



T-Cell/ Histiocyte-Rich Large B-Cell Lymphoma of Posterior Mediastinum - A Case of Diagnostic Dilemma

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ABSTRACT

T-cell/histiocyte-rich large B-cell lymphoma (THRLBCL) is a rare aggressive type of diffuse large B-cell lymphoma (DLBCL) characterized by presence of less than 10% of large atypical B lymphocytes i.e. malignant lymphocytes in the background of T lymphocytes. Pathophysiology is thought to involve cytokine mediated evasion of T cell immune response by malignant B cells. Mostly, affects lymph node, but can occur in extra nodal sites like bone marrow, liver and spleen. THRLBCL arising in mediastinum is extremely rare. Till date, there are only two case reports ascribing the occurrence of THRLBCL in mediastinum. Herein, we report another case of 49 years old female causing diagnostic dilemma initially but later on could be diagnosed accurately as THRLBCL of posterior mediastinum based on radiological and histopathological examination findings, immunohistochemistry (IHC) result and treated successfully.

Keywords: THRLBCL, Lymphoma, DLBCL, Posterior mediastinum

Introduction

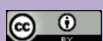
T-cell/histiocyte-rich large B-cell lymphoma (THRLBCL) is an aggressive type of diffuse large B-cell lymphoma (DLBCL) accounting for less than 10% of all DLBCLs. It is characterized by presence of less than 10% of large atypical B lymphocytes in the background of T lymphocytes. Predominantly, a nodal disease but can occur in extranodal sites like bone marrow, liver and spleen. [1] THRLBCL arising in mediastinum is extremely rare. Till date, there are only two case reports ascribing the occurrence of THRLBCL in mediastinum.[2,3] Herein, we report the another case of 49 years old female causing diagnostic dilemma initially but later on could be diagnosed accurately as THRLBCL of posterior mediastinum based on radiological and histopathological examination findings, immunohistochemistry (IHC) result and treated successfully.

Case Report

A 49 years old female presented to our hospital during January 2016 with history of pain in left side of chest, back alongwith decreased appetite and loss of weight since 2 months. The pain used to relieve with medication but aggravated during night. She had consulted an outside physician for the aforementioned complaints in December 2015. Outside magnetic resonance imaging (MRI) scan showed a large plaque like soft tissue mass in posterior mediastinum with craniocaudal extension from D4 to D10 level measuring 4.3x6.6x12.0 cm and in D11to D12 level measuring 5.0 cm occupying pre and paravertebral region (Figure 1a). The MRI findings

were suggestive of lymphoma. CT chest in our hospital revealed similar findings as MRI scan and also showed extension of mass into bilateral ventral foramina causing symmetrical foraminal widening at D6-7, D7-8, D8-9 vertebral levels alongwith lytic destruction of D7-8 vertebral bodies. She also underwent ultrasonogram (USG) and CT scan of abdomen. USG abdomen showed abdominal lymphadenopathy in paravertebral, para aortic, right iliac and pelvic region alongwith two well defined heterogeneous hypoechoic lesions in lower pole of spleen and a well defined, heterogeneous hypoechoic lesion in right iliac fossa extending into abdominal wall upwards and femoral canal downwards. CT scan of whole abdomen showed i). diffuse mass forming and discrete abdominal lymphadenopathy as that of USG findings, ii). a plaque like soft tissue density mass involving posterior mediastinal prevertebral space (D11-D12 space) completely encasing the descending aorta and displacing it anteriorly along with iii). moderate left sided pleural effusion. CT impression was suggestive of lymphoma/ neurogenic tumor whereas USG impression was in favour of lymphoma. CT guided FNAC was done from the soft tissue lesion in the pre and para vertebral region at the level of D11-D12 which was inconclusive due to lack of satisfactory aspirate.

