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Case Study

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MEDIASTINAL COMPOSITE LYMPHOMA COMPOSITE LYMPHOMA IN SUPERIOR MEDIASTINUM OF PRIMARY MEDIASTINAL B-CELL LYMPHOMA AND CLASSICAL HODGKIN LYMPHOMA

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ABSTRACT

Composite lymphoma (CL) of primary mediastinal B-cell lymphoma (PMBCL) and classical Hodgkin's lymphoma (CHL) is extremely rare specially in this age groups. In this article, we report a case of CL initially diagnosed as diffuse large B-cell lymphoma NOS, and CHL, then turned out as PMBCL with CHL. 14-year-old boy presented with several months of progressive cough, dyspnea, and generalized pruritus. Found to have massive left pleural effusion with lung collapse, computed tomographic imaging done which revealed large superior/ anterior mediastinal mass with multiple mediastinal lymphadenopathies as well as pleural, pericardial effusion along with lesions in kidneys. The patient underwent an excisional biopsy from the mediastinal lymph node, which found to have a composite lymphoma of CHL and PMBCL. He successfully treated with chemotherapy dose-adjusted EPOCH-R (etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab) and currently on regular follow up.

KEYWORDS: CHL, Composite lymphoma, EPOCH-R, mediastinum, PMBCL.

CASE STUDY

Composite lymphoma in superior mediastinum of primary mediastinal b-cell lymphoma and classical Hodgkin lymphoma.

INTRODUCTION

Composite lymphoma (CL) is a rare tumor composed of two or more distinct lymphomas arising in the same anatomic site or tissue.[1,2] The incidence of composite lymphoma is an estimated 1-4.7% of lymphoma cases.[6,9] Several combinations of B-cell non-Hodgkin lymphoma (NHL), T-cell NHL, and Hodgkin lymphoma can occur with different prognoses and treatments.[1] Primary mediastinal B-cell lymphoma (PMBCL) and classical Hodgkin lymphoma (CHL) is extremely rare and there are 4 reported case of composite lymphoma of PMBCL and cHL including our case.[1,3,5,11] Treatment and outcome are poorly covered in the recent literature, so we present how we managed this case and can guide other clinicians in managing such cases since there is no standard guidelines for treatment.

Case Presentation

The abstract states he is 14-year-old Saudi boy presented with 4 months history of shortness of breath and cough associated with B symptoms and generalized pruritus, both past medical history and family history for hematological diseases were negative. The patient was found to have massive left pleural effusion with collapsed lung, a left cervical lymph node (LN) measuring 3x4 cm and hepatomegaly. Laboratory studies revealed that blood count, renal, liver function tests and electrolyte were within normal range except erythrocyte sedimentation Rate and lactate dehydrogenase were high. Antibody testing for HIV, HBV, HCV, HTLV I/II were negative.

-Chest x ray: (Figure)

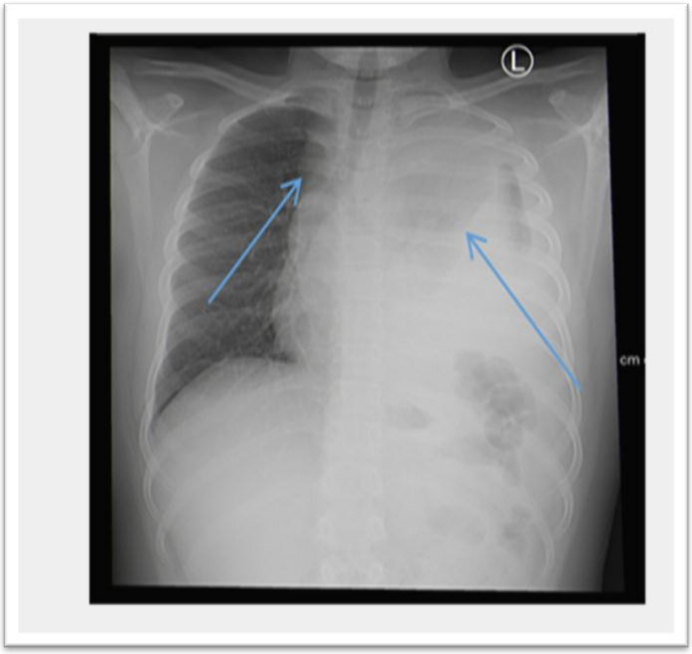

Figure 1: Showed diffuse opacity in left hemithorax with mild mediastinal shift. Opacity in paratracheal region due to enlarged paratracheal L.N.

CT scan of neck and chest showed multiple cervical, mediastinal and paratracheal lymph nodes the largest measuring 3.6x2.4 cm, large heterogenous superior mediastinal mass extending to the left side measuring 12.6 x11.7x.8.1 cm, significant left lung collapse with mild pleural effusion and minimal pericardial effusion. CT abdomen revealed hepatomegaly and multiple bilateral renal hypodense masses.

