CD138 (Fig. 2B) and CD45, and the renal biopsies were positive for CD79a, CD138, EBV-encoded RNA (EBER; Fig. 2D), CD30 and epithelial membrane antigen. The Ki-67 proliferation index was 99% for duodenal biopsies (Fig. 2C), and both renal and duodenal biopsies were negative for CD20. Ki-67 index is calculated visually by counting the total number of positive-stained tumor cells and dividing that by the total number of tumor cells in each high-powered field (7). The immunohistochemical features were comparable with those of PBL.

Bone marrow aspirate showed no increase in the number of plasma cells, no clonality and normal cytogenetics. Fluorodeoxyglucose (FDG)-positron emission tomography (PET)/CT was immediately performed, and FDG uptake was observed in the right submandibular regions, duodenum, bilateral perirenal space, aortocaval space and peritoneum. Therefore, the patient was diagnosed with recurrent PBL in the intra-abdominal lymph nodes, bilateral kidneys and duodenum associated with a bleeding duodenal ulcer. Systemic chemotherapy was initiated following the diagnosis with intravenous (i.v.) administration of etoposide (80 mg/day on days 1-4), vincristine (0.64 mg/day on days 1-4), doxorubicin hydrochloride (16 mg/day on days 1-4), and cyclophosphamide (1,200 mg/day for 60 min on day 5). Chemotherapy dosages were based on the guideline suggestions and adjusted according to the side effects of the drugs experienced by each patient individually. Between November 2020 and April 2021, the patient received six cycles of etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin hydrochloride (EPOCH) chemotherapy regimens. After six cycles of chemotherapy, PET/CT was repeated and a regressive change in previously noted FDG-uptake regions was observed.

Discussion

The present report described a case of an unusual presentation of flank pain and tarry stool caused by recurrent PBL in intra-abdominal lymph nodes, bilateral kidneys and duodenum. The clinical manifestation of PBL varies with extranodal masses in the head, neck and oral cavity the most common presentation (8). The median overall survival (OS) time is ~8 months (9). Once considered a malignancy that largely affected HIV-infected individuals, Castillo *et al* (10) analyzed 71 cases of HIV-negative PBL reported prior to August 2009 and revealed that these cases had distinct clinicopathological features, such as older age, high Ki-67 expression and negative for CD20. Moreover, Liu *et al* (11) indicated that EBV infection was common, being positive in 58.70% of patients with HIV-negative PBL, whereas 92.45% were negative for herpesvirus-8 (HHV-8). However, Morscio *et al* (9) reported that ~70% of HIV-positive PBL cases express EBER in malignant cells and 72% of cases express HHV-8; EBER detection is a sensitive technique for detecting EBV infection.

The patient in the current case report presented a rare clinical profile of flank pain and tarry stool, rather than head and neck masses. Additionally, the point-of-care ultrasound of the bilateral kidneys and subsequent contrast-enhanced abdominal CT indicated non-calculus hydronephrosis. Clinically, physicians should keep urothelial cell carcinoma, transitional cell carcinoma, retroperitoneal tumors and kidney cancers in mind when non-calculus hydronephrosis is found by abdominal CT. Serum viral tests showed positive for EBV-VCA IgG, but negative for EBV-VCA IgM and HIV rapid point-of-care test. A systematic review of 76 patients with HIV-negative PBL reported a median OS time of 9 months with a 2-year OS rate of 10% (12). Castillo *et al* (10) reported that patients with HIV-negative PBL had a poorer chemotherapy response compared with those with HIV-positive PBL. It was also reported that patients with HIV-negative PBL and Ki-67 expression >80% had a worse outcome, showing a poorer chemotherapy response and worse OS rate. Saraceni *et al* (13) reported a case of HIV-negative PBL with complete remission for 4 years, but the manifestations were in the usual sites of head and neck. In addition, Brahmania *et al* (14) reported a case of HIV-negative and EBER-positive PBL in the anorectal junction with complete remission after adequate concurrent chemoradiation therapy; however, Ki-67 expression in the anorectal tumor cells was <80%, indicating a better prognosis. In the present case, Ki-67 expression in duodenal biopsies was 99%. Moreover, Cao *et al* (15) reported a case of HIV- and EBER-negative duodenal PBL with Ki-67 expression of ~80%, wherein chemotherapy regimens such as CHOP included i.v. treatment of cyclophosphamide (750 mg/m^2; day 1), doxorubicin hydrochloride (50 mg/m^2; day 1), vincristine (1.4 mg/m^2; day 1) and oral prednisone (100 mg; days 1-50). However, the patient's disease progressed, and it was concluded that CHOP is not an optimal treatment regimen; thus, more intensive regimens are required. Conversely, the patient in the present case received six cycles of EPOCH chemotherapy regimens, and the repeat PET/CT showed a regressive change in previously noted FDG-uptake regions.

