Primary T-cell lymphoma of the central nervous system mimicking a brain abscess

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Abstract

Primary T-cell lymphoma is extremely rare in the central nervous system. We report a case occurring in an elderly Chinese male patient with underlying myeloproliferative disorder, who presented with fever and focal brain lesion on imaging mimicking brain abscess. Histological examination of the excised lesion showed extensive necrosis of brain tissue accompanied by marked perivascular infiltration of small to mid-sized lymphocytes with subtle nuclear atypia, while microbiological work up was negative and extensive immunohistochemical and histochemical staining failed to identify any pathogen. Immunohistochemistry revealed that the atypical lymphocytes were CD3+ CD56- EBER- T cells with attenuated BCL2 and CD2 expression. T-cell receptor analysis by PCR study confirmed monoclonal TRG gene rearrangement. The case highlights the importance of the awareness of T-cell lymphoma as a differential diagnosis of solitary brain tumour, despite its rarity and the need of attentive analysis of the histomorphology and immunophenotype and integration of molecular findings for accurate diagnosis. Recent findings on primary T-cell lymphoma of the central nervous system are discussed.

Case report

A 69-year-old Chinese elderly man presented with sudden onset of fever and confusion. He had history of JAK2-mutated myeloproliferative disorder favor polycythemia rubra vera with hydroxyurea treatment and hepatic hemangiomata. Initial physical examination showed no focal neurological deficit and CT scan identified a 3.3-cm left frontal lesion in the grey-white matter junction with solid-cystic component and hypodense core with peripheral contrast enhancement (Figure 1). Brain abscess was initially suspected and emergency craniotomy was performed. Intraoperative findings was atypical of brain abscess as no purulent material could be aspirated and the lesion was excised and submitted for pathological examination (tan-brownish piecemeal tissue, 2 x 1.5 x 0.5 cm in aggregate). Microbiological culture of blood, lesional tissue and cerebrospinal fluid were negative. Complete blood picture showed increased neutrophil counts with elevated baseline count due to preexisting myeloproliferative disorder. The patient was treated with broad-spectrum antibiotics empirically and the general conditions of the patient improved a few days after operation with no source of sepsis identified.

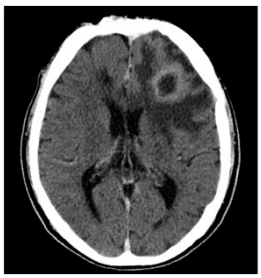

Figure 1. CT scan showing left frontal lesion with contrast-enhancing rim.

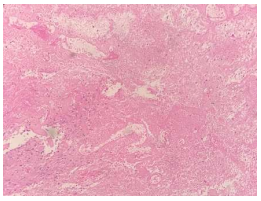

Figure 2. Microscopic examination showed extensive necrosis of brain tissue.

Histological examination showed brain tissue with extensive coagulative necrosis, focal viable areas featured brain tissue with concentric perivascular infiltrate of small to mid-sized lymphoid cells, notably lacking accompanying neutrophils and plasma cells (Figure 2 & 3). Thrombosis of the affected blood vessels was seen. The lymphoid cells showed subtle nuclear atypia with dented and angulated nuclear shape and were devoid of nucleoli or viral inclusions. Cytoplasm was scant and mitotic activity was inconspicuous (Figure 4).

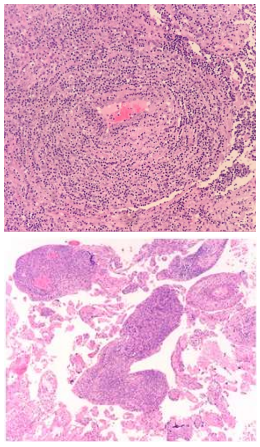

Figure 3. Perivascular cuffing by lymphocytic infiltrate.

Immunohistochemical studies revealed that the lymphoid cells were positive for CD3, CD2, CD5, CD4 and beta-F1, but they lacked CD20, CD8, CD56, CD30 and TIA-1 expression. Detailed assessment showed that the lymphoid cells displayed subtle but definite attenuated expression of BCL2 and CD7. In-situ hybridization study did not detect any EBV-encoded small RNA (EBER). T-cell receptor analysis by PCR confirmed the presence of monoclonal population with TRG gene rearrangement in background of polyclonal T cells. Extensive workup for infective agents by immunostaining (HSV, CMV, Treponema and toxoplasma) and histochemical staining (Grocott, Periodic acid–Schiff and Ziehl-Neelsen) were not revealing. Absence of mycobacterial infection was supported by PCR testing.

The overall features were consistent with peripheral T-cell lymphoma, not otherwise specified. The absence of evidence of primary T-cell lymphoma in other parts of the body supported the diagnosis of primary central nervous system T-cell lymphoma.

The patient received chemotherapy and follow-up imaging showed no evidence of disease progression at 11 months from diagnosis.

