Our Dermatology Online

Case Report

Triple-negative diffuse large B-cell lymphoma: A distinct entity

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ABSTRACT

The Hans algorithm categorizes the diffuse large B-cell lymphoma (DLBCL) into two major subtypes: the germinal center B-cell-like (GCB) DLBCL and the non-GCB DLBCL. This classification is based on three immunohistochemical markers: CD10, BCL6, and MUM1. The non-GCB subtype is associated with lower overall survival (OS) and progression-free survival (PFS) rates compared to the GCB. DLBCL without positive staining for these three markers (CD10$^-$, BCL6$^-$, MUM1$^-$), also called a triple negative or TN, are classified as the non-GCB subtype. However, they show different clinical characteristics and better prognosis than others assigned to the same cell-of-origin group. Herein, we report a case of a TN non-GCB DLBCL with a complete response after R-CHOP therapy. Together with previous reports of TN non-GCB DLBCLs, our case might depreciate the prognostic value of the Hans algorithm, which was already controversial in the literature, especially in the chemoimmunotherapy era.

Key words: Hans algorithm; Immunohistochemical markers; Diffuse large B-cell lymphoma (DLBCL); Germinal center B-cell-like (GCB) DLBCL; Non-GCB DLBCL; Chemoimmunotherapy

INTRODUCTION

Diffuse large B-cell lymphoma (DLBCL) is the most frequently encountered type of non-Hodgkin lymphoma (NHL), representing 30% to 40% of all adult NHLs [1]. It is a heterogeneous disease both clinically and morphologically [2]. In spite of advancements in clinical responses due to the advent of rituximab, the mortality rate is close to 40%. It is, therefore, essential to stratify patients conforming to its prognosis in an appropriate and cost-effective way. For this purpose, numerous immunohistochemical (IHC) algorithms have been proposed. The Hans algorithm is the most widely used in routine practice [3], relying on three markers (CD10, BCL6, and MUM1) to classify DLBCLs according to their prognosis. DLBCLs are categorized into two major subtypes: the germinal center B-cell-like (GCB) DLBCL and the non-GCB DLBCL. The non-GCB subtype is associated with lower overall survival (OS) and progression-free survival (PFS) rates compared to GCB. One category of DLBCL does not stain for the three markers CD10, BCL6, and MUM1, namely, the triple negative or TN (CD10$^-$, BCL6$^-$, MUM1$^-$), which is classified as the non-GCB DLBCL subtype. However, it shows different clinical characteristics and a better prognosis than others assigned to the same cell-of-origin group. Herein, we report a case of a TN non-GCB DLBCL with a complete response after R-CHOP therapy.

CASE REPORT

A 51-year-old male, with no significant past medical history, was referred to our department for the evaluation of a rapidly enlarging ulcerated tumor of the upper back with malaise, fever, night sweats, and weight loss. The lesion was first noticed one year ago. Bleeding after a minor frictional trauma was reported. A physical examination revealed a large polylobed

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ulcerated tumor of the upper back with multiples telangiectasias 15 cm in diameter (Fig. 1). A complete lymph node examination revealed left axillary and right inguinal lymphadenopathy. Palpation of the abdomen for hepatosplenomegaly was negative. An examination of the oral cavity showed no abnormality. Histology revealed a diffuse proliferation of round, large to medium-sized lymphoid cells (Fig. 2). On IHC, the tumor cells expressed CD45 and CD20 (Fig. 3). BCL2, CD10, BCL6, and MUM1 were negative (Figs. 4 and 5). The Ki-67 labeling index was high (60%). The complete blood count and the serum lactate dehydrogenase (LDH) level were normal. An excisional biopsy of an enlarged inguinal lymph node showed a large B-cell lymphoma. A Positron Emission Tomography (PET) scan was performed for staging. It gave evidence of widespread disease involving the liver (segment 1) and multiple lymph nodes (hepatic, pelvic, and deep inguinal). A bone marrow biopsy was negative. The patient was treated with systemic chemotherapy

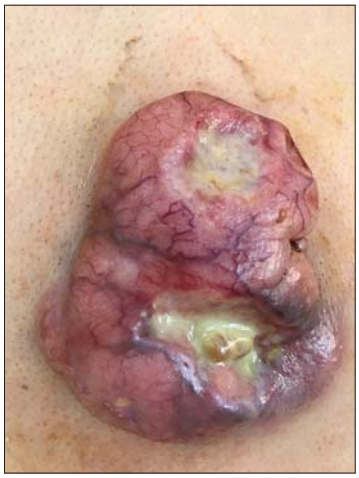

Figure 1: Large polylobed ulcerated tumor of the upper back.

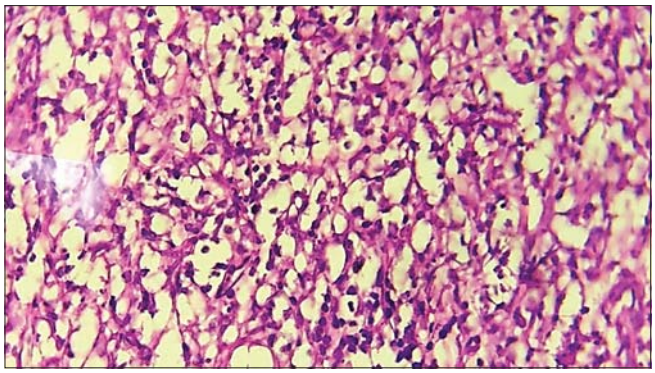

Figure 2: Diffuse proliferation of round, large to medium-sized lymphoid cells (H&E; 20×).

