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**Case Report**

# Case report of primary CD20 negative diffuse large B-cell lymphoma

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## Abstract

**Few groups of aggressive non-Hodgkin's lymphomas (NHL) that are refractory to standard chemotherapy are rarely reported. Primary CD20 negative diffuse large B cell lymphoma (DLBCL) without human immunodeficiency virus infection is an uncommon presentation and this case report is challenging in terms of diagnosis and treatment as well.**

## INTRODUCTION

The most common subtype of non-Hodgkin's lymphoma (NHL) is diffuse large B-cell lymphoma (DLBCL) which constitutes around 30–40% of all cases [1]. B-cell activation is dependent on CD-20 antigen which is a membrane protein and pan B-cell marker due to its expression on neoplastic B lymphocytes [1]. Primary CD20 negative DLBCL has rarely been reported and accounts for 1–3% of cases [2]. There are few known subtypes of CD-20 negative DLBCL [1]. Primary CD20 negative DLBCL is not common and has comparably bad prognosis as CD-20 negative DLBCL is refractory to standard treatment and this subtype is usually associated with extra nodal disease, unusual morphology and aggressive behavior. [2, 3]. We report a case of *de novo* CD20 negative DLBCL that did not respond to first-line treatment and required salvage chemotherapy to achieve partial remission.

## CASE

A 33-year-old male with no known comorbid presented with complaints of neck swelling which progressively increased in size for 3 months, associated with fever and difficulty in breathing. On examination he was vitally stable. General physical examination showed multiple skin lesions and bilateral cervical and axillary lymphadenopathy with the left cervical node measuring 4 × 6 cm in size. Systemic examination was unremarkable. His computed tomography (CT) scan of chest, abdomen and pelvis showed large infiltrative heterogeneously enhancing mass involving superior anterior and middle mediastinum involving root of aorta and other major vessels with extension of disease encasing trachea, superior vena cava, brachiocephalic veins, pulmonary trunk and veins (Fig. 1). Punch biopsy of the skin was done which showed mild irregular acanthosis and focal parakeratosis representing inflammatory hyperpigmentation which was managed with skin moisturizers. Excisional lymph node biopsy from left cervical area was sent for AFB smear culture, Gene-Xpert for tuberculosis (cartridge-based nucleic acid amplification test) and bacterial culture which were negative. Histopathology showed effaced architecture and infiltration with atypical lymphoid cells showing pleomorphic nuclei with prominent nucleoli. Immunohistochemistry (IHC) for leukocyte common antigen (LCA) was positive, while it was negative for CD-20 but positive for CD79a, PAX-5 which are other B cell markers (Fig. 2).

Considering diagnosis of CD20 negative DLBCL further work up including CD138 for possible plasmablastic variant, ALK protein, EBV, CD30 and HHV 8 was performed for other differential diagnosis, which were negative (Fig. 2). Human immunodeficiency virus (HIV) serology was also negative. Considering the diagnosis of primary CD20 negative DLBCL, which is a high-grade lymphoma, we started him on infusion chemotherapy regimen i.e. EPOCH (Etoposide, Prednisolone, Doxorubicin, vincristine along with bolus of cyclophosphamide). His follow-up interim scan done after four cycles of EPOCH did not show any change in the disease status (treatment failure). Subsequently he was started on second-line chemotherapy i.e. GCD (Gemcitabine, Cisplatin and Dexamethasone) and after two cycles his interim PET-CT scan showed partial remission. We are now planning for autologous stem cell transplantation (ASCT) once he achieved response on two more cycles of GCD.

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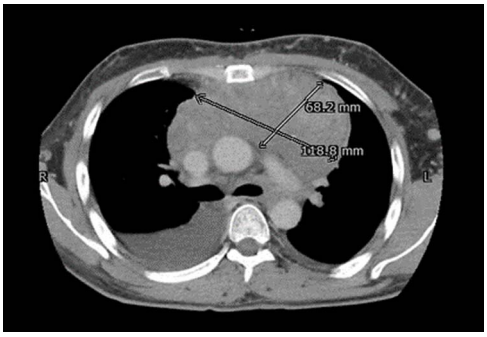


**Figure 1.** CT chest with contrast showing large heterogeneous mass.

## DISCUSSION

A rare entity like CD20 negative DLBCL is a heterogonous group of aggressive lymphomas [1]. They constitute 1–3% of all B-cell non-Hodgkin's lymphomas [2]. CD20 is a pan B-cell marker and cells can still survive even after loss of CD20 expression in CD20 negative DLBCL [1]. Known subtypes include plasmablastic lymphomas (PBL), primary effusion lymphomas (PEL), anaplastic kinase positive large B-cell lymphomas (ALK+ve LBCL) and large B-cell lymphomas arising in human herpes virus 8 associated multicentric Castleman disease (HHV-8 MCD-LBCL) [2].