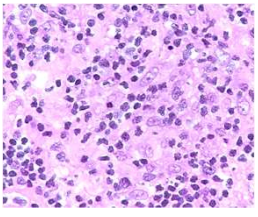

Figure 4. Small to mid-sized lymphoid cells with subtle nuclear atypia

Clinicopathological correlation and discussion

Primary central system lymphoma is rare, with majority being diffuse large B-cell lymphoma. T-cell lymphoma is even more uncommon. It appears to be relatively more prevalent in Asian populations with a slight male adult preponderance (1.5:1). The current case illustrates the difficulty in the diagnosis of primary T-cell lymphoma in the central nervous system. The clinical presentation was unusual, with fever, confusion and imaging suspicious of focal brain abscess. Primary T-cell lymphoma usually presents with headache, neurological deficits and seizure with radiological findings of a single mass lesion or multifocal lesions. Nevertheless, manifestations as cerebrovascular accident and fever have been reported. The neurological manifestations are probably the result of vascular compromise, due to the angiocentric growth of the neoplastic T-cells, exemplified by the microscopic findings of extensive tissue necrosis, perivascular cuffing and vascular thrombosis in our patient.

Important differential diagnoses include infection and autoimmune vasculitis. A wide spectrum of infective agents can present with fever and focal brain lesion, such as herpes simplex encephalitis, cerebral toxoplasmosis, amebic brain abscess, rhinocerebral mucormycosis, mycobacterial infection and neurosyphilis. Vasculitic causes such as primary angiitis or secondary to systemic autoimmune diseases should also be excluded by clinical correlation and serological studies. Another less entertained differential diagnosis is drug-related central nervous system vasculitis seen in cocaine users. Cocaine snorting can cause intense vasoconstriction and subsequent ischemic infarct and inflammation of the cerebral, especially frontal, blood vessels, mimicking lymphoma. The diagnosis is often difficult due to sensitivity of misuse history. Besides lymphoma, EBV-driven lymphomatoid granulomatosis can also show overlapping morphological features, and can be ruled out by absence of EBER+ atypical B-cells.

The significant overlap in the morphological features of small-sized CNS lymphoma and reactive lymphoid infiltrate prevents accurate diagnosis without ancillary testing. The aberrant immunoprofile supportive of a neoplastic process is subtle in this case, with the atypical lymphoid cells showing T cell markers and lacking NK cells or cytotoxic T cells phenotype, only subtle attenuated immunoreactivity of BCL2 and CD7 is seen. The diagnosis is eventually cemented by the demonstration of monoclonal population by TRG gene rearrangement testing. Detailed study on the pathological features of primary central nervous system T-cell lymphoma is scare due to its rarity. Menon et al. reported heterogeneous histological, genomic and clinical outcomes. In this series, 8 cases showed small or small to midsized neoplastic lymphoid cells. Majority (>70%) of the cases in the series showed cytotoxic phenotype and more than half were CD8+ and derived from alpha-beta T cells. Meanwhile, Yim et al reported similar observations that most cases were small-to-medium-sized cells and majority shows cytotoxic phenotype with alpha-beta T-cell receptors in a Korean series6. Nevertheless, CD4+ and CD8+ cases appear to be similarly common in Korean population. Clinical outcomes are variable in both Western and Korean series.

In additions to the diagnostic challenge in this case, interesting unresolved questions on the relationship of the lymphoma with the patient's underlying JAK2-positive myeloproliferative disorder are raised. Menon et al and Yim et al both detected activating mutations in the JAK/STAT pathway (JAK3, STAT3 and STAT5 genes) in some of their cases and the JAK/STAT pathway has been implicated in the pathogenesis in a number of T-cell malignancy. It would be interesting to search for JAK2 mutation in the neoplastic T cells, which maybe of theragnostic benefit for targeted therapy. Further mechanistic study is needed to clarify the interaction of the T-cell lymphoma and myeloproliferative disorder and its treatment.

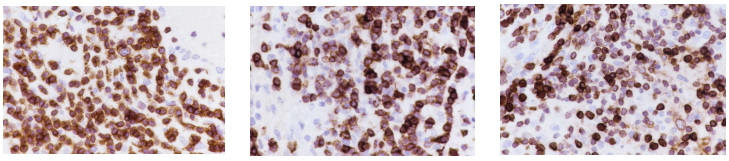

Figure 7. Preserved CD3 (left panel), attenuation of CD7 (mid panel) & BCL2 (right panel) expression in the atypical lymphoid cells.

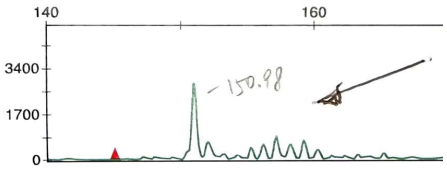

Figure 8. T-cell receptor gamma gene rearrangement analysis by BIO-MED2 PCR amplification showed monoclonal peak (size marked) in background of reactive polyclonal population.

Conclusion

In summary, primary T-cell lymphoma of the central nervous system is a rare tumour with broad differential diagnosis and subtle diagnostic features. Integrative assessment is essential in reaching the diagnosis.

Referemces

1. Menon et al. PMID: 26379152
2. Yim et al. PMID: 34980830