Original Research Paper

Volume-9 | Issue-4 | April-2019 | PRINT ISSN No 2249-555X

Neurosurgery

A RARE CASE OF PRIMARY ANAPLASTIC LARGE CELL LYMPHOMA OF CENTRAL NERVOUS SYSTEM

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ABSTRACT Primary central nervous system lymphoma is infrequently occurring lymphoma accounting for only 0.3-3% of all intracranial neoplasm. (1) We describe the case of primary central nervous system lymphoma which presented to us as extra calvarial swelling in previously operated case of craniotomy with biopsy which was suggestive of inflammatory lesion; exploration was done suspecting recurrence, but histopathological examination and immunostaining were suggestive of Primary CNS lymphoma.

KEYWORDS : Primary CNS Lymphoma, Anaplastic large cell lymphoma, Anaplastic lymphoma kinase positive

INTRODUCTION:

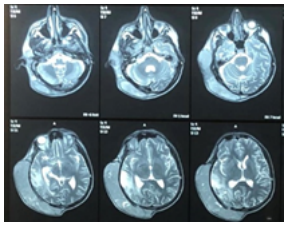
Primary central nervous system lymphoma (PCNSL) by definition is extra nodal lymphoma (Non-Hodgkin's type) originating in central nervous system in absence of systemic disease. [2,3] Primary central nervous system lymphoma are infrequently occurring lymphoma accounting for only 0.3-3% of all intracranial neoplasm.[1] PCNSL occurs in both immunocompetent and immunocompromised individuals.it has higher incidence in immunodeficient patients whether it is congenital or acquired.

CASE REPORT:

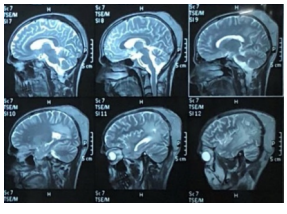
20 years old male came to us with complaints of swelling over right parieto-temporal region since 2 months. C/o Headache and vomiting since 15 days. C/o pain in left upper and lower limb since 15 days. Patient had only subtle weakness in left upper limb and left facial paresis; rest neurology was normal.

Patient had consulted for persistent headache since 4 months at outside hospital where MRI was performed which showed lesion in right parieto-temporal region with mass effect for which he had undergone right parieto-temporal craniotomy with biopsy from the lesion 3 months back; Histopathological examination suggested inflammatory lesion rich in macrophages. Patient was started on empirical AKT.

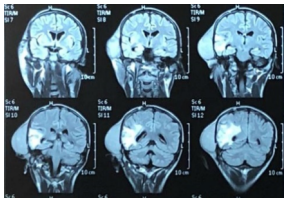
Patient came to us with above complaints; Subsequent MRI imaging showing presence of mass lesion in right parietotemporal region extending to extra calvarial space; suspecting recurrence re surgery was planned.



MRI Axial T2 weighted image of ALCL Patient



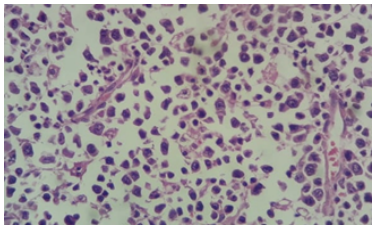
MRI Saggital T2 weighted image of ALCL patient



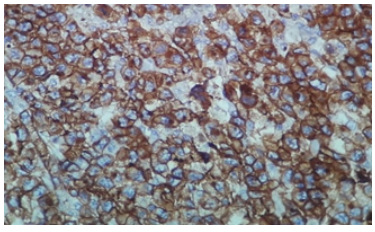
MRI Coronal Flair image of ALCL patient

Patient was operated; where extra calvarial mass of size 15×8×4 cm was seen coming out through previously performed craniotomy site through burr holes and bony defects which was in continuation with intraparenchymal lesion; Complete resection of intracranial SOL with its overlying bone and with its extra calvarial extension was performed.

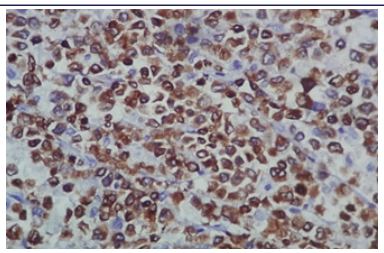
Patient made full recovery post-surgery. Specimen was sent to 2 independent histopathologist. Histopathological examination s/o Large cell lymphoma Anaplastic large cell type. Microscopic examination revealed non cohesive pleomorphic neoplasm; nuclei have finely dispersed chromatin and prominent nucleoli; malignant cells are admixed with lymphocytes and histiocytes; R-S like cells and wreath like nuclei are seen. Immunostaining was negative for CD 20 and positive for CD 3, CD 30, CD 68, LCA, S 100. Morphology was those of anaplastic large cell lymphoma. ALK 1 staining was positive.



