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Case Report

CD20-negative diffuse large B-cell lymphoma presenting with anuria: a case report

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Abstract: CD20-negative diffuse large B-cell lymphoma (DLBCL) is a rare novel subtype of non-Hodgkin lymphoma. Herein, we report a case of CD20-negative DLBCL in a 54-year-old male who had suffered with anuria for 5 days. Positron emission tomography/computed tomography (PET/CT) revealed lymphadenopathy, and biopsy of the right inguinal lymph node was performed. Lymph node sections revealed a 2 × 2 × 2-cm solid mass histopathologically suggestive of DLBCL. Immunohistochemical (IHC) analysis revealed the patient's lymphoid cells were CD10(+), CD21(+), CD79a(+), CD99(+), LCA(+), Myc(+), P53(+), PAX5(+), ALK(-), BCL-2(-), BCL-6(-), CD3(-), CD20(-), Mum-1(-), and TDT(-). Approximately 90% of his tested lymphoid cells reacted positively to Ki-67 antibody. A diagnosis of CD20-negative DLBCL (not otherwise specified) was made, and the patient was treated with seven courses of CHOP (cyclophosphamide, doxorubicin, vincristine, and dexamethasone) and one course of EPOCH (etoposide, cyclophosphamide, doxorubicin, vincristine, and prednisolone) chemotherapy. However, the treatment outcome was unsuccessful. To the best of our knowledge, this is the first reported case of CD20-negative DLBCL-induced acute renal failure presenting as anuria. Formulation of an optimized therapeutic strategy for this rare and aggressive disorder is urgently required.

Keywords: CD20-negative diffuse large B-cell lymphoma, acute renal failure, anuria

Introduction

Diffuse large B-cell lymphomas (DLBCLs) are a heterogeneous group of malignant disorders that present as large transformed lymphoid B cells and account for approximately 30-35% of non-Hodgkin lymphoma cases. According to the World Health Organization (WHO) classification, DLBCLs include many distinct disease entities [1]. DLBCLs generally express B-cell lineage antigens, such as CD20, CD79a, and PAX5. Rituximab, a chimeric anti-CD20 monoclonal antibody, has been used to treat DLBCLs with variable outcomes [2]. However, very few DLBCL patients do not express CD20 antigen, classified as CD20-negative DLBCL. This is a rare and heterogeneous group of lymphoproliferative disorders including plasmablastic lymphoma (PBL), primary effusion lymphoma (PEL), anaplastic lymphoma kinase (ALK)-positive DLBCL, and large B-cell lymphoma arising in human herpesvirus-8 (HHV-8)-associated multicentric Castleman disease (MCD) [3]. CD20-negative DLBCL has an aggressive clinical course with primary chemoresistance and poor prognosis. Due to lack of CD20 expression, rituximab therapy is not beneficial in these rare and aggressive disorders.

Patients with CD20-negative DLBCL typically present with rapidly enlarging nodal or extranodal masses with or without B symptoms (fever, night sweats, or weight loss). Enlarged lymph nodes may occur in any part of the body, causing diverse clinical manifestations such as lactic acidosis [4], nasal obstruction [5], melena, loss of appetite [6], abdominal distension, and vomiting [7]. The multiple enlarged lymph nodes with strong ^{18}F-fluoro-2-deoxy-D-glucose (FDG) accumulation, which caused urinary tract obstruction and followed by acute renal failure is very rare. Here, we report a case of CD20-

