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Research Article

PRIMARY CNS LYMPHOMA (PCNSL) IN AN IMMUNOCOMPETANT INDIVIDUAL - A RARE CASE REPORT

Shushruta Mohanty[1]., Pranati Mohanty[2]., Shilpa Dash[3] and Pragyan Paramita Mishra[4]

[1,3,4]Department of Pathology , S.C.B.M.C.H, Cuttack, Odisha, India
[2]Department of Pathology, P.R.M, M.C.H, Baripada, Odisha, India

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ABSTRACT

Primary CNS lymphomas are rare neoplasms with poor prognosis compared to other extranodal lymphomas.90% of primary CNS lymphomas are of B cell origin, predominantly of diffuse large B cell type and remaining 10% are poorly characterized low grade lymphomas, Burkitt lymphomas and T cell lymphomas. PCNSL accounts for 1-2 % of malignant brain tumors and 2-4% of all extranodal lymphomas. It can affect any age group but its occurrence in chidren is rare. We report a case of 42 years old male with headache and gradual decrease of vision as the only complaint. MRI scan revealed single intraparenchymal solid enhancing lesion of frontal and left lateral temporal lobe Surgical excision and biopsy showed diffuse large cell lymphoma with a B cell phenotype in IHC. Patient was screened for generalised and deep seated lymphadenopathy. CT Scan and MRI showed no enlarged lymphadenopathy. So a diagnosis of PCNSL was rendered which was further confirmed by IHC.

INTRODUCTION

Primary central nervous system lymphoma (PCNSL) can be defined as an extranodal Non-Hodgkin's lymphoma arising in and confined to the cranio-spinal axis(brain, eye, leptomeninges and spinal cord) to the brain, eyes, and/or leptomeninges with no evidence of a primary tumor elsewhere in the body [1]. PCNSL lesions may be divided into parenchymal, sub-ependymal, and leptomeningeal [2]. PCNSL is usually located in the craniospinal axis, particularily in the posterior fossa [1]. The most frequent locations are the frontal lobes, basal ganglia, and corpus callosum. It rarely affects childrens but its prognosis in childrens still remains unclear. PCNSL affects immunodeficient childrens (HIV)infected children (0.5%to1%) [3] and 4% of congenital immunodeficiency[4].

Case Report

A 42 years old male presented with headache and gradual decrease of vision since last 2 months. Headache did not respond to any medication nor was it related to any posture. Routine haematological parameters were within normal limits. He had no history of congenital immunodeficiency disease, previous organ transplantation, or was on any immunosuppressive therapy, and serological tests for HIV was negative. His family history was unremarkable for cancer or any immunodeficiency. Neurological examination revealed decreased visual acquity with normal light reflex on both sides. MRI scan revealed single intraparenchymal solid enhancing lesion of left cerebellar hemispheres measuring 3x2cm (Fig 1).

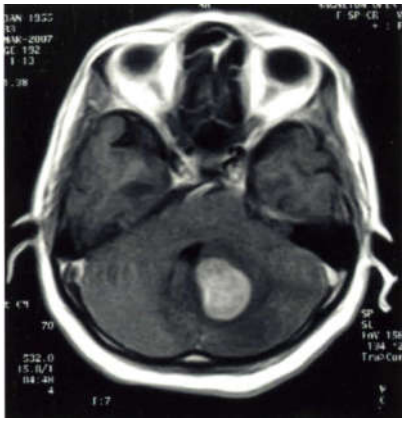

Fig 1 CT scan: single intraparenchymal lesion in the left cerebellar hemisphere measuring 3x2 cm.

Corresponding author:* **Shushruta Mohanty
Department of Pathology , S.C.B.M.C.H, Cuttack, Odisha, India

Intraoperative squash cytology study was done where a diagnosis of Glioblastoma multiforme was given. Following the intraoperative procedure the patient complained of total loss of vision of both the eyes. Surgical resection was planned immediately and biopsy was send to our department for histopathological analysis. Biopsy showed diffuse infiltration of medium to large pleomorphic lymphoid cells, with scanty cytoplasm, high N:C ratio, prominent nucleoli where the report was signed of as Diffuse large cell lymphoma (Fig 2a,2b) with a B cell phenotype which was confirmed by IHC(CD 45,CD20,CD3) (Fig 3a,b,c).