Notably, this unusual presentation of flank pain and tarry stool caused by recurrent PBL highlighted that genitourinary

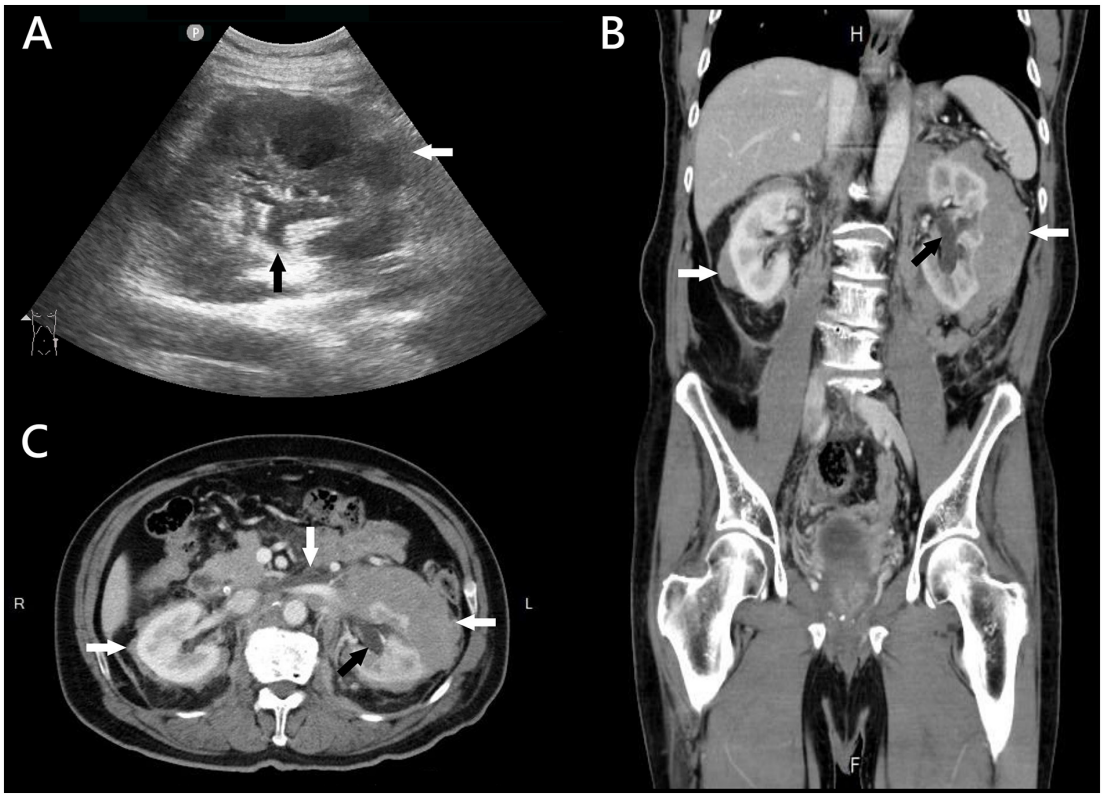

Figure 1. (A) Bedside point-of-care ultrasound of the left kidney revealed lobulated ill-defined hypoechoic foci in the perirenal spaces (white arrow) and mild hydronephrosis (dark arrow). (B) Coronal view of contrast-enhanced CT of the abdomen and pelvis showing low-density lesions in bilateral perirenal space and paraaortic space (white arrows), and mild hydronephrosis (dark arrow). CT, computed tomography. (C) Contrast-enhanced CT of the abdomen and pelvis with intravenous contrast (axial view) showing low-density lesions in bilateral perirenal space and paraaortic space (white arrows) and mild hydronephrosis (dark arrow).