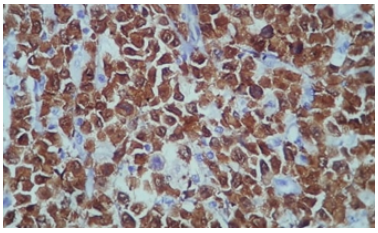
Micrograph of Anaplastic large cell lymphoma patient with ×20 resolution



Micrograph of Anaplastic large cell lymphoma showing CD 30 positive field



Micrograph of Anaplastic large cell lymphoma showing CD 3 positive field



Micrograph of Anaplastic large cell lymphoma showing ALK-1 positive field

CSF studies showed no evidence of malignant cells. Serum LDH was within normal limits. CT scan of neck, thorax, abdomen was done; there was no evidence of distant metastasis. Patient was seronegative for HIV.

Post operatively we discontinued AKT and patient was started with Inj. Dexamethasone iv to reduce perilesional oedema and anticonvulsant to avoid post-operative convulsion. DeAngelis protocol with high dose Methotrexate with leucovorin rescue with whole brain radiotherapy and cytarabine planned after 10 weeks of initial chemotherapy.

DISCUSSION:

Primary central nervous system lymphomas are infrequently occurring lymphoma accounting for only 0.3-3% of all intracranial neoplasm. [1] PCNSL occurs in both immunocompetent and immunocompromised individuals. It has higher incidence in immunodeficient patients whether it is congenital or acquired. The incidence being 4 cases per million persons per year. [4,5] Anaplastic large cell lymphoma (ALCL), also known as Ki-1, pleomorphic or histiocytoid lymphoma was reported first by Stein et al. in 1985. [18]

Diagnosis of Primary CNS Lymphoma was made as it fulfilled the criteria for PCNSL. [15]

1. The patient presented with neurological symptoms.
2. The diagnosis of lymphoma was made by biopsy.
3. At the time of initial evaluation, no evidence of lymphoma was found at any other site.

Primary central nervous system ALCL is extremely rare and most of the cases have been reported in young adults. Analysis of cases of primary ALCL described in the literature, indicate a bimodal age distribution with 50% below 20 years and 2nd peak is observed after fourth decade. [9,16,17] It is found to be more frequent in females than in males. No association with HIV is found and most of them are immunocompetent individuals. Though most cases showed multifocal lesions, there was a predilection for frontoparietal region and almost all had leptomeningeal involvement. Around half of the cases were Alk-1 positive. Few cases out of these had been clinically misdiagnosed as infectious lesions, mostly mycobacterial infection and treated accordingly, as it was in our case. [9,16]

Radiological differential diagnosis includes other malignant ICSOL such as Glioblastoma multiforme, metastatic brain lesion and benign lesions such as demyelinating disease, infectious or parasitic conditions. [7] Histologically PCNSL may be any type of NHL but more than 98% of PCNSLs are B cell lymphoma. T cell lymphomas are rare but have comparable outcome to B cell lymphomas. [6]

Intracranial lymphoma is often an unsuspected diagnosis following a brain tumour resection or biopsy. MRI is imaging modality of choice when PCNSL are suspected. Lesion appears isointense to hypointense on T2 Weighted MRI often with surrounding oedema. [8]

Anaplastic Large Cell Lymphomas (ALCL) are seen as large pleomorphic cells that express CD 30 antigen. Their histological appearance can be confused with metastatic carcinoma or melanoma or Hodgkin's lymphoma as their tendency to fill lymph node sinuses. [9] Majority of ALCL express T cell antigens and less common null cell variants often have genetic evidence of T cell origin. [10] ALCL have detectable anaplastic lymphoma kinase (ALK-1) protein expression resulting from a genetic alteration in ALK locus on chromosome 2.9 more specifically, there is distinct 2:5 translocation that fuses the ALK gene on chromosome 2 and the Nucleophosmin gene (NPM) of chromosome 5.9. Although the pathogenesis of PCNSAL is not clear, it could be suggested that in ALK-1 anaplastic lymphomas, translocation of ALK gene is partly responsible for the neoplastic transformation. [11] There is no evidence suggesting a familial inheritance of PCNSAL. [9]

PCNSL is a chemosensitive tumour and chemotherapy is backbone of treatment. The CHOP regimen has limited role in PCNSL as it has limited ability to cross Blood Brain Barrier. [12] The recent studies confirmed the efficacy of combination of antimetabolite methotrexate and cytarabine as first line treatment.

Radiotherapy has been treatment option for intracranial lymphomas for many years. Its use for residual disease after chemotherapy is recommended, however for patients that achieve complete response, there appears to be no additional benefit, particularly given the significant short term and long-term toxicities of Whole Brain Radio Therapy (WBRT). [13] Results from recent phase 2 study published in abstract form suggest that consolidation WBRT can be deferred until relapse. [14]

Since the reported cases are so few and management heterogenous, statements about treatment strategy and prognosis cannot be drawn with sufficient confidence. The overall therapeutic approach of PCNSLALCL patients does not seem to differ greatly from the current therapy of PCNSLs.

Rapid recognition of PCNSLALCL, even without the morphological features of classic variant, may therefore be helpful in permitting a more tailored therapeutic approach.

To summarize, PCNSL-ALCL is a very rare tumour and is seldom clinically diagnosed. It is often misdiagnosed clinically and radiologically as mycobacterial CNS infection. Hence an early recognition of PCNSL-ALCL by biopsy is important in permitting a more tailored therapeutic approach, as they may have a very rapidly deteriorating clinical course.

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