Primary spinal T cell/histiocyte-rich large B cell lymphoma (THRLBCL)—a rare diagnosis at a rare site

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Abstract

T cell/histiocyte-rich large B cell lymphoma (THRLBCL) is an unusual variant of diffuse large B cell lymphoma with poor prognosis. We describe a case of THRLBCL with an uncommon isolated spinal involvement. A 37-year-old male came to the neurosurgery outpatient department with weakness of both upper and lower limbs. Histopathology and immunohistochemistry revealed features consistent with THRLBCL. The patient was treated with D5-D6 laminectomy followed by six cycles of chemotherapy (CHOP; cyclophosphamide, hydroxydaunorubicin, oncovin, prednisolone) and was disease free for 5 years until he had relapse of disease at the same location in 2016 for which he is receiving palliative radiation therapy. Isolated spinal involvement as the first or only manifestation of THRLBCL is very rare and has been described very occasionally in the literature. It is important to correctly diagnose this entity and differentiate it from its mimics because of different prognostic and therapeutic implications.

Keywords Spine · THRLBCL · PCNSL · DLBCL

Introduction

Primary central nervous system lymphomas (PCNSL) represent a rare subcategory of extranodal non-Hodgkin lymphomas which are confined to the brain, leptomeninges, and rarely spinal cord. They account for 2.4–3% of all brain tumors and 4–6% of all extranodal lymphomas [1]. They rarely present as an isolated spinal cord tumor constituting < 1% of all CNS lymphomas [2]. Diffuse large B cell lymphoma (DLBCL) is the most frequent type of PCNSL. T cell/histiocyte-rich large B cell lymphoma (THRLBCL) is described as a rare specific subtype of DLBCL accounting for

less than 10% of all DLBCL and 1 to 3% of all B cell lymphomas [3]. In this variant, the neoplastic B cell population is overshadowed by reactive T cells and often a population of histiocytes [4]. Neoplastic cells may form less than 10% of the entire cell population. THRLBCL presenting as an isolated spinal mass is very rare. We hereby report this extremely rare presentation of THRLBCL as an isolated spinal mass in a middle-aged man with an emphasis on importance of diagnosing this entity and differentiating it from its mimics.

Case report

A 37-year-old male presented with weakness of both upper and lower limbs of 3-month duration. On examination, the patient was conscious and coherent. There was no neck stiffness, lymphadenopathy, or organomegaly. Vitals were normal. The weakness was predominantly proximal with power being 3/5 in upper limbs and 2/5 in lower limbs. Bilateral plantars were extensor. Sensory system was unremarkable. Routine blood and biochemical parameters were within normal limits. MRI dorso-lumbar spine showed hypointense focal intradural extramedullary lesion at D8/D9 and L2/L3 vertebral body level in posterolateral aspect on the left side causing significant thecal sac and cord compression displacing on the right

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and extending into left neural foramen (Fig. 1a). The patient underwent D8-D9 and L2-L3 laminectomy and removal of the mass. Histopathological sections showed cellular lesion with cells arranged mostly in sheets with some vague nodules formed by thin fibrous bands. Large pale histiocytes were seen admixed with small lymphocytic population. Amidst these, large cells were scattered which were mononucleate and binucleate with rare multinucleate forms. These cells showed 1–3 prominent nucleoli (Fig. 1b, c). Immunohistochemistry (IHC) revealed large cells to be positive for CD20, PAX5, MUM1, and EMA (Fig. 2a–d) and weak positive for BCL6 and negative for CD15, CD30, and EBV (Fig. 2e, f). CD68 highlighted the histiocytic population (Fig. 2g). CD3 (Fig. 2h) was positive in majority of the background lymphocytes with predominance of CD4 (Fig. 2i) over CD8 (Fig. 2j)-positive cells. CD21 stain did not reveal any dendritic meshworks (Fig. 1d).

Extensive clinical and radiological workup did not reveal any other site of primary disease. Therefore, correlating clinical and histological features with immunohistochemical profile, a diagnosis of primary spinal THRLBCL was made. The patient received six cycles of chemotherapy (CHOP; cyclophosphamide, hydroxydaunorubicin, oncovin, prednisolone) and was disease free for 5 years until he had relapse of disease at the same location in 2016 for which he is receiving palliative radiation therapy.

Discussion

THRLBCL was first described by Jaffe et al. in 1984 as an unusual B cell lymphoma mimicking peripheral T cell lymphoma [5]. Originally considered an uncommon variant of

DLBCL, it is recognized by the World Health Organization (WHO) as a separate clinicopathological entity since 2008 [4]. It predominantly affects middle-aged men often presenting with advanced stage disease frequently involving the spleen, liver, and bone marrow at the time of diagnosis. Isolated spinal involvement as an extranodal presentation of this rare entity has occasionally been described in the literature [6]. Weshi et al. [7] reported 61 cases of THRLBCL, and only one case was found to have central nervous system (CNS) as the initial site of presentation. Only 2 out of 30 patients of this entity reported by Lim et al. [8] presented as paraspinal mass with no involvement of the spine. Lymphoma involving the spine has a variety of patterns, including osseous, epidural, leptomeningeal, and spinal cord involvement. Intramedullary spinal involvement is the least common [9]. Leptomeningeal involvement predominantly occurs as a spread from intracranial lymphoma. Intradural extramedullary (IDEM) mass as seen in our patient forms a rare presentation [10]. Extensive workup did not reveal any intracranial or systemic lymphoma.