The case was referred to department of CTVS for thoracotomy and open biopsy. She underwent posterolateral thoracotomy. Intra operatively, a nodular hard mass was found around the descending aorta with adherence; excision was not attempted, biopsy was taken from the mass and sent for histopathological examination. Grossly,



the biopsy specimen comprised of multiple flap like gray white tissue bits together measuring 2.1x1.8x0.5 cm which was embedded entirely. Haematoxylin and Eosin (H&E) stained microsections revealed a tumor arranged in diffuse sheets and lobules separated by thin and dense fibrous bands. The tumor cells comprised of predominantly small lymphocytes characterized by round to oval cells with indistinct/scanty cytoplasm having round to oval nuclei with clumped chromatin alongwith few scattered atypical cells characterized by large round to polygonal cells resembling epithelial cells / Reed-Sternberg (R-S) cells having clear/ granular eosinophilic cytoplasm with vesicular nuclei and prominent nucleoli. Focal area showed spindle shaped cells (Figure 1b,1c,1d). Histopathological diagnoses were offered as – i. Thymoma Type B1, ii) Hodgkin's lymphoma (Nodular sclerosis/ Nodular lymphocyte predominant Hodgkin's lymphoma, iii). Non-Hodgkin's lymphoma and was advised for available immunohistochemistry (IHC) marker study with LCA, CD20, CD3, CD15 and pan CK (Cytokeratin) for further evaluation and confirmation. IHC revealed - i. LCA positivity in all the lymphoid cells and atypical large cells, ii. CD3 was positive in majority of back ground lymphoid cells but negative in atypical large cells, iii. CD20 was positive in large atypical cells but negative in background lymphoid cells (Figure 2a,2b,2c), iv. CD15 was negative in atypical cells and v. CK was

negative in all the lymphoid cells as well as atypical large cells. CK negativity in atypical large cells excluded the possibility of thymoma. LCA and CD20 positivity in the large atypical cells, CD15 negativity in large atypical cells, CD3 positivity in background lymphocytes ruled out the possibility of Hodgkin's lymphoma and Nodular lymphocyte predominant Hodgkin's lymphoma (NLPHL). Thus, basing on the imaging, histopathological and IHC findings, the case was finally diagnosed as non-Hodgkin's lymphoma –DLBCL (T-cell/ histiocyte rich-large B cell lymphoma) of posterior mediastinum belonging to stage III. Bone marrow aspiration did not show lymphomatous infiltration. She was planned for R-CHOP regimen (Rituximab, Donorubicin, Vincristine, Cyclophosphamide and Prednisolone) for 6 cycles, injection Zoledronic acid once in 3 weeks for 18 months, shelcal 500mg and RT to spine if required. The planned course of chemotherapy was completed on August 2017 when the patient was found to be comfortable. CT chest and abdomen findings did not reveal any residual disease indicating complete response to treatment. Chest x-ray and USG abdomen were also done in October 2017 and found to be normal; she was advised for review once in 6 months. Her last follow ups were in April and October 2018 when she was found to be asymptomatic clinically and CT chest and abdomen were also normal suggestive of no recurrence.