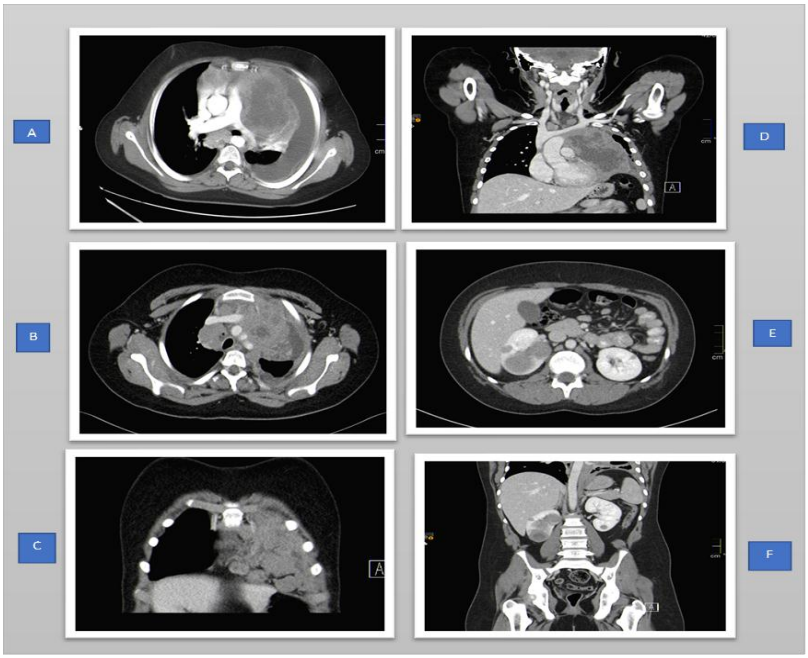

Figure 1: CT scan of neck and chest (A) Large heterogenous soft tissue mass occupying anterior mediastinum and causing shift of mediastinal structures to other side, measuring 12x11x8 cm.(B)mass shows hypodense areas of necrosis with mild left pleural effusion.(C)Multiple enlarged cardio phrenic L.N and minimal pericardial effusion. (D)Multiple large mediastinal lymph node the largest seen in superior mediastinum 2.5x1.7 cm ,right paratracheal measuring 3.6x2.4 cm, subcarinal 3.5x 2.3cm, left supradiaphragmatic 3.1x1.6 cm.(E,F) hepatomegaly and multiple bilateral renal hypodense masses largest 3.6x3.4 and 3.8x3.3cm2.

- Pathological examinations revealed 3 Mediastinal LN, One of which showed focal nodal effacement by sheets of atypical lymphoid cells with numerous mitosis and apoptosis. The background of remaining tissues and other lymph nodes reveal nodular appearance with scattered large Reed Sternberg -like atypical cells (R-S), noted within and in between the lymphoid follicles. Immunohistochemical (IHC) stains also revealed two different patterns; R.S cells: are positive for (CD30 and CD15, and MUM1), PAX5: weak positive and negative for LCA, CD20, CD79a, and CD3, while the effaced portion is positive for LCA, CD20, CD79a, PAX5 and negative for CD15, CD3. These findings indicate presence of two morphologically and immunophenotypically distinct lymphoma keeping with CL (Figure 2).

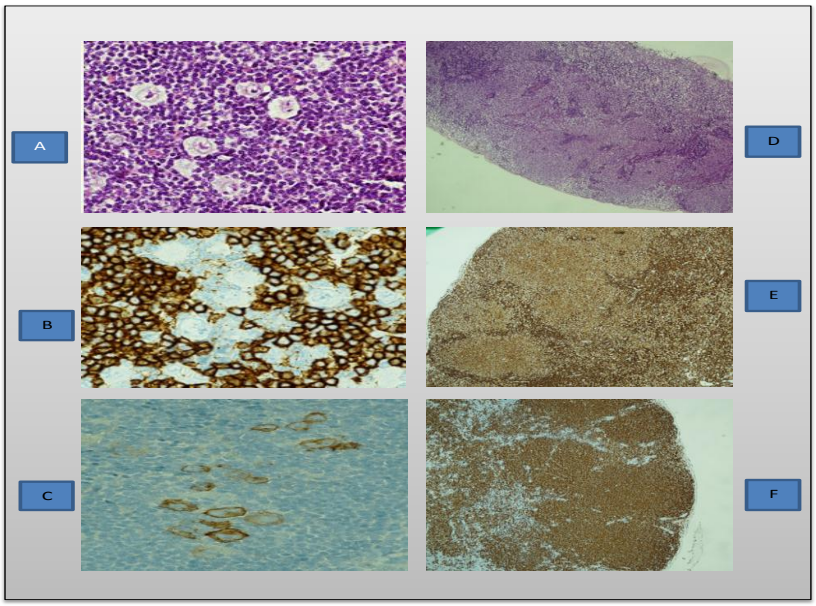

Figure 2: (A)CHL component (B) Reed-Sternberg cells (RS) with CD20 –VE. (C) Reed-Sternberg cells (RS) withCD30 +VE.(D) Diffuse component. (E) Diffuse component with LCA +VE. (F) Diffuse component with CD20.