THRLBCL is defined as a diffuse or less commonly vaguely nodular proliferation of a limited number of scattered, large, atypical B cells embedded in a background of abundant T cells, and frequently histiocytes [4]. The disease is considered a separate subtype of DLBCL in the WHO 2008 classification and is associated with an aggressive clinical course and poor outcome in comparison with its DLBCL counterparts with matched international prognostic index scores [7]. The main differential diagnoses for THRLBCL are classical Hodgkin lymphoma (cHL) and nodular lymphocyte predominant Hodgkin lymphoma (NLPHL) (Table 1).

Fig. 1 **a** MRI dorso-lumbar spine showing focal intradural extramedullary lesion at D8/D9 vertebral body level. **b, c** H&E-stained section showing scattered large cells with prominent nucleoli. **d** CD21 IHC stain demonstrating diffuse architecture characterized by complete absence of dendritic meshwork

Fig. 2 Immunohistochemistry revealed large neoplastic cells to be positive for CD20 (a), PAX5 (b), MUM1 (c), and EMA (d) and negative for CD15 and CD30 (e) and EBER-ISH (f, inset positive

control). Background population comprised of histiocytes positive for CD68 (g), T lymphocytes positive for CD3 (h) with predominance of CD4 (i) over CD8 (j)

THRLBCL can mimic cHL because of reactive background population and the large cells sometimes resembling Reed-Sternberg (RS) cells. However, in contrast to

RS cells in cHL, the large cells in THRLBCL are negative for CD15, rarely positive for CD30, and always positive for CD45 and CD20 [4].

Table 1 Differentiating pathological features between THRLBCL, cHL, and NPLHL

	THRLBCL	NPLHL	cHL	Our case
Overall architectural features	Diffuse or vaguely nodular	Six patterns have been described	Nodular or diffuse	Diffuse
CD21- or CD23-positive dendritic meshwork	Absent	Disturbed	Disturbed	Absent
LCA	+	+	–	nd
CD20	+	+	–	+
CD3	–	–	–	–
CD15	–	–	+	–
CD30	–	–	+	–
BCL6	±	+	–	Weak +
PAX5	+	+	+	+
MUM1	+	±	+	+
EBV	–	–	+	–

Distinguishing THRLBCL from NLPHL is more difficult and challenging. Fan et al. [11] observed six different patterns in NLPHL including a diffuse THRLBCL-like pattern (pattern E). Other patterns described were classic B cell rich (pattern A), serpiginous (pattern B), pattern with predominant extranodular LP cells (pattern C), T cell rich (pattern D), and diffuse with a B cell-rich background (pattern F). It has been suggested by the earlier studies that nodular pattern may be seen in 10% of THRLBCL cases [12]. The recent World Health Organization (WHO) classification however asserts that any nodular architecture excludes the diagnosis of THRLBCL. Both entities show significant overlap on IHC [4]. Similar to NLPHL, neoplastic cells in THRLBCL are positive for CD45, CD20, CD79a, PAX5 and negative for CD15 and CD30; there is less frequent expression of BCL6 and more frequent expression of IRF4/MUM1, a variable number stain for EMA [4]. In view of the overlap, the differential diagnosis in most instances relies on the background reactive population, which are predominantly B cells surrounded by T cell rosettes in NLPHL and they are rare or absent in THRLBCL. Expanded CD21+ or CD23+ follicular dendritic cell meshworks are always present in NLPHL but are lacking in THRLBCL [4]. Our case showed expression of CD20, PAX5, MUM1, and EMA in neoplastic cells, while CD15 and CD30 expression were lacking. Testing for EBV performed by EBER-ISH revealed negative results, further supporting the diagnosis of THRLBCL over cHL and spectrum of EBV-positive DLBCL having sparse neoplastic large cells that may also be T cell rich. Background population was comprised of T lymphocytes and histiocytes highlighted by CD3 and CD68 respectively. T cell rosettes around the large neoplastic cells and CD21 dendritic meshwork were absent. We observed predominance of CD4 over CD8 in background T lymphocytic population; a similar finding has been reported by Kunder et al. [13]

A worse outcome has been suggested for THRLBCL by some studies; however, treating it with standard CHOP chemotherapy seems to result in a relatively comparable outcome as conventional DLBCL [7] and is the current standard of care in such cases until new treatment strategies emerge.

Conclusion

T cell/histiocyte-rich large B cell lymphoma is a relatively newly recognized clinicopathological entity, characterized by an aggressive behavior. The spine has been described as an extremely rare extranodal site of THRLBCL and presentation as an isolated spine mass is even rare. It is important to correctly diagnose this entity and differentiate it from its mimics because of different prognostic and therapeutic implications.

Compliance with ethical standards

The manuscript is compliant with ethical standards.

Conflict of interest The authors declare that they have no conflicts of interest.

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