Case Report

Clear cell variant of diffuse large B-cell lymphoma: a case report and review of the literature

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Abstract: Diffuse large B cell lymphoma (DLBCL) is a diffuse proliferation of large neoplastic B lymphoid cells with nuclear size equal to or exceeding that of normal macrophage nuclei. The DLBCL morphological variants are centroblastic, immunoblastic, T-cell- and histiocyte-rich, anaplastic, plasmablastic, anaplastic lymphoma kinase-positive, and primary mediastinal large B-cell lymphoma (PMBCL). These histopathologically-recognized morphological variants respond differently to treatment and have distinct prognoses. We report a case of a 43-year-old patient who presented pain in the lower abdomen that had begun four months prior. Ultrasound-guided biopsy revealed epithelial cell features and a partial alveolar growth pattern. We discovered large diffuse areas comprising large cells with slightly irregular nuclei and very clear cytoplasm. These features were similar to those of clear cell carcinoma in renal tissue, suggesting the possibility of an epithelial neoplasm. To test this possibility, immunohistochemistry for cluster designation markers was performed, but the diffuse areas were found to be positive only for CD45. Additional immunohistochemistry was performed, and the diffuse areas were found to be positive for CD20, CD79a, P53, and Mum-1. Based on these characteristics, a diagnosis of a clear cell variant of DLBCL was made, and the patient was treated with chemotherapy. Precise histological diagnosis is crucial for clinical management and ultimately for patient survival. There has been one additional report of a case of clear cell DLBCL, outside the mediastinum. The features we identified can be used to define a new subtype of DLBCL. The expression of P53 and Mum-1 suggest a poor prognosis.

Keywords: Diffuse large B-cell lymphoma, retroperitoneal, CD45, CD20, clear cell, morphology, newly defined entities

Introduction

Diffuse large B cell lymphoma (DLBCL), a subtype of non-Hodgkin’s lymphoma (NHL), is the most common type of lymphoid tumor worldwide, accounting for 30%-40% of adult NHLs, according to the World Health Organization’s (WHO) classification of neoplastic diseases of hematopoietic and lymphoid tissues [1]. DLBCL exhibits striking heterogeneity at the clinical, genetic, and molecular levels [2]. The tumor may arise as a primary tumor or as a result of the progression and transformation of a less aggressive lymphoma [3-5].

This heterogeneous group of lymphoid neoplasms is characterized by diverse spectra of clinical and morphological features [5], responses to therapy, and survival [6-9]. In particular, histological examination has revealed considerable morphological diversity. Morphological variants include the centroblastic, immunoblastic, and anaplastic subtypes, among which the centroblastic is the most common, with better prognosis and overall survival [10, 11]. Additional variants have been described, and new evidence supports their distinction as independent diseases [12]. The WHO (2008) working group delineated some of these newly defined entities [10] on the basis of their distinctive clinical, pathological, or biological features. Their recognition is helpful in defining a more homogeneous group of DLBCL. However, a large number of biologically and clinically heterogeneous cases remain for which there are no clear and accepted criteria for subclassification; these are collectively termed DLBCL, not otherwise specified (NOS).
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We present a case of primary DLBCL with clear cell morphology in the retroperitoneal space, with a review of the literature. According to the results of immunohistochemistry (IHC), the patient presents non-germinat center B cell-like (non-GCB) DLBCL, suggesting a poor prognosis.

**Case presentation**

The patient was a 43-year-old woman who presented with the chief complaint of painful swelling in the lower abdominals. She was admitted to the hospital due to complaints of fatigue, dizziness and intermittent lower abdominal pain without obvious incentives. Symptoms had begun 5 months before admittance and had been aggravated for half a month. The patient first experienced fatigue, dizziness, and discomfort 5 months before her admittance. The symptoms worsened after activity and could be relieved temporarily after rest. Upon symptomatic treatment provided by a local hospital, the symptoms disappeared. Then one month after the symptoms began, the patient experienced a dull pain in her lower abdomen and developed a mass at the site of the pain. Initially, the patient ignored the symptoms and did not seek medical treatment. Over time, the pain aggravated gradually and presented intermittent features accompanied by fatigue, dizziness, and discomfort. The patient also experienced occasional nausea but no abdominal distention, vomiting, or melena. Half a month before admission, she received CT examination in a local county hospital due to persistent and unbearable aggravated lower abdominal pain. The result of the CT examination indicated a mass in her lower abdomen. Her weight had decreased by 8 kg since the onset of her condition. The patient reported no previous medical history and denied history of familial infective or genetic disease. Upon admission, the patient had a temperature of 36.4°C and blood pressure of 120/70 mmHg. Systemic superficial lymph nodes were not enlarged. Her abdomen was soft and flat, but a hard and relatively fixed mass with an irregular size of approximately 7 cm × 6 cm was palpated under the navel. The mass was tender without rebound tenderness. The liver, spleen and bilateral kidneys were not palpated. Repeated abdominal CT detected a soft tissue mass beneath the lower and medial peritoneum (Figure 1A). The mass wrapped the aorta, inferior vena cava and bifurcation area of the left and right iliac vessels. There was no

