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Case report

Large B-Cell Lymphoma with T-Cell–Rich Background and Nodules Lacking Follicular Dendritic Cell Meshworks: A Case Report with Complete Response to Chemotherapy and a Review of the Literature

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Abstract

In this report, we describe a 38-year-old male with a very rare type of lymphoma, large B cell lymphoma with T cell-rich background and nodules lacking follicular dendritic cell meshworks (THRLBCL). In 2016 the patient presented hot flashes and night sweats (B-symptoms) and peripheral edema. He was treated with R-CHOP (doxorubicin, vincristine, cyclophosphamide, rituximab and Prednisone) chemotherapy, a Positron emission tomography–computed tomography (PET-CT) scan was performed after four cycles of treatment which showed radiologic complete response and blood test (complete blood count (CBC)) results showed normal ranges. As of September, 2020 he patient remains in complete remission.

We searched the literature for descriptions of cases spanning the diagnostic spectrum of THRLBCL and we identified only five cases worldwide. The last reported case was in 2014 with distinctive features that were difficult to classify according to the World Health Organization criteria or previously described variants.

Our patient is the sixth case of THRLBCL to be reported. He is the youngest of the reported cases and the first from Israel and the Middle East.

Keywords: ***Large B-cell lymphoma, T-cell lymphoma, chemotherapy, R-CHOP Protocol***

Introduction

T cell histiocyte rich large B cell lymphoma (THRLBCL) is a sporadic sub-variant of lymphoma accounting for 1-2% of diffuse large B cell lymphomas (DLBCL). It is histologically characterized by a few scattered large malignant B cells, which are typically <10% of the cell population, in a background of reactive T cells and histiocytes [1], and needs to be distinguished from nodular lymphocyte-predominant Hodgkin lymphoma (NLPHL), which is characterized by nodular and diffuse growth of scattered large neoplastic B cells associated with follicular dendritic cell (FDC) meshworks [2]. Atypical patterns, which are associated with different clinical outcomes were previously reported by Hartmann and his colleagues [3], including one extreme rare variant expressing a T-cell–rich background with lacking FDC meshworks that could overlap with T-cell/histiocyte-rich large B-cell lymphoma [2,4]. We discuss the diagnostic challenge in this clinical scenario, as well as management considerations referring to the five other cases reported to date [5]. All cases completely lacked FDC meshworks despite a prominent nodular growth pattern. Large atypical cells in all cases were CD20+ CD30− CD15− B cells [5].

In this study, we present the clinical, histological diagnostic, and therapeutic features of the sixth known case of large B-cell lymphoma with a nodular or partially nodular growth pattern and abundant T cells in the background but lacking FDC meshworks within the nodules. We think this case should raise awareness about an under recognized variant with clinical and pathological overlap between NLPHL and THRLBCL, which require further guidelines for their diagnosis and management

Case report

A 35-year old male with a history of asthma, was referred to the emergency department in October 2016 by a primary care

physician due to chronic leukocytosis average of 14 (normal range 4.8-10.8 *10^3/ul) and thrombocytosis average of 450 (normal range 130-140*10^3/ul), hot flashes, night sweats and peripheral edema over the past two months. There was no family history of cancer.

Physical examination revealed peripheral edema. Remainder of physical examination including cardiac auscultation was normal. Electrocardiogram showed normal sinus rhythm .Routine laboratory investigations (complete blood count, and biochemical profile) showed: anemia, monocytosis, leukocytosis neutrophilia and thrombocytosis (Table 1.). He was admitted to the hospital for further evaluation (Tables 2 and 3.). The patient underwent total body CT-scan (computed tomographic) which showed significant lymph node enlargement with retroperitoneal lymphadenopathy (Figure.1 A red square), (The largest retroperitoneal node was 1.8cm in diameter) more on left side and several enlarged nodes in the left iliac area, the largest 4 cm in diameter (Figure.1 A and B yellow square) around and edema. A lymph proliferative disorder was suspected. Deep venous thrombosis was excluded by ultrasound (US) of the lower extremities. TSH was in normal range, excluding pretibial myxedema.

For further investigation the patient underwent a positron emission tomography–computed tomography (PET-CT) (Figure.2 A) which showed hyper-metabolic uptake and lymphadenopathy of the retroperitoneal and left iliac areas.