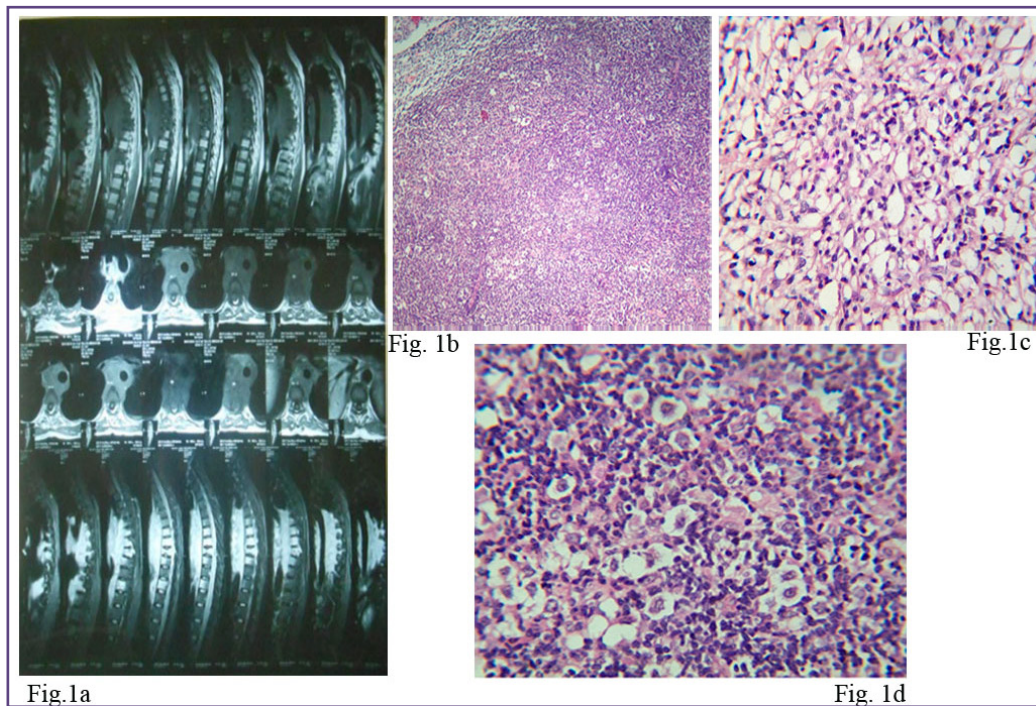


Fig. 1: 1a. MRI scan image showing plaque like posterior mediastinal mass;1b-1d (H&E stained microphotographs): 1a. Large atypical tumor cells in a background rich of lymphocytes[x100], 1c. Spindly tumor cells[x400],d. Large atypical tumor cells with clear/ eosinophilic cytoplasm vesicular nuclei, prominent nucleoli[x400].

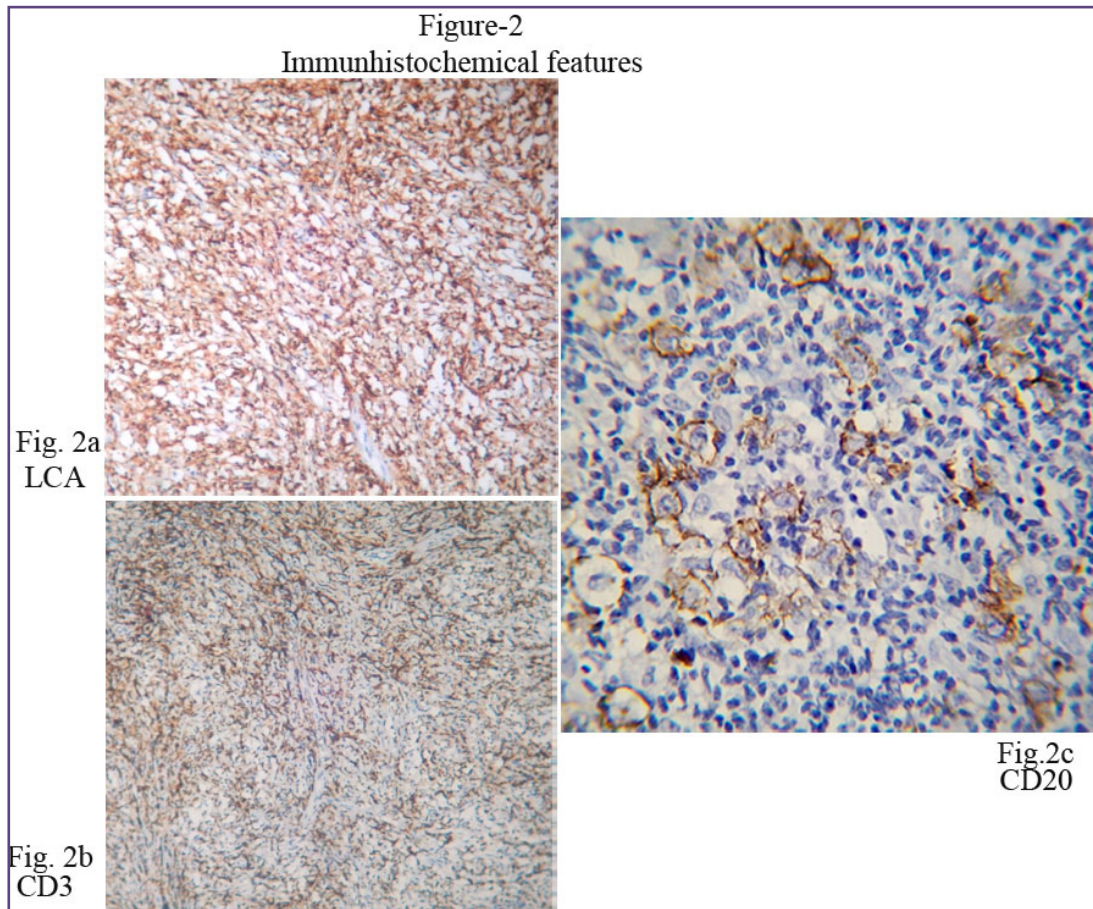


Fig. 2: 2a. LCA positivity in all the tumor cells[x100], 2b. CD3 positive background lymphocytes, 2c CD20 positive atypical large tumor cells[x400].