![Figure 1](image_url)
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obvious invasion in the vertebral body. The mass had a CT value of 44.0 HU, a maximum area of 5.28 cm × 4.27 cm, and unclear boundaries with the surrounding tissues. When enhanced scanning was performed, arterial phase enhancement was not obvious and the CT value was approximately 48.9 HU. The intra-peritoneal lymph node was not enlarged. Plain film X-rays of the anteroposterior and lateral chest were normal without mediastinal enlargement. CT inspection revealed no masses in liver, kidney, lung, adrenal gland and brain. B ultrasound examination showed a homogeneous and relatively hypo-echoic area with a size of 6.2 cm × 3.5 cm around the abdominal aorta, behind the peritoneum and in front of the vertebral column. This area presented clear boundaries, a fairly regular shape, and regular internal echo. Blood routine examination, liver function testing, and biochemical testing found no abnormalities. B ultrasound-guided tumor puncture was performed two days after the patient was admitted to our hospital. A gray-white tissue with a length of 2 cm and a diameter of 2 mm was extracted. Conventional sectioning showed relatively homogeneous transparent cells that were analogous to renal clear cell carcinoma of medium size. Most cells were irregularly polygonal or ovoid in shape, with distinct cell boundaries and clear cytoplasm (Figure 1B). Nuclei were oval or irregular in shape and were deeply stained. Large nucleoli were observed in some of the nuclei. Massive necrosis accounted for 15% of the tumor tissue. A small number of fat cells were found in the tumor tissue without obvious interfibrillar substance. The preliminary consideration was an epithelial mesenchyme-derived malignant tumor. To test this possibility, IHC was carried out using antibodies for vimentin, Syn, CD34, CD117, S-100, HMB45, CKpan, CKlow, and CD45. CD45 was strongly expressed, but the tissue was negative for the rest of the epithelial and mesenchyme antibodies, suggesting that the tumor was not an epithelial mesenchyme-derived malignant tumor. Next, retroperitoneal lymphoma was considered, and a second round of IHC staining was performed. Antibodies were selected for their roles in the diagnosis and classification of lymphoma. Strong positive labeling was observed for CD20 (Figure 1C) and CD79a (++) as well as for P53 and MUM-1 (+++) (Figure 1D). In addition, approximately 70% of nuclei were positive for Ki67 (Figure 1E). The tissue was negative for CD10, CD21, CD30, Bcl-2, bcl-6, CD3 and ALK. Based on these characteristics, we diagnosed the tumor as a clear cell variant of DLBCL, non-GCB type. R-CHOP was chosen as the clinical therapeutic protocol.

Discussion

DLBCL is a moderately to highly malignant B cell-derived tumor with significant heterogeneity. This heterogeneity is present not only in its complex and diverse clinical manifestations, histological features [4], immune phenotypes, and genetic characteristics, but also in the inconsistent responses of DLBCL patients to treatment and their different prognoses [5, 13, 14]. In the WHO classifications of 2001 and 2008 [15, 16], variants of DLBCL were defined according to the belief that they represent distinct clinico-pathologic entities [17]. As such, the pathomorphological changes found in tumors can be used for diagnostic purposes and to guide treatment. In the case we presented, the tumor cell morphology was different from that of common variants of DLBCL. Instead, the transparent and lightly stained tumor cell cytoplasm gave the initial impression that the condition was metastatic clear cell carcinoma or another clear cell tumor. This case suggests that the heterogeneity of DLBCL is greater than previously thought, as tumor cells can have morphological changes outside of those present in more common variants of DLBCL. Such differences in morphology present a great challenge for pathological diagnosis. Had no IHC techniques been applied, the pathological diagnosis in this case would have been incorrect. In pathological and differential tumor diagnosis, a variation of DLBCL should be considered after epithelial and mesenchymal tumors are excluded by IHC. This case emphasizes that correct pathological diagnosis requires the use of several pathological techniques, especially IHC.

In diagnosing the tumor, we had to differentiate our case from other variants of DLBCL, including PMBCL. PMBCL is classified by the WHO and Maurizio Martelli classifications [18] as a subtype of DLBCL due to its distinct clinical presentation in younger patients, tumor site, and expression of CD30. PMBCL is thought to arise from asteroid B-cells of the thymus [19] and has often been recorded in young women presenting with a large mediastinal mass that fre-
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We performed a search of the literature worldwide and found a case reported by Suzana Manxhuka-Kerliu in 2011 [4]. Both this patient and the one in our case are at middle age and are pathologically typed as non-GCB.

**Conclusion**

Based on our IHC findings, we diagnosed the present case as a clear cell variant of DLBCL of activated cell type, post-germinal center cell origin. Clear cell morphology is atypical of DLBCL, and may represent an otherwise unspecified variant of DLBCL. Our patient is alive and undergoing R-CHOP chemotherapy treatment. Due to time restrictions, the treatment has not been completed and further observation is required.

**Disclosure of conflict of interest**

None.

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**References**


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