A lymph node biopsy was taken (from the left iliac area) under US guidance. Histopathologic findings were suspicious for a large B cell lymphoma. JAK2 mutation and BCR-ABL mutation were negative. The case was sent for consultation to the Department of Pathology, Stanford University, USA. The histopathologic findings at consultation were: Large B-cell lymphoma with T-cell rich background and nodules lacking follicular dendritic cell meshworks (Table 4.)

A multidisciplinary conference came to the conclusion that the patient should be treated with six cycles of chemotherapy (R-CHOP protocol). He received systemic intravenous therapy consisting of doxorubicin 50 mg/m2, vincristine 1.4 mg/m2, cyclophosphamide 750 mg/m2, rituximab 375 mg/m2 all given on day 1 every 21 days. After four cycles the patient underwent PET-CT (Figure.1 C), (Figure.2 B) which showed no evidence of disease (NED) and CBC tests were in the normal ranges. After the sixth cycle the PET-CT also showed NED. Most recent PET-CT done in July 2020 which also showed NED (Figure.1 D), (Figure.2 C).

Table 1: Patient's Complete Blood Count (CBC), Coagulation and Chemistry.

Parameter	Lab Reference	Result
WBC (10^3 cells/ul)	4.8-10.8	14.2
Neutrophils.(10^3 cells/ul))	1.9-8	10.88
Eosinophil's	1-3%	2.5%
Basophils	0-1.5%	0.1%
Monocyte's (10^3 cells/ul)	0.16-1	1.15
Platelets (10^3/ul)	130-400	439
Hemoglobin (g/dL)	12-16	12.5
Hematocrit	42-52%	37.4%
Red cell distribution width	11.5-14.5 (%)	15.4%
Red blood cell (10^3 cells/ul)	4.7-6.1	4.03
PT-INR	0.89-1.16	1.13
PT-SEC (sec)	10-13.5	13.8
APTT-sec (sec)	26-39	34.1

**Chemistry tests did not show any pathological findings.*

Table 2: Patient's Virology Tests.

Parameter	Lab Reference	Result
Hepatitis A	Positive/Negative	Negative
Hepatitis B	Positive/Negative	Negative
Hepatitis C	Positive/Negative	Negative
Q-FEVER phases	Positive/Negative	Negative
Epstein–Barr virus	Positive/Negative	Positive
BRUCELLA Ab R.Bengal	Positive/Negative	Negative
CMV	Positive/Negative	Negative

Table 3: Patient's Rheumatologic Tests.

Parameter	Lab Reference	Result
Antinuclear antibody (ANA)	Positive/Negative	Negative
Anti-Neutrophils Cytoplasmic Antibodies (ANCA)	Positive/Negative	Negative

Table 4: Patient's Stanford University Pathology Lab Findings.

Label	Marker For	Results	Special Pattern or Comments
HGAL	(Human Germinal center Associated Lymhpoma): Germinal center Bcells.	POSITIVE	NON
CD10	Calla, follicular lymphoma, B-ALL	NEGATIVE	POS INTERNAL CONTROL
EMA	Epithelial membrane antigen: anaplastic lymphoma	NEGATIVE	POS INTERNAL CONTROL
CD23	FcRigE, CLL, FDC	EQUIVOCAL	NO+INTL CONTROL
BCL6	Follicular Lymphoma	POSITIVE	NON

Table 5: The immunohistologic differences between our reported patient comparing with the previous reported five patients

Immunohistologic Findings Results	CD-20	EMA	CD-30	CD-15	PD-1staining
Our Case	Positive	Negative	Positive	Expression	Negative with rosette formation around the large atypical B cells
Previous Five Patients	Positive	Negative	Positive only in one patient	Expression in 4 cases	Positive with prominent ringing pattern around the large atypical B cells