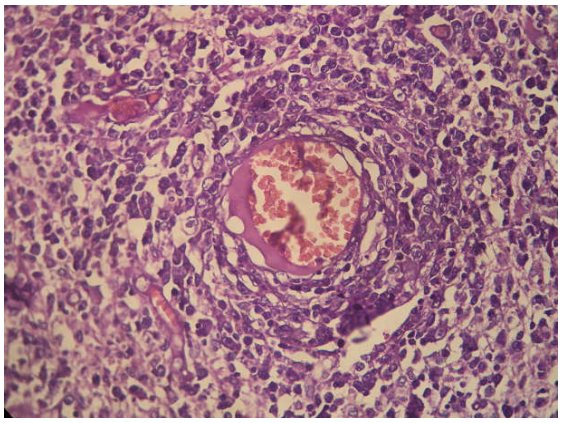

Fig 2 a Photomicrograph- LP 100 X-Showing pleomorphic tumour cells clustering around blood vessels.(Vasocentric pattern)

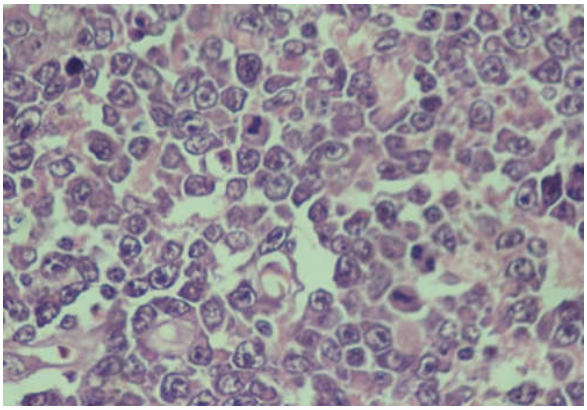

Fig 2 b Photomicrograph -HPX400- Showing Pleomorphic tumour cells with high N:C ratio, scanty cytoplasm, prominent nucleoli at places.

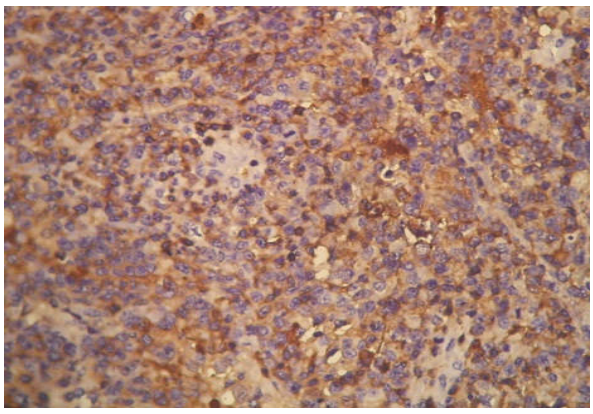

Fig 3 a Diffuse positivity of IHC- CD45 in tumour cells

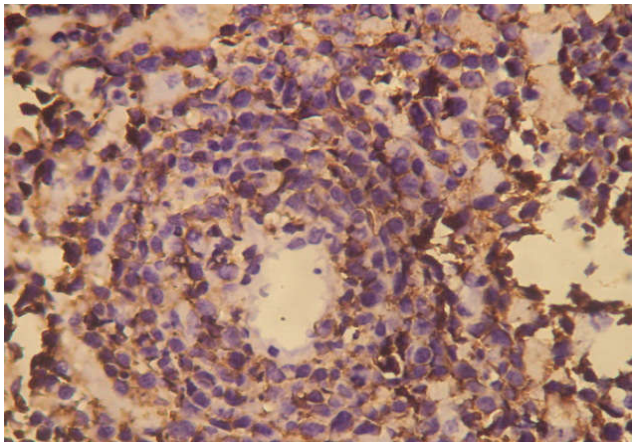

Fig 3 b Diffuse positivity of IHC-CD20 of tumour cells around blood vessels.

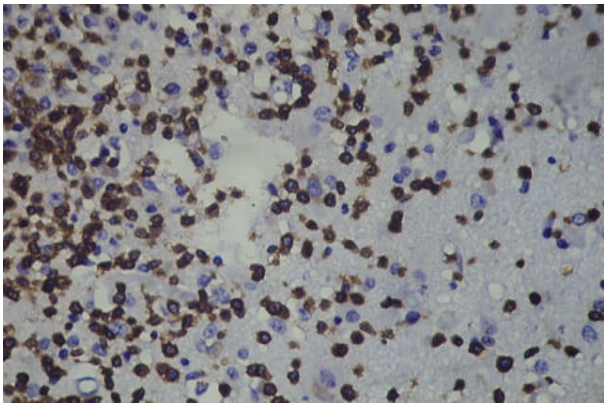

Fig 3 c IHC CD3 –staining of Peripheral T lymphocytes.

A systemic work up for NHL was carried out and patient was screened for generalised and deep seated lymphadenopathy. CT Scan and MRI showed no enlarged lymphadenopathy. Bone marrow aspiration study, bone scan, opthalmologic examination, including slit lamp, whole body PET Scan showed no evidence of neoplasia elsewhere. Immunoglobulin levels were normal, and ELISA for EBV and HIV were negative. LDH was below 450 mg/dl. Thus, confirming the diagnosis of PCNSL.

