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Case Report

Diffuse large B-cell lymphoma, multilocalized and extranodal in adult with complete remission: a case report

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ABSTRACT

Diffuse large B-cell lymphoma (DLBCL) is a heterogeneous group of lymphomas. The current classification recognizes an expanding group of distinct entities, with this being the most common. Up to one-third of DLBCL cases may originate in nearly any organ, most commonly in the gastrointestinal tract, skin and soft tissues, bones, or genitourinary tract. A 52-year-old woman with no history of chronic degenerative diseases presented with severe abdominal pain, weight loss, and night sweats. As part of her evaluation, an abdominopelvic CT scan was performed, revealing splenomegaly with internal nodular lesions of undetermined origin, inguinal lymphadenopathy, and cutaneous involvement. A lymphoproliferative process was suggested among the differential diagnoses. Immunohistochemical studies confirmed DLBCL. The patient subsequently received treatment with R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone), achieving a cure rate of approximately 50% after six cycles with an adequate response to treatment.

Keywords: Diffuse large B-cell lymphoma, Lymphoproliferative, Immunohistochemistry

INTRODUCTION

Non-Hodgkin lymphoma (NHL) is the most common hematologic malignancy worldwide, accounting for nearly 3% of all cancer diagnoses and deaths. It primarily presents as lymphadenopathy or the presence of solid tumors. According to the WHO, the most common NHL in Western countries is diffuse large B-cell lymphoma (DLBCL), representing about 31–40% of adult cases.[1,2] The classification of lymphoid neoplasms includes various subtypes within the DLBCL group, each characterized by unique clinical and/or pathological features. These include primary mediastinal large B-cell lymphoma (PMBL), primary DLBCL of the central nervous system, primary cutaneous DLBCL, T-cell/histiocyte-rich large B-cell lymphoma, Epstein-Barr virus (EBV)-positive DLBCL, and unspecified subtypes, among others. However, most DLBCL cases fall under the unspecified category.[2-4] Immunophenotypically, the neoplastic cells express B-cell markers, including CD19, CD20, CD22, PAX5, and CD79a. Surface and/or cytoplasmic immunoglobulins (IgM > IgG > IgA) can be demonstrated in up to 75% of cases.

Markers commonly used in characterizing DLBCL include CD10, BCL6, BCL2, and IRF4/MUM1. Aberrant cytoplasmic CD3 expression has been documented primarily in extranodal presentations, without expression of other T-cell markers.[5] CD5 expression in DLBCL is observed in approximately 5–10% of cases. Most cases exhibit an activated B-cell phenotype with extranodal distribution.[6] Up to one-third of DLBCL cases may

originate in almost any organ, most commonly in the gastrointestinal tract, skin and soft tissues, bones, or genitourinary tract.

Furthermore, advanced DLBCL can spread to extranodal organs, particularly the bone marrow, pleura, peritoneum, liver, and central nervous system (CNS), occasionally obscuring the primary site of origin.[2,7,8] DLBCL is an aggressive disease, with patients often presenting with rapidly enlarging lymphadenopathy and constitutional symptoms, requiring immediate treatment. While most patients exhibit lymphadenopathy, extranodal disease is also possible. The most common initial treatment is chemoimmunotherapy with R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone), achieving a cure rate of approximately 50% of patients.[4]

CASE REPORT

A 52-year-old woman with no history of chronic degenerative diseases presented with severe abdominal pain, weight loss, and night sweats. She underwent evaluation to rule out intestinal infectious processes and differential diagnoses of abdominal pain syndrome. As part of her workup, an abdominopelvic CT scan revealed splenomegaly with internal nodular lesions of undetermined origin, as well as inguinal lymphadenopathy. A lymphoproliferative process was suggested as part of the differential diagnosis. Laboratory findings included.

Complete blood count, WBC 7,000, Hb 11.9 g/dl, HCT 35.2%, platelets 223,000, neutrophils, 73.6%, reticulocytes 3.2%, myelocytes 2%. Samples were obtained from the lesions identified in the initial CT scan, including a biopsy of an inguinal lymph node. The immunohistochemistry report indicated CD3 positive with reactive pattern. CD20 positive with reactive pattern. BCL2 positive with reactive pattern (paracortical expression, negative in lymphoid follicles). CD10 positive in a few follicular and paracortical lymphocytes. KI67 positive in germinal centres with appropriate polarization.

Subsequently, due to symptom follow-up and evaluation by hematology, a positron emission tomography (PET-Scan) was performed, along with immunohistochemistry from a different location (peripancreatic lymph node).

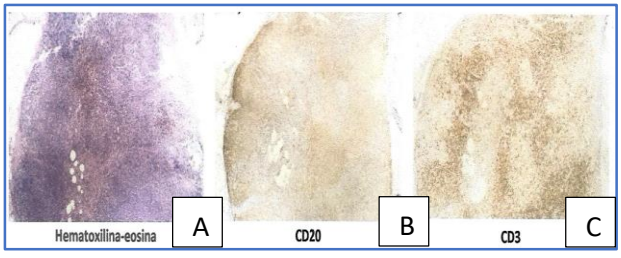

Figure 1 (A-C): Lymphoid follicular hyperplasia in an inguinal lymph node sample.

