Primary intracranial peripheral primitive neuroectodermal tumor in an adult patient with aphasia: a rare case report

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Abstract

Primary intracranial primitive neuroectodermal tumors (PNETs) are extremely rare malignancies, affects children and adolescents with only 10 cases has been reported over 33 years old. we present a case of PNET in a 36 years old female patient with the chief complaint of aphasia for the first time

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Running title: Intracranial adult pPNET

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"Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy"

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Abstract

Primary intracranial primitive neuroectodermal tumors (PNETs) are extremely rare malignancies, which affects children and adolescents with only 10 cases has been reported over 33 years old. They have an aggressive behavior and a high tendency for local recurrence and distant metastasis. Here we present a

case of supratentorial PNET which occurred in left frontoparietal lobe of a 36 years old female patient with the chief complaint of aphasia for 2 month duration. Aphasia is being reported for the first time as a consequence of a PNET brain tumor. T1-weighted MRI showed a large mass with mixed isointense to hypointense signals. The tumor was completely removed. Histopathologic examination was indicative of a small round cell tumor. Immunohistochemical analysis showed positivity for CD99. Presence of EWSR1 gene rearrangement confirmed the diagnosis. The patient's aphasia gradually resolved post operation. Six months follow-up showed no evidence of local recurrence or metastasis.

Key Words:

Brain Neoplasms, Primitive Neuroectodermal Tumors, Skull

Introduction

Primary intracranial primitive neuroectodermal tumors (PNETs) are extremely rare malignancies that usually originate from the meninges and show varying degrees of neuroectodermal differentiation [1-4]. About 66 cases of these tumors have been reported so far. PNETs are poorly differentiated, highly malignant, and aggressive small round cell neoplasms. They had a high propensity for local recurrence and distant metastasis. Intracranial PNETs commonly affect children and adolescents [1, 2, 5]. It is noteworthy that the incidence of PNETs in adults is exceedingly rare. Only about ten cases of these tumors have been reported over the age of 33 years [1, 2]. Fusion of the EWSR1 gene with a member of the gene family is considered the primary cause of the PNETs [1, 4]. Due to the scarcity of cases of patients with PNETs, the clinical and imaging features, treatment and prognosis are not clear [1, 2].

Case report

A 36 years old female patient referred to neurosurgery department, Razi hospital of Birjand, Iran, with the chief complaint of aphasia for 2 month duration. Her past medical history was not significant. Her family history was not noticeable. On examination, the patient was afebrile, with normal vital signs. Tongue was in midline. She had full strength in all extremities and had no other neurologic symptoms. Her laboratory tests were unremarkable. Brain CT scan and T1-weighted, T2-weighted and post-contrast MRI Images were made. T1-weighted MRI showed a large mass with mixed isointense to hypointense signals in left frontoparietal lobe; T2- weighted MRI showed isointense to hyperintense signals; post-contrast MRI showed a mass with heterogeneous enhancement in the left frontoparietal lobe. CT scan demonstrating a large mass with isodensity signals (Figure 1). A preoperative diagnosis of astrocytoma was suspected. It was decided that the patient would undergo surgery. Stereotaxic surgery was performed and the tumor was completely removed.

The biopsied tissues were processed to formalin fixed paraffin embedded (FFPE) preparation, hematoxylin and eosin (H&E) and immunohistochemistry (IHC). Immunohistochemical analysis was performed for CD99 immunomarker. Reverse transcription polymerase chain reaction (RT-PCR) was done to assess gene rearrangement for EWSR1 gene.

The tumor was sent for histopathological examination. On microscopic examination, at lower power, the tumor was undifferentiated and densely cellular. Sheets of small, round to oval, uniform cells with scant clear cytoplasm were seen infiltrating the brain tissue. Some large pleomorphic cells were also evident (Figure 2). Histopathologic findings were suggestive of a malignant small round cell tumor with following differential diagnosis: 1- Ewing sarcoma / primitive neuroectodermal tumor (PNET); 2- neuroblastoma; 3-lymphoma. Immunohistochemical analysis showed diffuse membranous positivity for CD99 but negative staining for LCA. Reverse transcription polymerase chain reaction showed EWSR1 gene rearrangement and confirmed the diagnosis of PNET. Whole-body CT scan was recommended and performed and did not demonstrate any lesion in other parts of her body.

After surgery, the patient's condition was stable and after two months, the patient's aphasia gradually resolved. Six months after surgery, follow-up images including MRI of the patient's brain and whole body

scans were performed. There was no evidence of tumor recurrence in these images and no metastatic focus was evident in the images.

Discussion

PNETs occur primarily in children and adolescents; the median age at initial diagnosis is about 15 years of age with a slight male predisposition [1, 5]. The age of our case does not correspond to the common age of intracranial PNETs, which adds to the importance of our case. Our case was observed in a female patient that did not agree with the predominance of males [1].

Supratentorial cerebral hemispheres are the most common sites of involvement for adult intracranial PNET [1]. The location for PNET of our case was also supratentorial.