DISCUSSION

A primary central nervous system lymphoma (PCNSL) also called as microglioma and primary brain lymphoma[5] is a primary intracranial tumor appearing mostly in patients with severe immunodeficiency (AIDS). There is no predilection for any age group and an association with EBV is seen in greater than 90% cases of immunodeficient individuals.[6], on contrary it is also known to affect certain group of immunocompetant individuals of age groups 50's-60's with rare association of EBV detected in these individuals .

Incidence of PCNSL in immunocompetant population is gradually increasing more than 10 fold from 2.5 cases to 30 cases per 10 million population but the cause for such increase incidence in these individuals is unknown.[7,8]

No clear risk factors for PCNSL in immunocompetant patients are known, on the contrary prolonged glucocorticoid use (>6months),low CD4counts(<30 cells/microlitre), IV drug

abuse are risk factors in immunocompromised patients. The most typical presentation of PCNLS in an immunocompetant patient is focal symptoms due to mass effect. Varied presentation like headache, seizure, visual disturbances may also occur. Patient with AIDS more likely to present with an encephalopathy, with history of concurrent infections, low CD4 count<20 cells/micro lit. Progressive dementia, stupor with little or no enhancement on MRI seen in patients with AIDS who have PCNSL.

A careful history taking should be done to establish if the patient has immunodeficiency and if the patient is a transplant recipient, then nature and duration of immune suppression must be taken. Thorough physical examination is vital to exclude possible extraneural sources of lymphoma. Examining any lymphadenopathy, abdominal masses and neurological examination for focal deficiets, examination of peripheral nerves for evidence of neuropathy(s/o neurolymphomatosis), eye examination for vitreous involvement (for vitreous lymphoma) and slit lamp examination for patients with raised ICP(as papilledema may be present)should be done.

Differential diagnosis of a patient with suspected PCNSL depends on patients immune status and the radiographic appearance. Differential diagnosis in an immunocompetant patient with solitary lesion are high grade primary brain tumor such as glioblastoma and isolated metastasis. In patient's with AIDS multifocal ring enhancing lesions on MRI brings toxoplasmosis and other opportunistic infections as differential diagnosis.

Investigations required to reach a final diagnosis of PCNSL includes CBC count, Chest xray to detect any metastatic lesion and lumbar puncture for CSF cytology (r/o meningeal dissemination). MRI gives information about leptomeningeal enhancement, hydrocephalus or concurrent infections in patients with AIDS. Patients with focal spine, root or cord symptoms (Neurolymphomatosis) should undergo MRI to localise deposits of lymphoma if any. Lesions are 70% multifocal in immunosupressed individuals as compared to immunocompetant individuals. Stereotactic brain biopsy is appropriate method for diagnosis of PCNSL, however open brain biopsy is preferred in cases where it is difficult to access like the brain stem. The diagnosis of PCNSL, on histopathology is based on the facts that PCNSL(DLBCL type) is composed predominantly of immunoblastic or centroblastic morphology that have a predilection for blood vessels. Lymphoid clustering around cerebral vessels (vasocentric pattern) and T lymphocyte infiltrate are common in immunocompetant patients. IHC showed positivity for CD20 and CD 45. Optimal treatment for PCNSL has not been established. Standard CHOP regimen is ineffective due to difficulty in penetration of the drugs through blood brain barrier, combined chemotherapy and radiotherapy though doubles the median survival duration but poses a risk of leucoencephalopathy and dementia in 50% cases. Current active protocol as described by Hoang-Xuan and Delattre is high dose systemic methotrexate which is considered most successful treatment strategy.

According to the International Extranodal Lymphoma Study Group for PCNSL, an age of more than 60 years, a performance status (PS) greater than 1, an elevated LDH serum level, a high CSF protein concentration, and involvement of deep brain regions (periventricular regions, basal ganglia, brainstem, and/ or cerebellum) are significantly and independently associated with poorer survival [9]. In our case patient succumbed to death following few days of surgery.

Prognostic value of serum markers in PCNSL was reported in a prospective study of 45 cases of PCNSL[10] Length of survival correlated with serum levels of YKL-40 and MMP-9.YKL-a tissue marker of inflammation related to carcinogenesis, MMP-9 controls remodelling permeability are associated with "active disease".

CONCLUSION

Patients should be routinely monitored with monthly MRI scans after initiation of methotrexate chemotherapy, and those with leptomeningeal disease should undergo lumbar puncture with CSF cytologic sampling at monthly intervals. Diagnosis of primary CNS lymphoma is challenging and a definitive diagnosis of this rare tumor depends on distinctive histomorphology, IHC, and a panel of investigations to rule out extraneural spread of lymphoma. A better understanding of the characteristics and features of this CNS lymphoma is required, and an optimal therapeutic strategy is needed to improve survival rate in these patients.

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