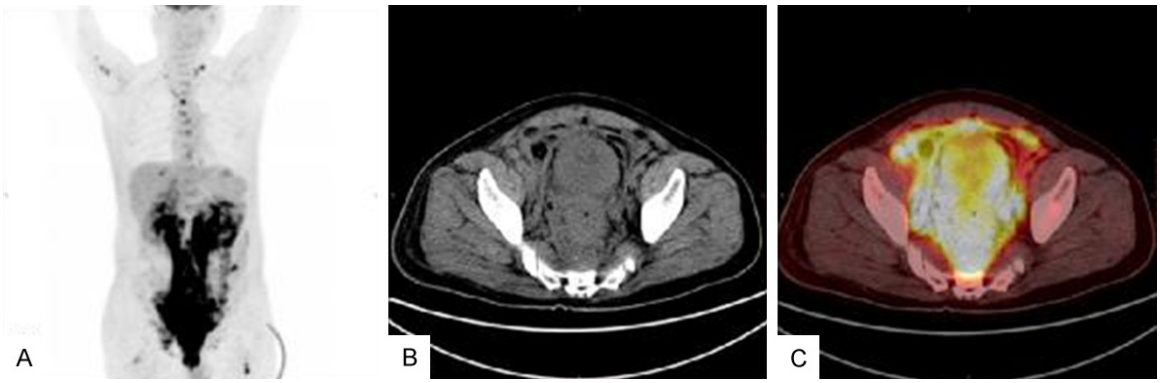

Figure 1. FDG-PET/CT images. A. FDG-PET reveals multiple swollen lymph nodes and FDG accumulation in the abdominal pelvic peritoneum (standardized uptake value; SUVmax 19.9). B. CT image of the pelvic cavity reveals multiple swollen lymph nodes. C. FDG-PET shows pelvic lymph nodes that have taken up FDG (SUVmax 19.9).

negative DLBCL presenting as anuria. To the best of our knowledge, this is the first reported case of CD20-negative DLBCL-induced acute renal failure presenting as anuria.

Case presentation

A 54-year-old male was referred to our hospital with a chief complaint of anuria, from which he had been suffering for 5 days. He was in otherwise good health with no antecedent trauma. The history of the present illness revealed he experienced nonspecific diffuse abdominal discomfort and reduced urine output, followed by anuria. On the fifth day, he was referred to the department of urology. He had no B symptoms (fever, night sweats, or weight loss). Physical examination revealed double kidney percussion pain, no ureteral tenderness, and no prostate gland enlargement. There were several palpable superficial lymph nodes, but no hepatosplenomegaly or any other mass. Laboratory tests revealed mild anemia. His serum biochemistry results were within normal ranges with the following exceptions: serum lactate dehydrogenase (LDH), 813 (109-245) U/L; serum creatinine (CRE), 1227.9 (53.0-106.0) mmol/L; and blood urea nitrogen (BUN), 28.2 (3.2-7.1) mmol/L. All other examinations were either within normal limits or no significant abnormality, including a negative result for human immunodeficiency virus (HIV) antibody detection. Ultrasound examination revealed bilateral hydronephrosis and diffused bladder-wall thickening. Computed tomography (CT) results were suggestive of colon cancer with metastatic carcinoma of multiple lymph nodes in peritoneum and pelvic cavity, and bilateral hydronephrosis. The patient underwent hemodialysis treatment and ureteroscopy, which failed to locate the ureteral orifice. ^{18}F-fluoro-2-deoxy-D-glucose-positron emission tomography/computed tomography (FDG-PET/CT) examination was performed. As shown in **Figure 1**, PET/CT revealed multiple lymphoid swelling and strong FDG accumulation, which was considered indicative of lymphoma. Biopsy of the right inguinal lymph node (2 × 2 × 2 cm) was performed, and the histopathology results indicated DLBCL. Subsequently, the patient was transferred to the hematology department for further treatment.

Bone marrow puncture and biopsy were performed; however, bone marrow cytology and pathology showed no evidence of lymphoma.

Immunophenotype analysis was performed by multiparametric flow cytometry (FCM) on the patient's biopsied bone marrow cells. As shown in **Figure 2**, his bone marrow cells were CD10(+), CD19(+), CD22(+), CD20(-), and immature B lymphocytes (3%) were obtained from the bone marrow aspirate.

Immmunohistochemical (IHC) analysis revealed his lymphoid cells were CD10(+), CD21(+), CD79a(+), CD99(+), LCA(+), Myc(+), P53(+), PAX5(+), ALK(-), BCL-2(-), BCL-6(-), CD3(-), CD20(-), Mum-1(-), TDT(-), and approximately 90% of his tested lymphoid cells reacted positively to Ki-67 antibody (**Figure 3**).