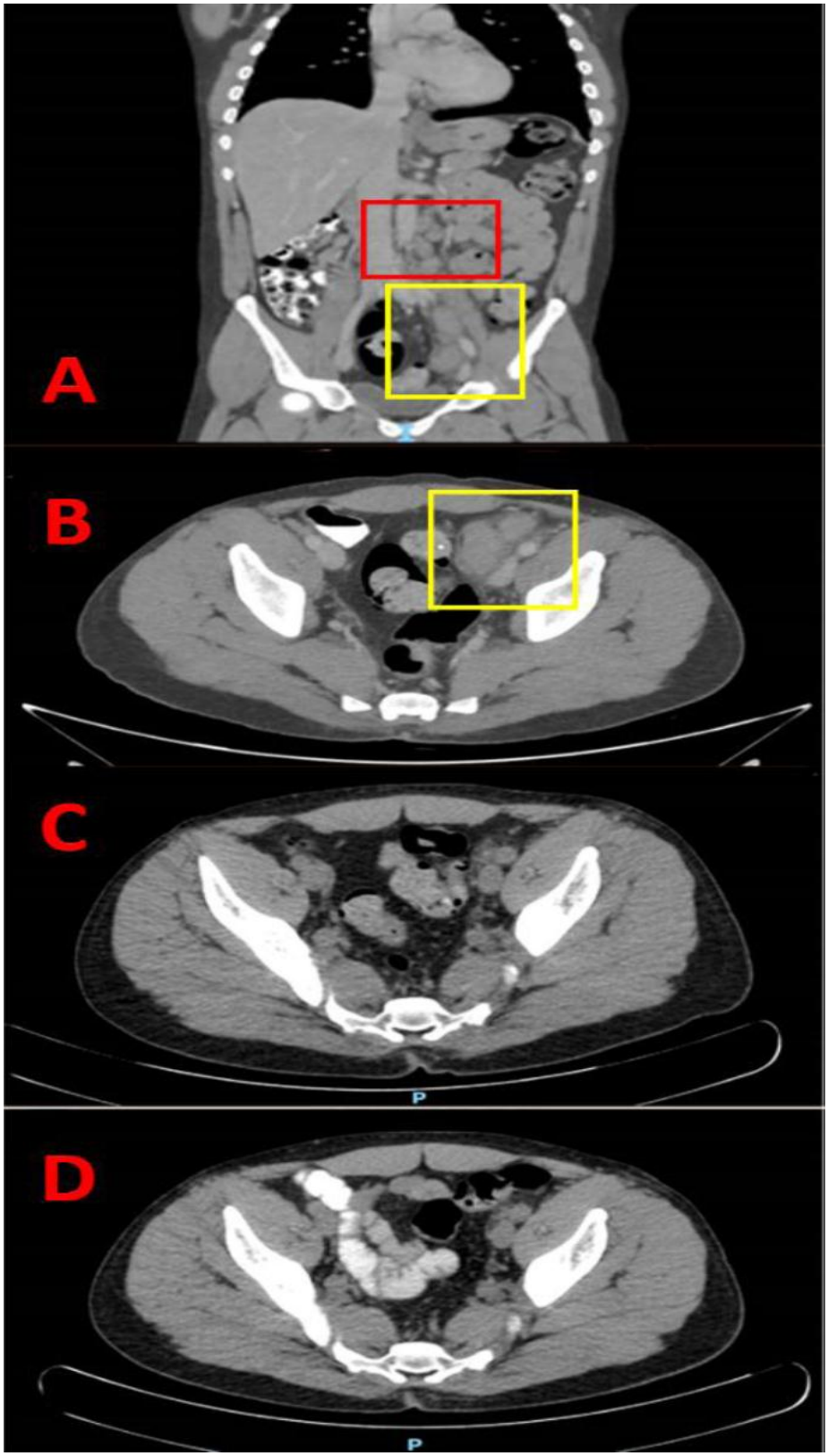

Figure 1: Shows the patient's radiological response (CT sections) to the treatment. (Red square- significant lymph node enlargement with several enlarged retroperitoneal nodes at presentation), (Yellow squares- lymphadenopathy in the left iliac area and edema at presentation).