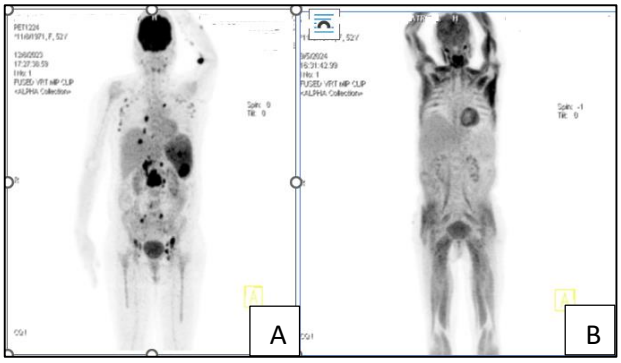

Figure 2 (A and B): Comparison of Computed Tomography (PET-Scan) after treatment, showing in the first image the multifocal and extranodal manifestation of DLBCL.

The PET-Scan report shows images with adenomegaly localized in the following areas: head and neck with 20 lymph nodes on each side of the neck (12 mm), thorax with mediastinal lymph nodes (1.5 cm in diameter) in the anterior and middle mediastinum, predominantly in the right pulmonary hilum, as well as multiple bilateral axillary lymph nodes (10 on each side) up to 1 cm in diameter.

The abdomen and pelvis show splenic masses up to 3.5 cm, two of which are dominant and tend to converge, and another smaller one of 1 cm. The pancreas shows a 5 cm conglomerate of peripancreatic nodes at the head of the pancreas. The liver has 5 lymph nodes in the hepatic hilum and one retrocaval lymph node on the left.

The retroperitoneum contains 30 lymph nodes up to 12 mm, extending throughout the entire retroperitoneum, including intracanal aortic, paraaortic, and paracervical nodes, as well as 2 lymph nodes of 1.5 cm in common iliac chains (10 lymph nodes in total). The musculoskeletal and cutaneous areas show 4 cutaneous nodules in the left forearm region.

The decision was made to manage the patient with R-CHOP for 6 cycles, with complete remission of both nodal and extra nodal lymphoma activity (Figure 2). The patient is currently under surveillance.

Table 1: Biopsy product (TRU-CUT) of a peripancreatic lymph node with histopathological and immunohistochemical findings consistent with diffuse large B-cell lymphoma (DLBCL).

Antibodies	Results
CD20	Positive (+++)/ Difuso L26
CD3	Positive (++)/Focal/MRQ-39
CD10	Negative/56C6
BCL-6	Positive (+++)/LN22
MUM-1	Negative/MRO-43
Ki-67	Positive (+++)/80%/sp6

DISCUSSION

Cases of DLBCL originating in almost all organs and tissues have been described, although there are frequent locations and others that are diagnosed only as anecdotal cases. While percentages vary, the most common extra nodal DLBCL locations are: gastrointestinal DLBCL, Waldeyer's ring DLBCL, salivary gland and other cervicofacial DLBCL, cutaneous DLBCL, central nervous system DLBCL, bone DLBCL, thyroid DLBCL, breast DLBCL, testicular and genitourinary DLBCL, ocular and orbital tissue DLBCL, extradural DLBCL, pleuropulmonary DLBCL, and gynaecological DLBCL. The first five account for more than 65% of all extra nodal DLBCL cases.[3] In our patient, the involvement was at the splenic and cutaneous levels.

The so-called B symptoms (fever higher than 38ºC, night sweats, and weight loss greater than 10%) are indicative of advanced disease. They are present in 47% of aggressive lymphomas but can also appear (<25%) in patients with indolent lymphoma. Other less frequent symptoms include fatigue, anorexia, malaise, pruritus, headache, cough, shortness of breath, and bone or abdominal pain.[9] The recognition that the appearance of DLBCL in specific organs can be associated with distinct clinical or molecular features, as well as consistent recurrence patterns, has generated interest in examining both extranodal origin and secondary involvement as prognostic factors.[10]

Our immunohistochemistry report correlates with DLBCL cases with CD20 positivity (B cells) following up with CD10 negativity, BCl-6 positivity, and MUM-1 negativity, which is consistent with a germinal center profile, with a very high cell proliferation rate (80%), compatible with the multiple nodal and extranodal locations reported in our patient's CT scan. Despite the findings in the initial inguinal lymph node tissue sample, which only showed follicular lymphoid hyperplasia without malignancy, this could be due to many of these malignant neoplasms presenting as extranodal and multifocal masses.

Their clinical and radiological presentations may mimic non-hematopoietic neoplasms, and initial biopsies may give a clinical or radiological impression favoring metastatic tumors or other primary tumors.[11] Various studies have established differences in clinical aggressiveness and response to standard immunochemotherapy using the rituximab, cyclophosphamide, adriamycin, vincristine, and dexamethasone (R-CHOP) regimen. For DLBCL, the complete remission rate can reach 60% but there are cases of aggressive clinical progression in which only 30% of patients achieve complete remission, and 10-15% experience refractory or progressive disease, showing primary resistance to treatment.[12-14] In our patient's case, the involvement was multiple and extranodal, meeting the characteristics of an aggressive DLBCL. However, the treatment employed was conventional R-CHOP, with a good response that did not correlate with the immunohistochemistry report. It is important to note that despite the adverse prognosis of our clinical case due to the evolution, aggressiveness (Stage IV DLBCL), and multilocalization of both nodal and extra nodal involvement, the response to conventional treatment was good. The response to treatment suggests that both splenic and cutaneous involvement originate from the same cell lineage and share similar molecular and metabolic characteristics, although the cutaneous involvement could have been analysed immunohistopathologically to determine its cell lineage.

CONCLUSION

Non-Hodgkin lymphoma (NHL) is the most common hematologic malignancy worldwide and primarily presents as lymphadenopathy or the presence of solid tumors. The most common NHL in Western countries is DLBCL, which represents about 31-40% of adult cases. Extranodal involvement at unusual locations (splenic and cutaneous) is aggressive; however, it responds well to conventional treatment with R-CHOP.

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