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Oncology

PRIMARY INTRACRANIAL PRIMITIVE NEUROECTODERMAL TUMOR IN ADULT FEMALE: AN UNUSUAL OCCURRENCE

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ABSTRACT Non-Osseous intracranial PNET is a very rare and aggressive malignant tumor with only 40-cases reported in adults. We hereby report a 25-years-old female presenting with altered sensorium and seizures for 4-months. Contrast enhanced magnetic resonance imaging (CEMRI) of brain revealed hyper-intensity in the left posterior frontal region. Left frontal craniotomy with total excision of mass was done. Histopathology and immuno-histochemistry confirmed a primitive neuro-ectodermal tumor and post-operative external beam radiation was given to prevent recurrence. Patient is asymptomatic and on regular follow-up for last 20-months. Further consensus is needed to establish a universal guideline for peripheral primitive neuroectodermal tumor management.

KEYWORDS :

INTRODUCTION

Primitive neuroectodermal tumors (PNETs) are a group of embryonal rare tumors with a specific immune-phenotypic characteristic of diffuse cytoplasmic membrane staining for CD99.[1] These tumors are common among children and adolescents but rarely present in adulthood. Incidence is more common among males as reported in literature. Bone and soft tissues are usual sites of presentation, intracranial (especially meningeal) location is extremely rare and intra-parenchymal occurrence is almost non-existent.[1] Due to rare occurrence of this tumor, no much information is available regarding clinical features, treatment protocol and prognosis. We aim to highlight clinical, immune-histochemical and treatment outcome in a rare case of non-osseous intracranial PNET in adult female.

Case Summary

A young female, 25 years of age presented with altered sensorium and generalized seizures for last 4-months. She also complained of frontal headache, pulsatile in nature persisting for 2-3 hours every day for same duration. No focal neurological deficit was elicited on central nervous system examination. Routine complete blood count, liver function test, renal function test were found to be within normal limits. T2W FLAIR view contrast enhanced magnetic resonance imaging (CEMRI) of brain (figure-3A) showed heterogeneous area of abnormal signal intensity in the left posterior frontal region with associated edema and associated left parasagittal lesion measuring 3.1 × 3.7 × 3.1 cm. Magnetic resonance spectroscopic (MRS) finding revealed elevated choline uptake in mentioned lesion. Patient underwent left frontal craniotomy with total excision of mass in department of neurosurgery. Post-operative histopathology report revealed features of small round blue cell tumor {Figure-1 (A&B)}. On immune-histochemical analysis it was found to be cluster differentiation- 99 (CD 99) (Figure-2A) and neuron specific enolase (NSE) positive (Figure-2B) and glial fibrillary acidic protein (GFAP)(Figure-2C), synaptophysin (Figure-2D), chromogranin, CD56 and S100 negative. Thus, confirmed as Primitive neuroecto dermal tumor.

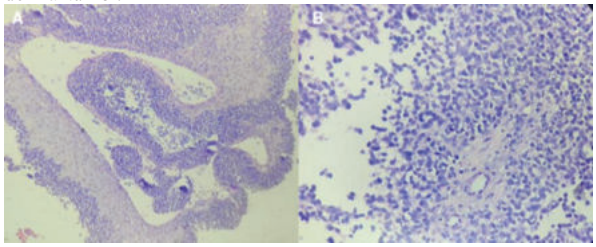

Figure1: Photomicrograph - Hematoxylin and eosin-stained paraffin sections A) Low power view B) High power view- showing packed small, round to oval, undifferentiated cells with hyperchromatic nuclei and little basophilic cytoplasm.

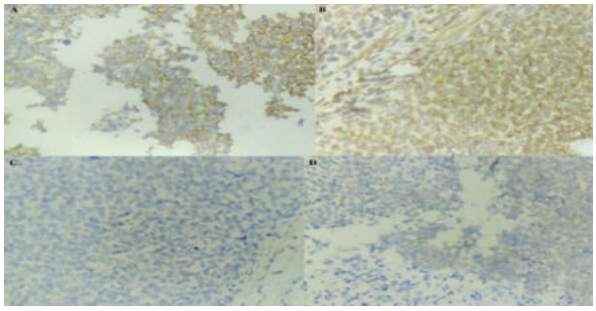

Figure 2: Photomicrographs of the immune-histochemical analysis (magnification ×20) showing (A) diffuse positive cytoplasmic membrane staining for CD99, (B) neoplastic cells positive for neuron specific enolase (C) neoplastic cells negative for glial fibrillary acidic protein. D) neoplastic cells negative for synaptophysin.

Post-operative contrast enhanced CT of brain revealed heterogeneous non-enhancing area of abnormal hyper attenuation with internal cystic areas and air locules in left fronto-parietal lobe and mild associated edema suggestive of resection cavity with post-operative parenchymal changes. No evidence of any significant soft tissue enhancement (Figure-3B). For adequate local control and to prevent recurrence, patient was given option of adjuvant chemotherapy with vincristine, adriyamycin and cyclophosphamide (VAC) regimen alternating with ifosfamide and etoposide (IE) and post-operative whole brain radiotherapy (WBRT). After receiving detailed information about benefit and toxicity profile of both treatment modalities patient decided to go ahead with adjuvant radiotherapy. Patient received whole brain radiation therapy (WBRT) 2-weeks after the initial surgery with 36 Gray (Gy) in 20 fractions, 1.8 Gy per fraction over 4-weeks by cobalt-60 tele-therapy machine. Post-radiation therapy CEMRI of brain shows no associated diffusion restriction or post contrast enhancement. Patient was kept on regular follow up after radiation therapy. 6-month follow up scan (CEMRI) did not show any sign of residual or recurrent disease (Figure-3 C&D). The patient is doing well after 24-months of surgery and adjuvant radiation therapy, without any neurological symptoms/ deficit.