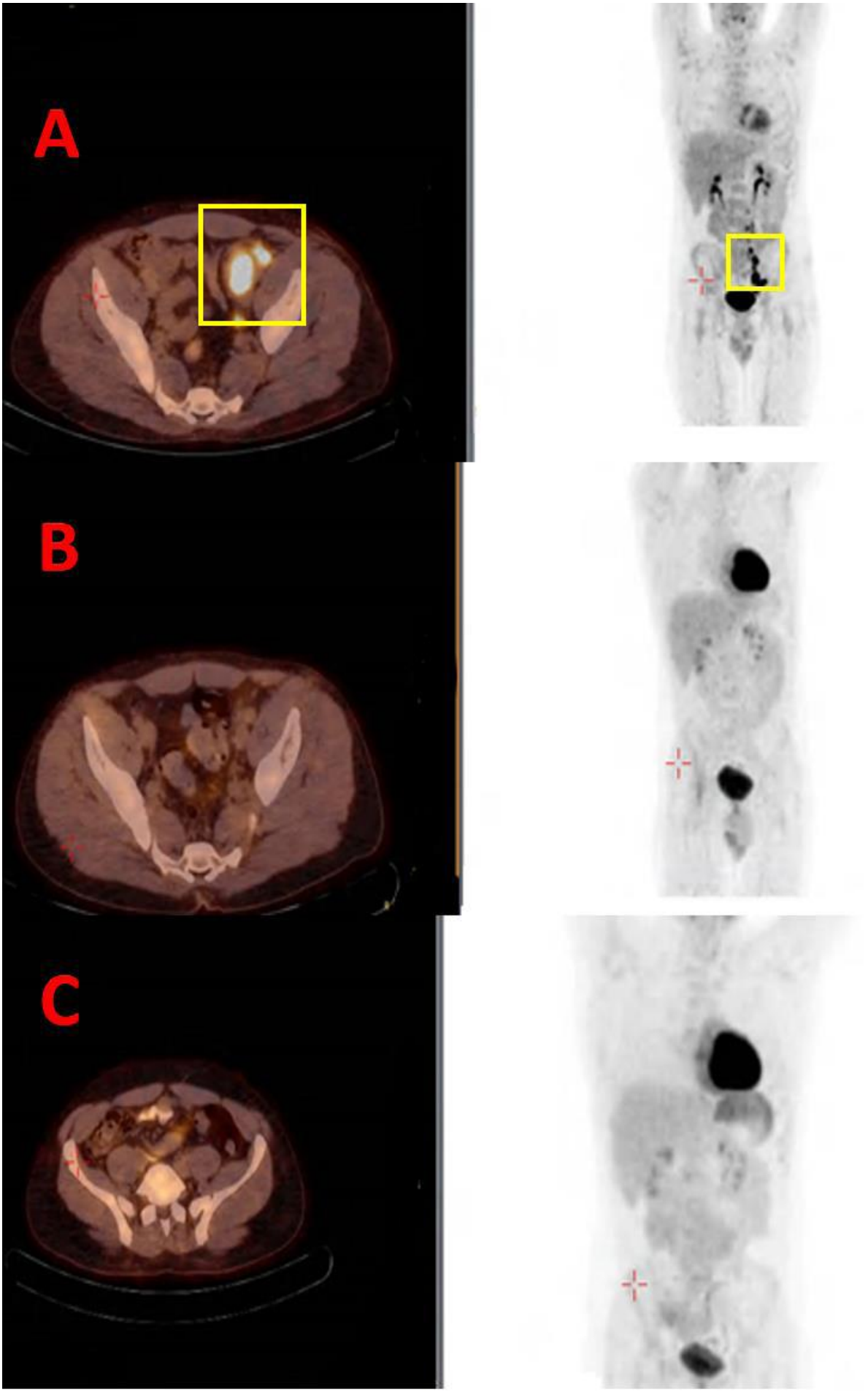

Figure 2. Shows the patient's radiological response (PET-CT selections) to the treatment. (Yellow squares- hyper-metabolic uptake and lymphadenopathy of the left iliac areas.

Discussion

We have described a patient who had one of the rarest types of lymphoma (5 previous reported cases, the last in 2014). Our case is the youngest patient to be reported and the first to be reported from the Middle-East.

Furthermore, if we compare (immunohistologic findings) our patient with the previous five reported patients we see that the large atypical cells in all five cases expressed CD-20, the same was in our case. Epithelial membrane antigen (EMA) was negative in the previous five reported patients, the same was in our case. CD-30 was positive only in one of the five cases, also in our case it was positive. Lack of CD-15 expression was seen in four of the previous reported cases, also in our case it was expressed. The previous five reported patients were all positive for PD-1staining and showed a prominent ringing pattern around the large atypical B cells, but our patients' staining for PD-1 was negative and showed rosette formation around the large atypical B cells (Table 5.). [5].

We suggest that in a patient of any age it is important to consider the possibility of unusual malignancies when the diagnosis at first is not clear-cut, particularly today in the era of molecular medicine and tumor subtyping.

Data Availability

Not applicable

Disclosure Statement

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Statement of Ethics

The authors have no ethical conflicts to disclose.

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