Right Para-tracheal LN: reveal diffuse infiltrate with atypical lymphoid cells and the background show mixture of reactive cells including lymphocytes, histiocytes and eosinophils. IHC stains were positive for (LCA, CD20, CD79a, PAX5, focally positive for CD30 and MUM1, BCL6 (35%) and negative for CD3, CD5, CD15, CD10, CD68, CK5/6, CD1a, S100, TdT, which keeping with DLBCL. (Figure 3)

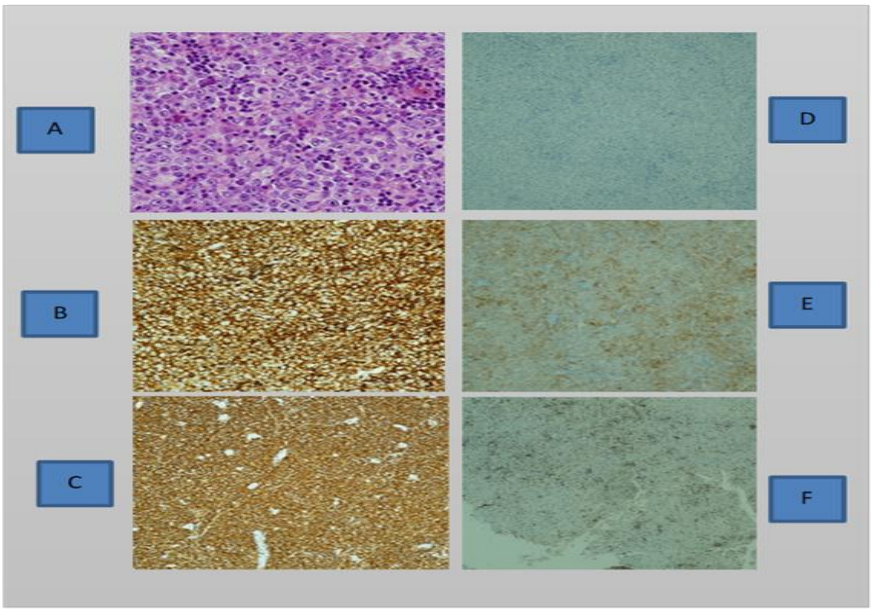

Figure 3: Para tracheal LN Biopsy/IHC.(A) Histology of para tracheal LN. (B) LCA +VE. (C) CD15 –VE. (D) CD15 –VE. (E) Para tracheal CD30 Focal +VE (F) Para tracheal CD3-VE.

Bone marrow biopsy revealed no evidence of lymphoma.

Molecular study is positive for clonal IGH gene rearrangement and MYC (8q24) translocation, and negative for BCL6 and BCL2 rearrangement.

Our case initially diagnosed as composite of CHL with DLBCL, then discussed in the tumor board meeting and we raised the possibility of PMBCL which this distinction will reflects the best treatment regimen and prognosis.

Based on that, additional IHC done such as CD23, which turned to be diffuse and strong positive, in addition to negative CD10, CD68, OCT2, and bone marrow biopsy, the diagnosis of PMBCL was made.

The patient's age was particularly a challenge in this case as no established treatment guidelines available. The decision was made to use a protocol to act on the most aggressive component, which is PMBCL. The long-term complications of mediastinal radiation on young patients were considered so dose-adjusted R-EPOCH (Etoposide, Prednisone, Vincristine, Cyclophosphamide, Doxorubicin, and Rituximab) was used. The question was which central nervous system (CNS) prophylaxis is better? Systemic or intrathecal chemotherapy (IT) especially with high CNS risk like our patient. The decision was to use IT to avoid compromising dose adjustments with systemic one.

Patient started on DA-REPOCH protocol and received 8 doses of IT from cycle 3 to 6. After 4 cycles the patient was re-evaluated by CT which revealed interval reductions in size of all lesions.

Fluorodeoxyglucose-positron emission tomography (FDG-PET-scan) after 6 cycles showed persistence of anterior mediastinal mass with moderate FDG uptake (Deauville score 3), he received 2 additional cycles according to protocol (total of 8 cycles) followed by FDG-PET-scan which revealed residual supra-diaphragmatic nodal mass mostly in the thorax with (Deauville score 3). This was another challenge, is this patient need consolidative radiations or not? So mediastinal biopsy was taken and showed necrotic tissue only and the patient kept on a watch and wait plan with close monitoring.