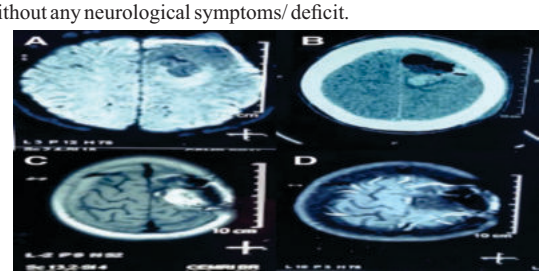

Figure 2: A) CEMRI of brain DW T2 FLAIR image showing heterogeneous area of abnormal signal intensity in the left posterior frontal region with associated edema and left parasagittal lesion measuring 3.1×3.7×3.1 cm. B) Post-operative CECT of brain showing heterogeneous non-enhancing area of abnormal hyper attenuation with internal cystic areas and air locules in left fronto-parietal lobe and mild associated edema suggestive of resection cavity. C&D) CEMRI of Brain done (T2/FLAIR) revealed hyperintensities noted in the left superior frontal cortex and subcortical white matter with no associated diffusion restriction or post contrast enhancement.

DISCUSSION

Non-Osseous intracranial PNET is a very rare and aggressive malignant tumor. Only 40 cases are reported in literature among adults more than 18 years of age. Intracranial ES/peripheral PNETs account for only 0.03% of the total number of intracranial tumors. 15 years is median age of onset with peak in 2nd decade.[2,3] Due to uncommonness of PNET in the intracranial (non-osseous) location, it is not considered for differential diagnosis in most clinical situations. In the recent WHO 2016 classification of primary central nervous system (CNS) tumors, the term PNET has been removed instead primitive embryonal tumor, NOS (not otherwise specified) was introduced for primitive embryonal tumors which are not showing any classic genetic alterations.

Variable clinical features are observed based on tumor location, size and invasion. Tumors are usually located in temporal lobe but in our case it was located in fronto-parietal lobe.

Microscopically primary intracranial peripheral PNETs (pPNET) are mainly composed of small, round and undifferentiated cells with small cytoplasm and hyperchromatic nuclei.[4,5] Differential diagnoses of intracranial pPNETs on the basis of histo-pathological sections include central neuroblastoma, primary leptomeningeal medulloblastoma and intracranial central PNET.[6,7] In order to make accurate diagnosis, immunohisto-chemical and molecular genetic analysis is needed. Central nervous system embryonal tumors are negative for CD99 but all intracranial ES/pPNETs show diffuse cytoplasmic membrane staining for CD99.
CD99 is not a specific immune-histo-chemical marker as it is also positive in round blue cell tumors. But distinct membranous staining pattern is characteristic feature of pPNET/ES where-as cytoplasmic staining is seen in all other round blue cell tumors.[3,8,9,10]

The gold standard for diagnosis of ES/pPNET is molecular testing which depicts EWSR1 gene rearrangement that can be detected by reverse transcription polymerase chain reaction and fluorescent in-situ hybridization (FISH). Most frequent chromosomal translocation is t(11, 22)(q24;q12).[8] However, chromosomal studies were not performed during our investigation due to financial constraints.

On MRI Imaging, pPNET is characterized by mixed isointense-to-hypointense signals on T_1-weighted imaging and isointense-to-hyperintense signals on T_2-weighted imaging as mentioned in literature. Our findings are consistent with literature.

Due to the scarcity of cases of this tumor, no proper guidelines are framed for management of such tumors. However, primary therapy is surgical resection of the tumor. Chen et al. reported that patient undergoing gross total resection (GTR) was found to be having significantly longer survival (i.e 38 months) when compared to partial resection (20 months).[3]

As this is a rare occurrence, the standard first-line adjuvant treatment remains unclear. Few studies have showed that adjuvant chemotherapy improved the long-term survival rates from 5%-10% to 70%-80 %.[11,12] Chemotherapy (CT) regimen most commonly used is VAC ± IE. Radiotherapy play a significant role as adjuvant treatment for ES/pPNETs. It is observed that the 1- and 2-year survival rates of patients who received adjuvant radiotherapy (88.9 and 66.7%) were remarkably better than those of patients who did not receive any adjuvant treatment (60.0 and 0%). Median survival time improved significantly (38 months vs. 13 months).[3]

Literature review shows that GTR combined with adjuvant chemotherapy and radiotherapy is the preferred line of treatment .[2,3,8,9] However, close follow-up is necessary to look for any reoccurrence.

CONCLUSION

In adults we rarely encounter Primary intracranial ES/pPNETs with aggressive clinical course and a high tendency for local recurrence and distant metastasis. Thus, more cases with long term follow up are needed to understand pPNETs in the adult population. Awareness of intracranial occurrence of this tumor is necessary to acknowledge its biological, therapeutic and prognostic implications. Immunohisto chemistry and molecular genetic analysis are necessary for accurate diagnosis of these tumors. GTR combined with radiotherapy and chemotherapy is considered as standard of care. Therefore, our present case report will enhance the existing scarce reported pool and may serve as a potential guide for oncologists.

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