The patient was diagnosed with CD20-negative DLBCL-NOS (not otherwise specified), Ann Arbor stage IV, group A, and international prog-

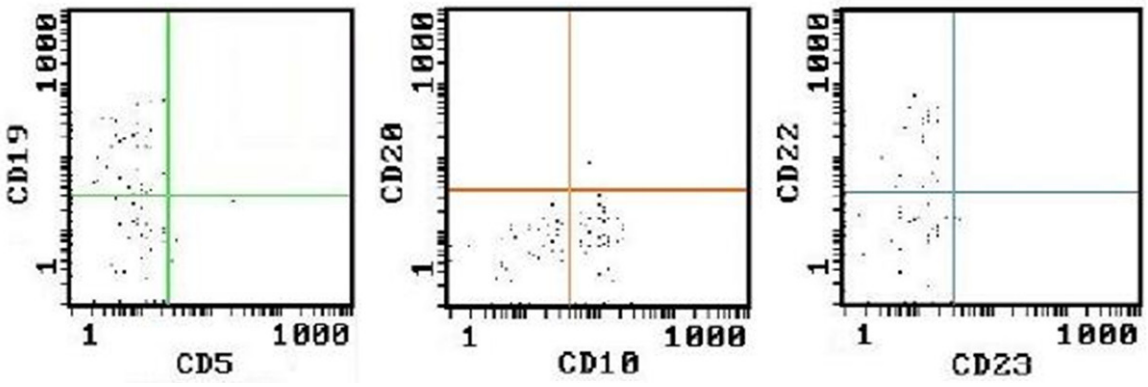

Figure 2. Flow cytometry (immunophenotype) analysis of bone marrow cells. The cells were positive for CD10, CD19 and CD22 and negative for CD20 expression.

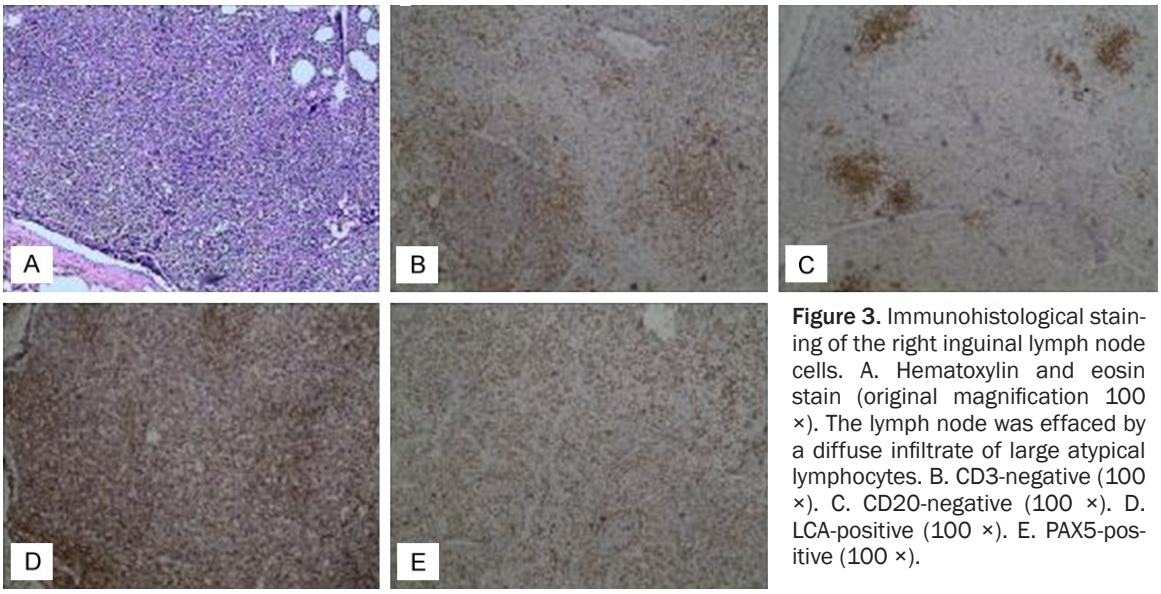

Figure 3. Immunohistological staining of the right inguinal lymph node cells. A. Hematoxylin and eosin stain (original magnification 100 ×). The lymph node was effaced by a diffuse infiltrate of large atypical lymphocytes. B. CD3-negative (100 ×). C. CD20-negative (100 ×). D. LCA-positive (100 ×). E. PAX5-positive (100 ×).

nostic index (IPI) intermediate-risk. He was treated with seven courses of CHOP (cyclophosphamide, doxorubicin, vincristine, and dexamethasone) and one course of EPOCH (etoposide, cyclophosphamide, doxorubicin, vincristine, and prednisolone) chemotherapy. His symptoms decreased after the first course, but relapsed after six cycles of chemotherapy.