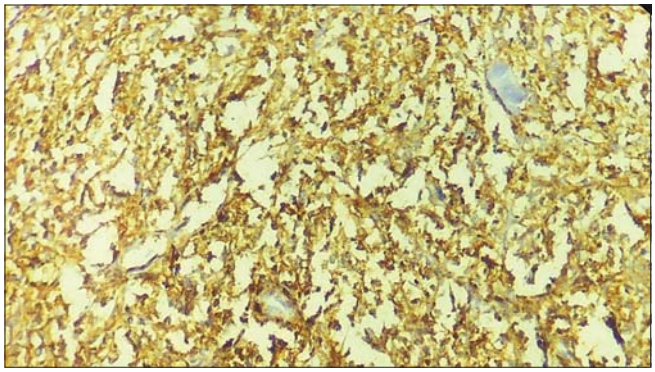

Figure 3: Expression of CD45 on IHC (H&E; 40×).

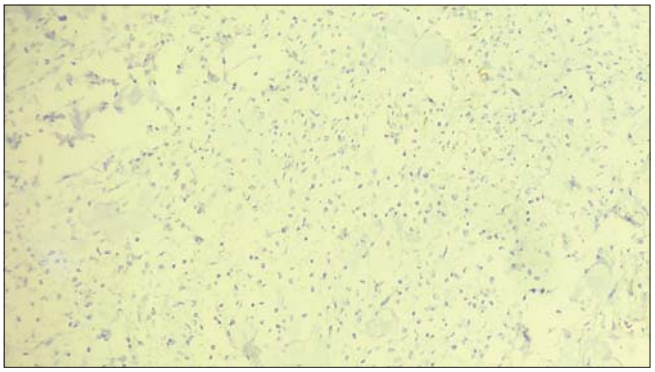

Figure 4: The tumor cells being negative for CD10 (H&E; 40×).

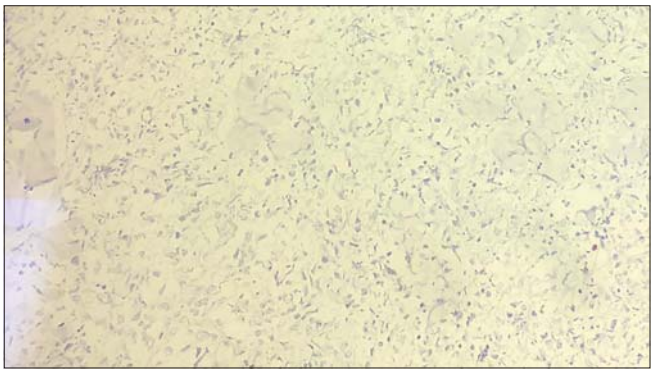

Figure 5: The tumor cells being negative for MUM1 (H&E; 40×).

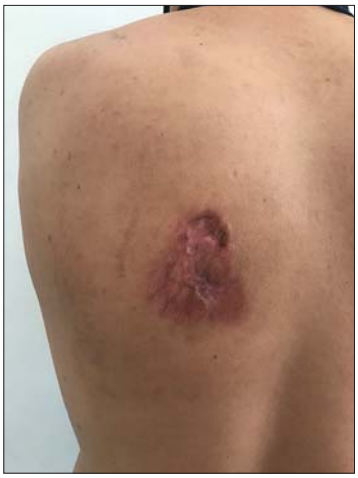

Figure 6: Complete regression of the tumor of the upper back six months after R-CHOP therapy.

(cyclophosphamide, doxorubicin, vincristine, and prednisone) together with rituximab (R-CHOP). Six months after the treatment, a follow-up examination revealed a complete regression of the tumor of the upper back and lymph nodes (Fig. 6). A PET scan showed complete clearance of all lesions. There was no relapse of the disease after three years of follow-up.

DISCUSSION

We report a case of a TN non-GCB DLBCL ($CD10^-$, $BCL6^-$, $MUM1^-$) with a complete response after chemoimmunotherapy. In the literature, the reported incidence of the TN non-GCB DLBCL is 5.5–19.1% [4,5]. In a study on the Hans algorithm, it was 19.1% [3]. The Hans algorithm is known to be a substantial and reasonable strategy for determining the prognosis in DLBCL patients. It involves IHC staining for CD10, BCL6, and MUM1 to classify cases of DLBCL into the GCB and non-GCB groups [3]. Past studies have reported a significant correlation between the non-GCB subtype and lower OS and PFS compared with the GCB [6]. However, TN DLBCLs, which should be classified as the non-GCB subtype according to the Hans algorithm, were found to have different clinical characteristics and better OS and PFS when compared with other non-GCB DLBCLs. The reason for this observation remains unknown [7]. In a study on the prognostic value of each of the markers, the expression of neither CD10 nor BCL6 was predictive of OS or PFS. However, the expression of MUM1 was a significant predictor of worse OS and PFS [8]. Immunohistochemical negativity for MUM1 in TN DLBCL may explain its relatively good prognosis, as in our patient. The existence of an entity such as ours, together with previous reports, might depreciate the prognostic value of the Hans algorithm, which has already been disputed in the literature, especially in the chemoimmunotherapy era [9-11]. The TN non-GCB DLBCL remains an ill-defined entity and, to our knowledge, there are no studies that have accurately characterized the clinical and biological behavior of this type of lymphoma. In conclusion, given the heterogeneity of DLBCLs, it is important to search for new compelling biomarkers to predict the outcome and to help in the management of the patients.

Consent

The examination of the patient was conducted according to the principles of the Declaration of Helsinki.

The authors certify that they have obtained all appropriate patient consent forms, in which the patients gave their consent for images and other clinical information to be included in the journal. The patients understand that their names and initials will not be published and due effort will be made to conceal their identity, but that anonymity cannot be guaranteed.

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