Discussion

A wide spectrum of neoplasms occurs in posterior mediastinum which include neurogenic and non-neurogenic tumor. Neurogenic tumors comprise of i. peripheral nerve sheath tumors (Schwannoma, neurofibroma, malignant peripheral nerve sheath tumor), ii. parasympathetic ganglion tumors (paraganglioma, pheochromocytoma, chemodectoma) and iii. sympathetic ganglion chain tumors (neuroblastoma, ganglioneuroma). Non neurogenic tumors comprise of chordoma, chondrosarcoma, Ewing's sarcoma, lymphoma, invasive thymoma, metastatic tumors and oesophageal tumors.

THRLBCL is a rare type of B cell type non-Hodgkin's lymphoma (NHL) and its occurrence in mediastinum is extremely rare. Extensive literature search revealed only two cases of THRLBCL in English literature of which one was a case of 17 years old female having mediastinal mass alongwith multiple liver lesions as well as splenic and mesenteric lymphadenopathy whereas the other one was a 52 years female having a thymic mass with a past history

of Sjogren's syndrome.^[2,3] Histopathologically, THRLBCL is characterized by malignant B cells with reactive T lymphocytes. Pathophysiology is thought to involve cytokine mediated evasion of T cell immune response by malignant B cells. Macan et al. suggested that IL4 could play a role in histogenesis of this lymphoma.^[4] Histologically large lymphoid cells are scattered in a background of reactive T lymphocytes which are CD3+,CD5+,CD8+ T cells. The low number of neoplastic cells is explained by tumor cell apoptosis mediated by cytotoxic CD8+ cells.^[5] These lymphoma cells express CD20 but lack CD5, CD10, and CD138. The histology of THRLBCL mimic Hodgkin's lymphoma (HL) i.e. lymphocyte rich classical Hodgkin's lymphoma (LRHL) and NLPHL. In LRHL, Reed-Sternberg cells (R-S cell) are CD15, CD30 and EBV positive and negative for pan B marker (LCA). In NLPHL, R-S cells are negative for CD15 and CD30 but positive for LCA and CD20. Both NLPHL and THRLBCL progress to DLBCL.^[6]

The present case initially caused diagnostic dilemma with one of the differential diagnosis offered as Thymoma B1

due to mediastinal origin and finding of spindly cells, abundant lymphocytes as well as large cells resembling thymic epithelial cells. Although, thymomas are commonly seen in anterior mediastinum, invasive thymomas with clinical stage III (Masaoka's clinical staging) and TNM stage- $T_3N_0M_0$ - stage III (Yamakawa-Masaoka TNM staging) can be seen in posterior mediastinum.^[7,8] Histopathological observations of nodular arrangement of tumor cells with large atypical cells having clear cytoplasm, central vesicular nuclei and prominent nucleoli further confused with R-S cells; thus, Hodgkin's lymphoma (Nodular sclerosis/ NLPHL) was considered as the second differential diagnosis. But finally, the case was diagnosed as NHL of THRLBCL type due to LCA positivity in all the tumor cells, CD3 positivity in background lymphocytes and CD20 positivity in large atypical tumor cells by IHC markers study. THRLBCL patients have poor prognosis as majority of patients present with Ann-Arbor stage III or IV.^[9] They belong to intermediate to high risk as per international prognostic index score and 3 year survival is only 46%.^[1,6] Patients with extension to adjacent organs or thoracic structures, pleural or pericardial effusion or poor performance status have been associated with unfavourable clinical outcome. Recurrence of lesion shows increased number of atypical cells resulting in picture of DLBCL which has bad outcome. The present case was below 60 years with Ann-Arbor stage- III showing evidence of visceral involvement and pleural effusion; thus belonged to a higher risk group. But with the accurate diagnosis and planned treatment she could be well managed and is asymptomatic till her last check up.

Conclusion

In conclusion, we present the third case of THRLBCL arising in posterior mediastinum. Though such cases are extremely rare and usually belong to higher risk group, but can be managed properly with early and accurate diagnosis and appropriate treatment.

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