

Rapid Intra-operative Diagnosis of CNS Lymphoma on Squash & Imprint Smears – a Boon for the Surgeon: Case Report

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ABSTRACT

Primary CNS Lymphoma [PCNL] accounts for 3% of all brain tumors. Diagnosing PCNL on squash and imprint cytology is a challenge for the pathologist but a boon for the operating surgeon as the knowledge of the nature of the lesion determines the nature of surgery. We report a case of 59 years old immunocompetent male who presented with right hemiparesis and headache. MRI Brain was suggestive of Left frontal Glioma. Intra-operatively, squash cytology and imprint smears of tissue from the lesions showed scattered lymphoid cells which also exhibited perivascular cuffing. Cytology was suggestive of lymphoma with differential of an inflammatory pathology. Histopathological examination and positivity for LCA, CD 20, Bcl 2 and Mum 1 on IHC confirmed the diagnosis of Diffuse Large B Cell Lymphoma-Brain. It is important to distinguish lymphoma from glioma or metastasis in CNS because of totally different lines of management. Knowledge of empirical diagnosis during surgery can guide the surgeon to ensure that adequate tissue is excised so that sample for immunophenotyping or further tests is available.

Keywords: CNS, cytology, imprint, lymphoma

Introduction

Microscopy provides the morphological diagnosis of any Central Nervous System (CNS) lesion, in spite of conflicting radiological opinion. We report a case where Magnetic Resonance Imaging (MRI) findings suggested left frontal Glioma while squash cytology and imprint smears from intraoperative tissue suggested lymphoma which was confirmed on histopathology and Immunohistochemistry [IHC]. Diagnosing Primary CNS Lymphoma (PCNL) on squash and imprint cytology can be a challenge for the pathologist but a boon for the operating surgeon as the nature of the lesion determines the nature of surgery and further management. [2,3]

Case Report

A 59 years old immunocompetent male presented with right hemiparesis and headache. MRI showed a heterogeneously enhancing mass with lobulated contours, suggestive of glioma in left frontal lobe. [Figure 1 a & b] So frontal lobe lesion excision was planned. Intra-operatively, the tissue was sent to the Department of Pathology for squash cytology. On microscopy, the smears were cellular with dispersed atypical lymphoid cells, plasmacytoid cells, mature lymphocytes and foamy macrophages against fibrillary background. Some lymphoid cells adhered to capillaries, giving rise to perivascular cuffing [Figure 2

a& b]. May Grunwald Giemsa (MGG) smear showed lymphoglandular bodies in the background [Figure 2 c & d]. No glands or cell clusters were present. The cytological impression was lymphoma. Based on this report, the surgeon abandoned the previous plan of total excision and biopsied only a part of the tumor so that adequate tissue was available for histopathology and IHC studies. Histopathological examination of the stereotactic biopsy showed sheets and angiocentric pattern of arrangement of atypical lymphoid cells having vesicular chromatin and scanty cytoplasm. [Figure 3 a & b]. On IHC, the cells were uniformly positive for LCA and CD 20 and focally positive for Mum 1 and Bcl 2. MiB 1 index was 50% in the highest proliferating areas. So, the final diagnosis was PCNL - Diffuse Large B Cell type of Non - Hodgkin's Lymphoma. The patient was started on Rituximab – CHOP regimen and intrathecal Methotrexate. The patient is planned for Radiotherapy after completing Chemotherapy cycles. Written informed consent has been taken from the patient for using his data for academic purpose.

Discussion

PCNLs account for 3% of all brain tumors and occur between fifth to seventh decade with male predominance. In immunocompetent patients the etiology is unknown. [1,2]

Patients present with cognitive dysfunction, psychomotor slowing, focal neurological deficits and signs of raised

