

CASE REPORT

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

Kazem Ghaemi¹ | Mahdieh Rajabi-Moghaddam² | Hamid Abbaszadeh³ 

¹Department of Neurosurgery, School of Medicine, Birjand University of Medical Sciences, Birjand, Iran

²Department of Pathology, School of Medicine, Birjand University of Medical Sciences, Birjand, Iran

³Department of Oral and Maxillofacial Pathology, School of Dentistry, Birjand University of Medical Sciences, Birjand, Iran

Correspondence

Hamid Abbaszadeh, Faculty of Dentistry, Oral and maxillofacial Pathology Department, Birjand, South Khorasan province, Iran.
Email: hamidabbaszade@yahoo.com

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Abstract

Primary intracranial peripheral primitive neuroectodermal tumors (pPNETs) are extremely rare malignancies that commonly affect children and adolescents. Only 10 cases over the age of 33 have been reported. pPNETs have an aggressive behavior and a high tendency for local recurrence and distant metastasis. Here, we present a case of supratentorial pPNET that affected the left frontoparietal lobe of a 36-year-old female patient. The patient complained of aphasia during the last 2 months. Aphasia is reported for the first time as a result of a pPNET. In T1-weighted MRI, a large mass with mixed isointense to hypointense signals was observed. 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 was gradually resolved post-surgery. Six months follow-up showed no evidence of local recurrence or metastasis.

KEYWORDS

brain neoplasms, primitive neuroectodermal tumors, skull

1 | INTRODUCTION

Primitive neuroectodermal tumors (PNETs) of the central nervous system (CNS) are heterogeneous groups of embryonal tumors. PNETs arising outside the CNS are classified as peripheral PNETs/Ewing's sarcomas (pPNETs/ESs); they can occur in osseous and extra-osseous tissues, including inside the skull (extraparenchymal in location). Primary intracranial pPNETs/ESs are extremely rare malignancies that usually originate from meninges and show varying degrees of neuroectodermal differentiation.¹⁻⁴ About 66 cases of these tumors have been reported so far. pPNETs are poorly differentiated, highly malignant, and aggressive small round cell neoplasms. They have a high tendency for local recurrence and distant metastasis.

Primary intracranial pPNETs commonly affect children and adolescents.^{1,2,5} It is noteworthy that the incidence of pPNETs in adults is exceedingly rare. Only about 10 cases over 33 years have been reported.^{1,2} Fusion of the EWSR1 gene with a member of the ETS gene family is considered the primary cause of the pPNETs.^{1,4} Due to the rarity of primary intracranial ES/pPNETs, the clinical characteristics, imaging features, treatment, and prognosis of these tumors are unclear.^{1,2}

2 | CASE REPORT

A 36-year-old female patient referred to neurosurgery department, Razi hospital, Birjand, Iran, with the chief

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complaint of aphasia during the last 2 month. The past medical history and family history were not noticeable. On examination, the patient was afebrile, along with normal vital signs. Tongue was in midline. She had full strength in all extremities without any neurologic symptoms. Her laboratory tests were unremarkable. CT scan, T1-weighted, T2-weighted, and post-contrast MRI images were taken. T1-weighted MRI image showed a large mass with mixed isointense to hypointense signals in left frontoparietal lobe; T2-weighted MRI image showed isointense to hyperintense signals; post-contrast MRI image showed a mass with heterogeneous enhancement in the left frontoparietal lobe. CT scan image demonstrated a large mass with isodensity signals (Figure 1). Preoperative diagnosis of astrocytoma was suspected. It was decided that the patient would undergo surgery. Stereotaxic method was performed for incisional biopsy.

The tumor was sent for histopathological examination. On low power microscopic examination, the tumor was undifferentiated and densely cellular. Sheets of small, round to oval, uniform cells with scant clear cytoplasm were seen that had infiltrated the brain tissue. Some large pleomorphic cells were also evident (Figure 2).

Histopathologic findings were suggestive of a malignant small round cell tumor with the following differential diagnoses: 1- pPNET/ES; 2- neuroblastoma; 3-lymphoma.

Immunohistochemical analysis was performed for CD99 immunomarker. Reverse transcription polymerase chain reaction (RT-PCR) was done to assess EWSR1 gene rearrangement. Immunohistochemical analysis showed diffuse membranous positivity for CD99 but negative staining for LCA immunomarker. RT-PCR showed EWSR1 gene rearrangement and confirmed the diagnosis of pPNET.