Discussion

CD20-negative DLBCL is a novel rare subtype of non-Hodgkin B-cell lymphoma that exhibits a more aggressive clinical course with resistance to chemotherapy and worse prognosis compared with typical DLBCL. Due to lack of CD20 expression, rituximab is seldom used in the treatment of these cases, which are characterized by primary chemoresistance and early relapse [3]. Taken together, the outcomes of patients with CD20-negative DLBCL are poor, with the median survival time ranging between several months and a few years. In the present study, we report a case of CD20-negative DLBCL that was treated with seven cycles of CHOP and one cycle of ECHOP chemotherapy over 9 months. His symptoms decreased after the first course, but relapsed after six cycles of treatment. A new strategy is needed to cure these rare and aggressive disorders.

Many factors and mechanisms contribute to the occurrence of CD20-negative DLBCL. These include environmental agents, genetic mutations, chromosomal translocations, and patient immunological abnormalities. Deregulation of

BCL-6 gene expression may be specific to DLBCL [8]. An early study illustrated that plasmablastic lymphomas of the oral cavity are associated with HIV infection [9]. However, recent cases have emerged in HIV-negative patients involving other sites, such as the nasal cavity [10], liver [11], small intestine [12], and central nervous system [13]. In this case, the patient had no HIV infection, tobacco or alcohol abuse, or toxic or other known exposure. Increasing age and decreasing immunity may be considered risk factors in this case.

Patients with DLBCL typically present with rapidly enlarging nodal or extranodal masses with unusual symptoms and presentations. A recent study reported a rare case of CD20-negative DLBCL presenting with lactic acidosis [4]. An early study reported a case of CD20-positive DLBCL presenting as acute renal failure, for which anti-CD20 targeted therapy could be beneficial [14]. In the present case, nodal and extranodal masses induced urinary tract obstruction and acute renal failure. The patient's prognosis was poor due to lack of CD20 expression.

PET/CT plays a vital role in the diagnosis of DLBCL [15]. In the present case, the CT results suggested colon cancer with metastatic carcinoma, and surgery was considered. PET/CT revealed multiple swollen lymph nodes with strong FDG accumulation, indicative of lymphoma. Histopathology, the diagnostic golden standard for neoplasms, confirmed the diagnosis. IHC examination revealed the subtype was CD20-negative DLBCL, thus providing evidence required for treatment.

CD20-negative DLBCL is a rare and aggressive lymphoproliferative disorder that represents a therapeutic challenge. As CD20 expression is negative, rituximab plus combination chemotherapy is not efficacious. To date, many treatment strategies for CD20-negative DLBCL have been proposed in case reports and small retrospective case series. However, no prospective trials have been conducted to establish treatment standards for these patients. Standard treatment strategies for DLBCL, such as CHOP and EPOCH, have been used for the treatment of CD20-negative DLBCL. However, outcomes may vary depending on individual patient characteristics, cancer subtype, and Ann Arbor stage. A recent study reported a patient who responded to EPOCH regimen therapy with partial regression of the disease [7]. The present case was Ann Arbor stage IV, which may have contributed to the poor outcome. Thus, it is crucial to diagnose DLBCL early and start treatment immediately.

In the present study, we report a very rare case of CD20-negative DLBCL-induced acute renal failure presenting as anuria. Given the poor prognosis of these lymphomas and the lack of therapeutic efficacy of anti-CD20 therapy, additional cases should be collected, as formulation of an optimized therapeutic strategy is urgently required.

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Disclosure of conflict of interest

None.

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