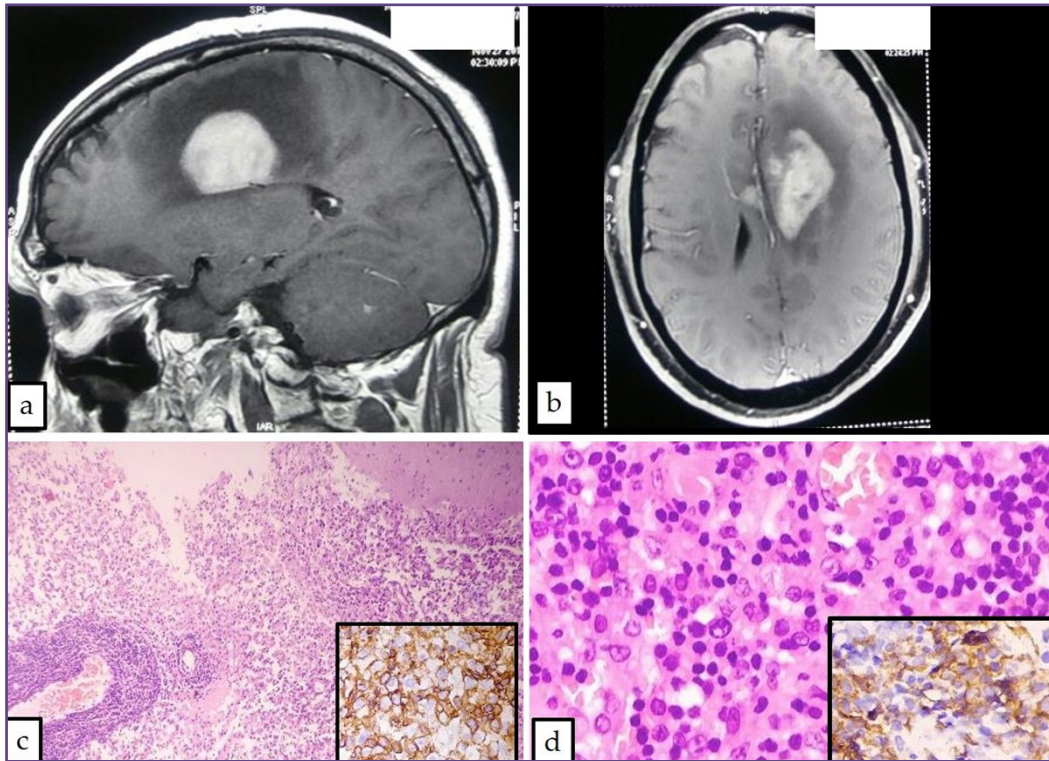


Fig. 1: a) & b) MRI images showing heterogeneously enhancing mass with lobulated contours in left frontal lobe, involving genu and body of corpus callosum & producing perilesional white matter edema with mass effect on frontal horn of both the lateral ventricles.

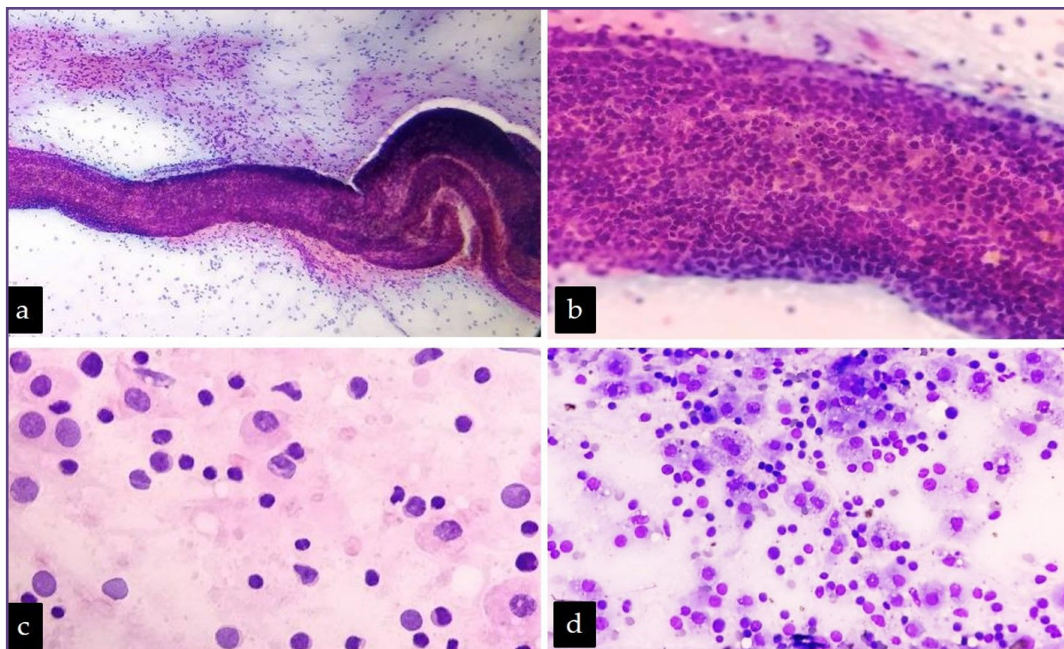


Fig. 2: a) Squash smear showing scattered lymphoid cells with perivascular cuffing (H&E, 40x); b) Atypical lymphoid cells adherent to capillary (H&E, 400x); c) H&E stained imprint smear showing atypical lymphoid cells admixed with lymphocytes & macrophages (400x); d) MGG stained imprint smear showing dispersed lymphoid cells, foamy macrophages and mature lymphocytes. (400x).