PET-CT image was taken and did not demonstrate any metastatic lesion in other parts of her body.

Combined microsurgical and endoscopic methods were used for total removal of the tumor. Histopathologic examination of excisional biopsy revealed similar findings as incisional biopsy.

After surgery, the patient also underwent local radiotherapy. The patient's condition was stable and the patient's aphasia was gradually resolved within 2 months. Follow-up images including MRI and PET-CT image were taken 6 months post-surgery. There were no evidence of tumor recurrence or metastatic focus in these images.

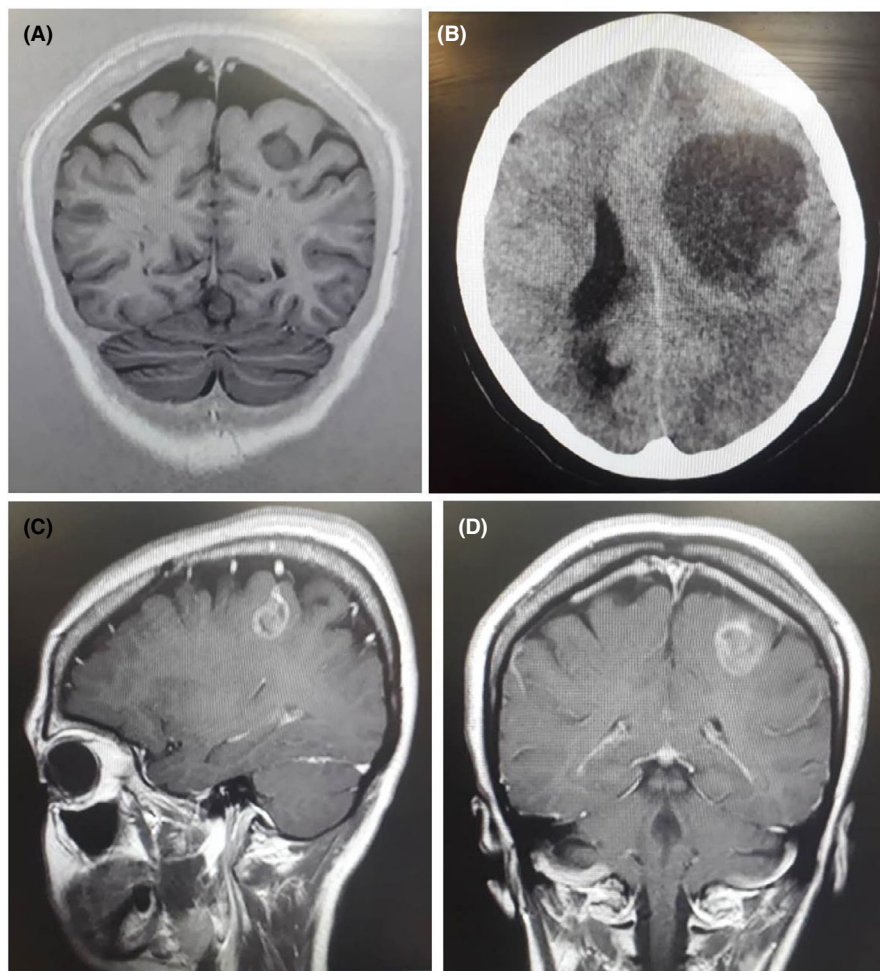
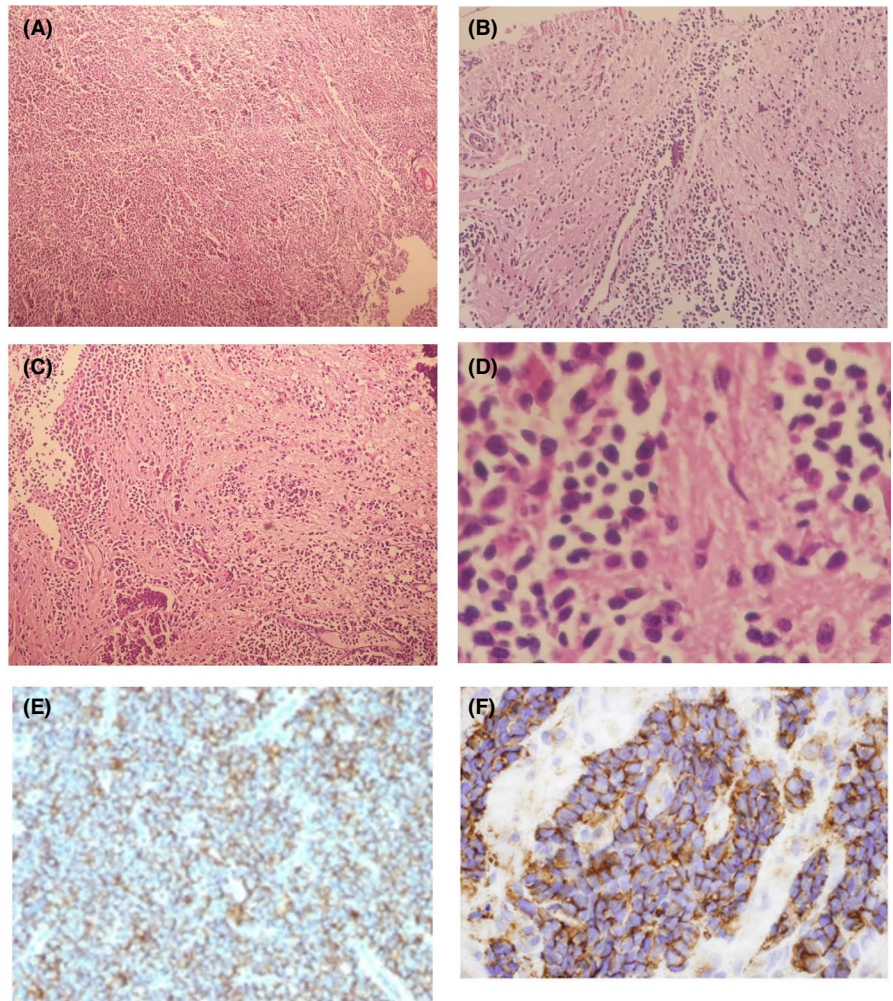