Our case showed that DA-R-EPOCH with IT CNS prophylaxis appears to be effective and appropriate choice for CL of PMBCL component. However, continuing follow-up is necessary to determine the long-term outcome of this treatment.

Final diagnosis
Mediastinal composite lymphoma.

DISCUSSION

Our case represents an extremely rare entity of lymphoma, which is CL of PMBCL and CHL, and based on our literature review, there are only one reported case was successfully treated with dose-adjusted R-EPOCH regimen.[1]

CL is a rare disease defined as a type of lymphoma composed of two or more distinct lymphomas arising in a single patient and at same time of diagnosis.[1,3,5,6] The exact pathogenesis of composite lymphoma remains unclear. The different combinations of composite lymphoma described in the literature, but the most common form is composed of two non-Hodgkin B-cell lymphomas.[9] The combination of classical Hodgkin lymphoma and non-Hodgkin lymphoma coexisting in the same tissue is rare and much more uncommon than other combinations.[5,6,8]

From reviewing the literature, the diagnosis of mediastinal lesions can be particularly challenging for the pathologist specially distinguishing PMBL from CHL and a lot of studies and publications were introduced this challenge[12,18]

PMLBL frequently demonstrates clinical, morphologic and/or IHC features that overlap with mediastinal-CHL.[12,16,19] but in the era of modern immunophenotypic and molecular genetic techniques, most cases of lymphoma can be diagnosed and classified as one of the currently recognized distinct disease entities, but there are some lymphomas, however, with histologic, biologic, and clinical features overlapping between various types of lymphomas.[18]

PMBCL is a subtype of diffuse large B-cell lymphoma (DLBCL) that derived from a Thymic-B cell. Accounting for up to 10% of cases of DLBCL, it usually presents in the third and fourth decades of life with female predominance.[6] PMBCL is typically confined to the mediastinum and sometimes invade local structures. Disseminated disease may occur at diagnosis with involvement of extra nodal sites such as liver, kidney, and adrenal gland. PMBCL expresses B cell-associated antigens including CD19, CD20, CD22 and CD79a[1,5,6] like our case.

Recently, Mediastinal grey zone lymphoma (MGZLs) with clinical and pathologic features intermediate between PMBCL and CHL have been recognized. MGZLs predominantly affect men and appear to have an inferior outcome compared with PMBCL and CH.[4,5]

From what described in the literatures, we need more biological and immunohistochemistry tools in addition to more molecular studies to help in distinguish between these overlapping lymphomas and to develop a guideline to diagnose these overlapping lymphomas which could help to accurately define the optimum management.

Dose -adjusted EPOCH has been used successfully in patients with PMBCL with overall survival rate of 97% at median of 5-year follow-up and obviated the need for radiotherapy in patients with primary mediastinal B-cell lymphoma.[1,5,10]

At the completion of treatment of PMBCL, a residual mediastinal mass is commonly present, and It is not uncommon for these masses to persist for several months after the completion of therapy, which should be considered the interpretation of follow-up imaging.[10]

CONCLUSION

Due to the complexity in treating multiple types of lymphoma simultaneously, composite lymphoma (CL) presents a challenge. Therapeutic decision of CL should be based on the components, of which malignant degree is higher. Dose adjusted EPOCH-R with IT CNS prophylaxis seems to be effective and appropriate therapy for CL with PMBCL component. Assessment of a residual mass by FDG-PET is not an exactly accurate at end of treatment so alternative and more specific imaging modalities should be investigated.

CONFLICT OF INTEREST

The author declares that there is no conflict of interest that could be perceived.

AUTHOR CONTRIBUTIONS

Abotaleb Alia A: Writing - Review & Editing, developed the original idea, wrote the manuscript-review and editing (equal). Bin Abbas Elham S: review and editing (equal).

1 Abbreviations: CHL, classical Hodgkin's lymphoma; CL, composite lymphoma; CNS, central nervous system; DLBCL, diffuse large B cell lymphoma; ESR, erythrocyte sedimentation rate; EPOCH-R, etoposide, prednisone, vincristine, cyclophosphamide, doxorubicin, and rituximab; FDG-PET-scan, Fluorodeoxyglucose-positron emission tomography; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; IHC, Immunohistochemical; IT, intrathecal chemotherapy; MZGLs, Mediastinal grey zone lymphoma; NHL, non-Hodgkin lymphoma ; NSHL, nodular sclerosing Hodgkin lymphoma; PMBCL, primary mediastinal B-cell lymphoma; R S, Reed Sternberg -like atypical cells.

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