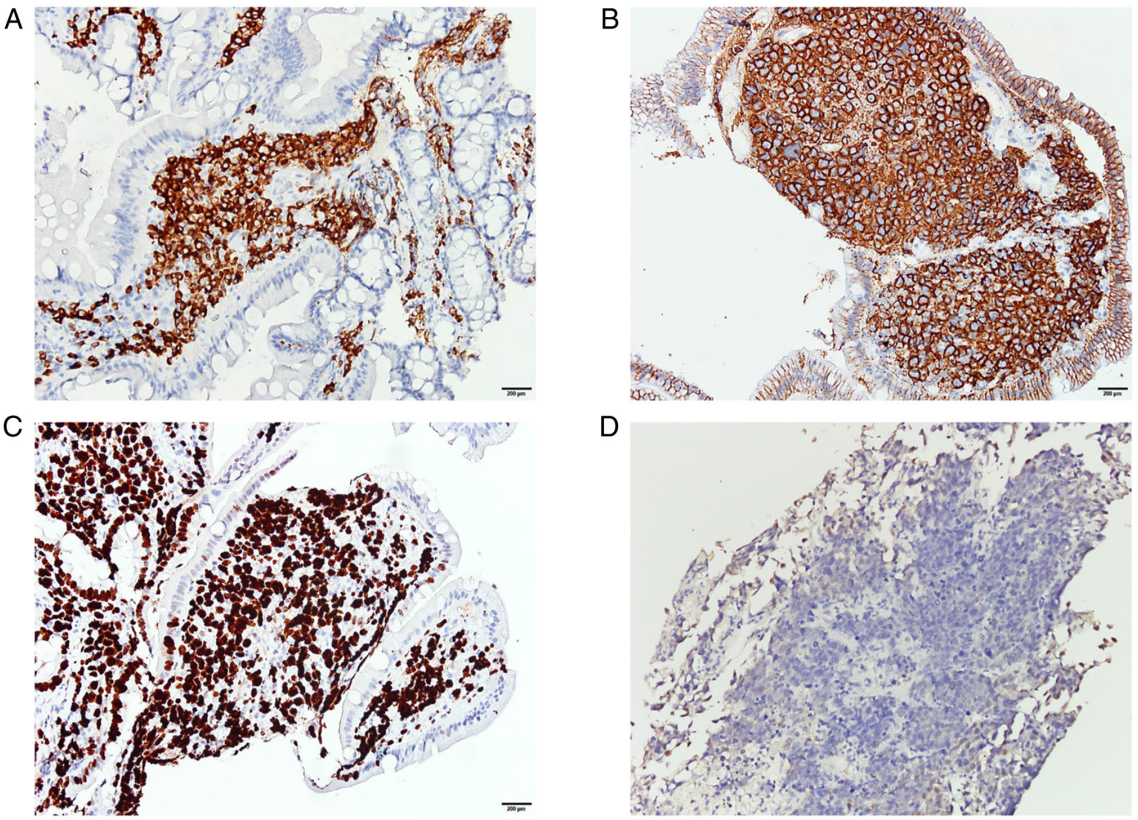

Figure 2. Immunohistochemical analysis of neoplastic cells of (A-C) duodenal and (D) renal biopsies stained with hematoxylin and eosin. The cells were positive for (A) CD79a, (B) CD138 and (C) Ki-67. (D) Epstein-Barr virus-encoded RNA. Scale bars, 200 μm.

or gastrointestinal manifestations can occur in cases of PBL recurrence, as well as head and neck manifestations. Additionally, more intensive chemotherapy regimens, such as EPOCH instead of CHOP, may be necessary for patients with HIV-negative PBL with >80% Ki-67 expression, a diagnostic and therapeutically challenging malignancy.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

YCL and YTS were major contributors in writing the manuscript. CKH, YCT, YCC and PFL were involved in critically revising the manuscript for important intellectual content. YCL and PFL confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The institutional review board of the Tri-Service General Hospital (Taipei, Taiwan) approved this study (IRB No. B-202105167). Written informed consent was obtained from the patient. All procedures were performed according to the World Medical Association's Declaration of Helsinki.

Patient consent for publication

The patient provided written informed consent regarding the publication of all case details and any accompanying images.

Competing interests

The authors declare that they have no competing interests.

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