The clinical features of intracranial PNETs are diverse. The reported symptoms for adult intracranial PNETs included headache and vomiting (most common symptoms), hemiplegia, muscle strength decrease, facial palsy, deafness and hearing disturbance, drowsiness, fatigue, epilepsy, memory decline, and ataxia [1]. Our case was the first case which manifested as aphasia. The major causes of aphasia are a cerebral vascular accident (stroke) or head trauma. Aphasia can also be the result of brain tumors, brain infections, or neurodegenerative diseases [1].

Adult intracranial PNETs predominantly show mixed isointense to hypointense signals on T1-weighted on MRI images, and isointense to hyperintense signals on T2- weighted on MRI images [1, 5]. The MRI findings in our case were consistent with these findings. For post-contrast MRI, Jiang et al. reported the heterogeneous enhancement of in 6 cases of adult intracranial PNETs, and intense enhancement in 4 cases [1]. Our case showed heterogeneous enhancement.

Histopathological differential diagnosis for intracranial PNETs includes central nervous system (CNS) embryonal tumors (such as medulloblastoma, neuroblastoma, atypical teratoid/rhabdoid tumor), malignant meningioma, lymphoma, rhabdomyosarcoma and melanoma [1, 3]. However, it is necessary to identify PNET correctly and differentiate it from other CNS embryonal tumors due to different treatment and prognosis (PNET requires focal radiotherapy while other CNS embryonal tumors require craniospinal irradiation) [3].

Membranous expression of CD99 is a highly reliable and sensitive, but not specific, diagnostic marker for intracranial PNETs and was detected in almost all patients [1, 3, 5]. Molecular cytogenetics showing EWSR1 gene rearrangement is the golden standard for diagnosis of PNET. Because chromosomal translocations are not unique to this tumor the diagnosis of PNETs can be confirmed based on the comprehensive histopathological, immunohistochemical and molecular cytogenetics examinations [1, 3]. It is noteworthy that CNS embryonal tumors are negative for CD99 and negative for EWSR1 molecular rearrangement [5].

Jiang et al. [1] present a case of intracranial PNET located in the left frontoparietal lobe of a 55-year-old female patient who presented with memory decline and treated by gross total resection (GTR) with adjuvant radiotherapy. In terms of age, symptoms and adjuvant treatment, there are differences between our case and their case, but in terms of tumor location, there is similarity between the two cases.

Chen et al. [2] reported a case of intracranial PNET located in the right parietal lobe of a 43 years old male patient who presented with the chief complaint of epilepsy and treated by GTR with adjuvant chemoradiotherapy; he died after 48 months post operation.

VandenHeuvel et al. [3] reported a case of intracranial PNET located in the right temporal lobe of a 61 years old male patient who presented with left hemiparesis and left-side facial drooping, He underwent just biopsy. In terms of age, tumor location, symptoms and treatment there was no agreement between our case and their case.

A standard treatment plan for intracranial PNETs has not yet been established. Surgical resection (GTR) is the main therapeutic option [1]. Radiotherapy plays a significant role in improving the survival of patients

with intracranial PNETs. Chemotherapy can significantly improve the survival rate. GTR with adjuvant radiotherapy and chemotherapy is probably the best treatment plan for these tumors [2, 5].

Intracranial PNETs are aggressive malignancies with a poor prognosis. The overall 5-year survival rate is estimated to be 19.0% [2]. Wide surgical resection margins could significantly reduce local recurrences. GTR is accompanied with better survival than incomplete tumor resection [1]. Early recurrence and old age may not be associated with a good outcome [5].

To conclude, primary intracranial PNETs in patients > 33 years are extremely rare. Because clinical and imaging characteristics, treatment and prognosis of these tumors remain unclear, further reports are necessary to fully understand them.

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Declarations

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Conflicts of interest/Competing interests

The authors declare that they have no conflict of interest.

Ethics approval

This case report has observed the ethical guidelines.

Consent to participate

Patient informed consent has been obtained for this case report.

Consent for publication

This is the author's own work and there is no need for special permission to publish it

Availability of data and material

Code availability

Not applicable.

Authors' contributions

KG, MRM and HA have made substantial contributions to conception and design of the study. MRM, and HA have been involved in data collection. KG, MRM and HA and have been involved in data interpretation and drafting the manuscript. KG, MRM and HA have critically revised the manuscript. All authors have given final approval of the version to be published.

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Figure legends:

Figure 1: Radiologic findings of the primitive neuroectodermal tumor. (A) T1-weighted MRI showing a mass with mixed isointense to hypointense signals in left frontoparietal lobe. (B) CT scan demonstrating a large mass with isodensity signals. (C, D) Post-contrast MRI showing a mass with heterogeneous enhancement in the left frontoparietal lobe.

Figure 2: Histopathologic findings. (A) An undifferentiated and densely cellular tumor. (B, C) Small, round, uniform cells infiltrating the brain tissue. (D) Round cells with scant cytoplasm. (E, F) Diffuse membranous positivity for CD99. Scale bars: 100 μm (A), 50 μm (B, C, E). 20 μm (D, F)