The most prevalent and well-known sub-type is PBL, which accounts for 75% of the reported cases [3]. Both HIV-positive and -negative patients have been found to have primary CD20 loss in DLBCL [1]. Pathologically, CD20 negative DLBCL is more closely associated with aggressive pathologic parameters with a high proliferation index and a higher proportion of non-GCB type [1]. Only a few cases of well-established sub-types of CD-20 negative DLBCL have been reported that could not be categorized as known variants of CD20 negative DLBCL [4]. This might broaden the spectrum of unclassifiable primary CD20 negative DLBCL which shows genetic and immunophenotypic aberrancy and results in diagnostic and therapeutic challenges [4]. Morphology and the results of immunohistochemistry and flowcytometry are used to identify DLBCL. Positivity of CD19, CD79, PAX5 are the major immunohistochemical biomarkers used to establish a diagnosis of CD20 negative B cell lymphomas, while flowcytometric analysis shows positivity for CD19, CD79a, CD5 and CD10 in cases of CD20 negative B cell lymphomas [5]. Molecular analysis using cytogenetic and fluorescence *in situ* hybridization (FISH) to detect rearrangement or translocation of BCL-2, BCL-6 and C-MYC is an important part of diagnosis and the most frequently found mutation is BCL-2 [6].

Patients with CD20 negative DLBCL do not respond to standard cyclophosphamide, doxorubicin, vincristine and prednisone (CHOP), and still no standard of care for CD20 negative B-cell lymphomas has been identified. Considering poor prognosis, high-dose chemotherapy

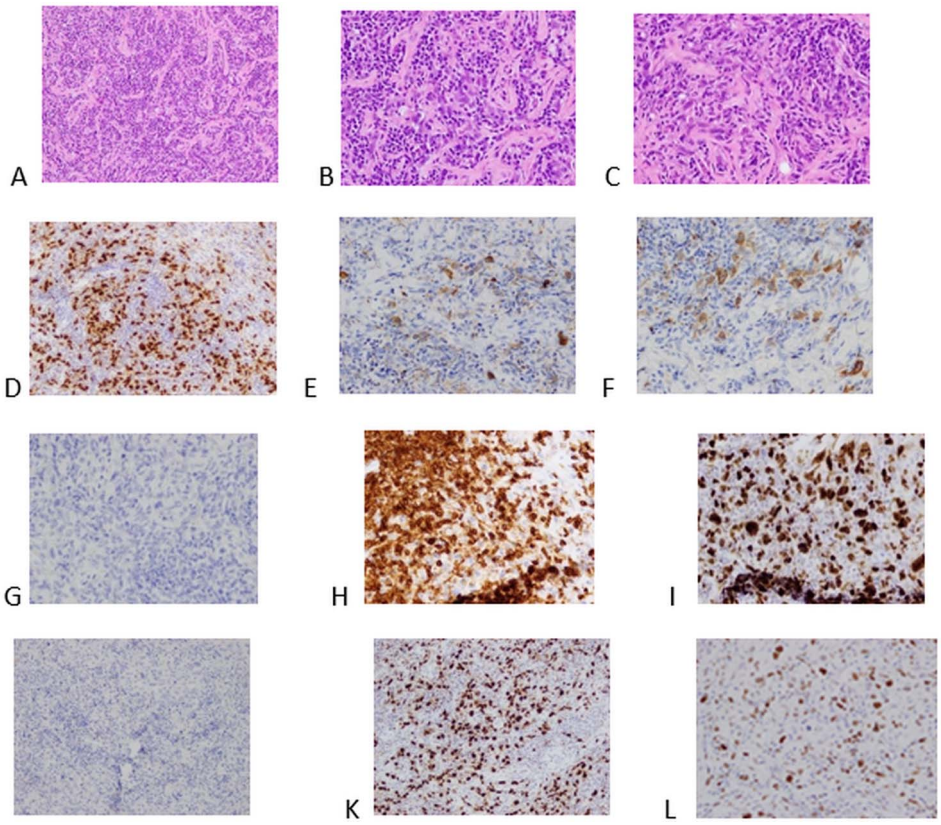


**Figure 2.** (A), (B) and (C) showing Lymph node biopsy HE at 20-X and 40-X show effaced architecture by group of atypical lymphocytes. (D) PAX-5, (E) and (F) CD 79a at 40X shows positive staining in neoplastic cells. (G) CD 20 negative. (H) CD 3 negative in neoplastic cells. (I) Ki-67 increased. (J) CD 30 negative. (K) MUM-1 and (L) C-MYC positive in neoplastic cell.

had been suggested i.e. either cyclophosphamide, vincristine, doxorubicin and dexamethasone alternating with high-dose cytarabine and methotrexate (hyperC-VAD), EPOCH with modified dose, or cyclophosphamide, vincristine, doxorubicin, methotrexate alternating with ifosfamide, etoposide and cytarabine (CODOX M/IVAC) [7–9] as per previous literature review.

Our patient did not respond to EPOCH chemotherapy regimen. He was therefore started on salvage chemotherapy and has been planned for autologous stem cell transplant considering poor prognosis of disease course [10].

## FOLLOW UP OF CASE

Post 4 cycles of GDP he achieved partial response and went autologous stem cell transplant and is doing well with engraftment of all cell lines.

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## CONFLICT OF INTEREST

Nothing to declare.

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## ETHICAL APPROVAL

N/A.

## CONSENT

Informed written consent taken.

## GUARANTOR

Kanta Devi is the guarantor of this manuscript.

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