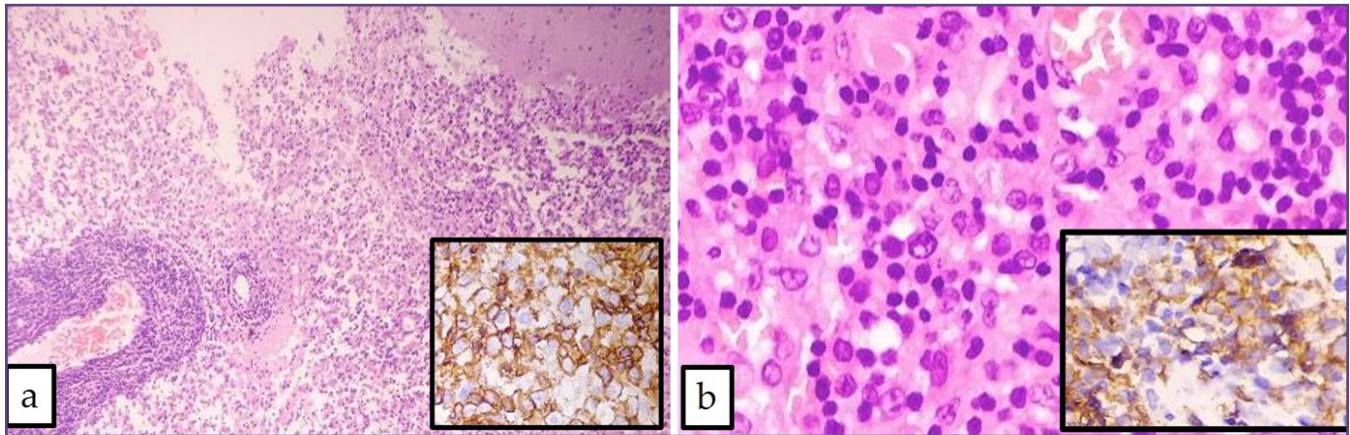


Fig. 3: a) Histopathological section showing lymphoma cells in perivascular pattern and also infiltrating the brain parenchyma (H&E, 40x). Inset showing LCA positivity on IHC; b) High power view showing pleomorphic lymphoma cells with vesicular chromatin and prominent nucleoli. (H&E, 400x) Inset shows CD 20 positivity.

intracranial pressure like headache, vomiting and ocular symptoms.^[1,2] Clinically and radiologically, the differential diagnosis includes glioma, metastasis, demyelinating disorders, sarcoidosis, abscess or infection like toxoplasmosis which necessitates a histological diagnosis for confirmation.^[3]

On cytology, the characteristic perivascular arrangement of atypical lymphoid cells clinches the diagnosis of lymphoma. Lymphocytes and foamy macrophages may confuse the cytological picture with vasculitis, infection or demyelinating disorder.^[3,4] During smearing, the cytoplasm of foamy macrophages may get stripped and the naked nuclei may resemble nuclei of lymphoma. However, neutrophils are more commonly seen in infections and macrophages are seen in demyelination or infarcts.^[2] Reactive astrocytes may totally obscure the underlying lymphoma, resulting in false negative intra operative diagnosis due to sampling error.

Histopathology shows large areas of necrosis with viable cells around blood vessels, giving rise to the characteristic perivascular arrangement of lymphoma cells which even grow within the blood vessels. Tumor cells may also be present as dispersed population or in small clusters. Focally, reactive astrocytes, microglial cells and reactive T lymphocytes are also seen.^[2-4]

Causes of discrepancy between frozen section and formalin fixed paraffin embedded sections include sampling error and inaccurate assessment of histological grade or cell type of tumor.^[2,4] Squash Cytology and imprint smears circumvent the problem caused by freezing artifact, are cheaper, faster and use minimal tissue, thus conserving tissue for histopathology and immunophenotyping tests.^[4,5]

The diagnostic accuracy of imprint and squash cytology ranges from 83.7 %-94.6 % when compared with final histological diagnosis.^[1,5-7] On comparing imprint smears and squash cytology smears for the same case, Sharma et al have reported diagnostic accuracy of 89.3% for squash cytology, 92% for imprint smears and 94.6% when both squash and imprint smears were studied. The thickness of the crush smears depends on the pressure applied while smearing, producing uneven smears. On the other hand, imprint smears have uniform thickness, thereby ensuring better assessment of cellularity. The tiny bit of tissue used for making crush smear may not contain representative areas, resulting in erroneous diagnosis. The architecture of lesion is preserved in imprint smears. Besides, unlike squash cytology, the tissue used for making imprints is preserved and can be utilized for histopathological examination.^[1] Few studies have advocated concomitant use of frozen section with squash and imprint cytology to improve the accuracy of intraoperative rapid diagnostic techniques.^[4]

Rapid intraoperative diagnosis of lesion as lymphoma is invaluable for the operating surgeon as extensive excision is avoided and only tissue adequate for histopathology and immunophenotyping studies is taken while extensive surgical resection and intracavitary radiation is done in case of glioma.^[2-4,8] Lymphoma is treated by chemotherapy with high dose methotrexate followed by radiotherapy.^[3]

Conclusion

This case highlights the challenge faced by the pathologist in diagnosis of PCNL intra-operatively on squash and imprint cytology smears. It is important to distinguish lymphoma from glioma or metastasis in CNS because of totally different lines of management.

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Competing Interests

Nil

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