FIGURE 1 Radiologic findings of the primitive neuroectodermal tumor. (A) T1-weighted MRI showing a mass with mixed isointense to hypointense signals in left frontoparietal lobe. (B) CT scan demonstrating a large mass with isodensity signals. (C, D) Post-contrast MRI showing a mass with heterogeneous 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 μ m (A), 50 μ m (B, C, E), 20 μ m (D, F)



3 | DISCUSSION

In this case report we aimed to present a case of pPNET in a 36-year-old adult patient which was accompanied by aphasia.

3.1 | Supratentorial PNET

The supratentorial PNETs are a category of small round and blue cell tumors which was included in the 2007 world health organization (WHO) CNS tumor classification to separate them from medulloblastomas. Classic medulloblastomas show small blue round cells with syncytial arrangement of densely packed undifferentiated cells (embryonal cells). Differential diagnoses include anaplastic ependymoma, atypical teratoid rhabdoid tumor (ATRT) and other forms of highly proliferative malignant neuroectodermal tumors. In fact, PNET is a name used for tumors which appear histopathologically similar to medulloblastoma but occur primarily in the cerebrum (medulloblastoma originates in the cerebellum).⁶

3.2 | CNS PNETs (cPNETs) versus intracranial pPNETs

Although CNS PNETs (cPNETs) and intracranial pPNETs cannot be distinguished on morphology, their distinction from each other is necessary as their treatment and prognosis vary. They have distinct genetic properties and immunohistochemical profiles; for example, intracranial pPNETs show characteristic chromosomal translocation t(11; 22; q24; q12). CD99 is positive in nearly all pPNET with distinct membranous staining. Central PNETs are negative for CD99 staining.^{2,7}

3.3 | Primary intracranial pPNETs

Primary intracranial pPNETs occur primarily in children and adolescents; the median age at initial diagnosis is about 15 years of age with a slight male predilection.^{1,5} The age of our case does not correspond to the common age of intracranial pPNETs, which shows the importance of our case. Our case was observed in a female patient that

does not correspond to the gender superiority of men in primary intracranial pPNETs.¹

Supratentorial cerebral hemispheres are the most common sites of involvement for adult primary intracranial pPNETs.¹ The location in our case was also supratentorial.

The clinical features of primary intracranial pPNETs are diverse. The reported symptoms for adult primary intracranial pPNETs include headache and vomiting (the most common symptoms), hemiplegia, muscle strength decrease, facial palsy, deafness, 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 cerebral vascular accident (stroke) or head trauma. Aphasia can also be the result of brain tumors, brain infections, or neurodegenerative diseases.¹

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

Histopathological differential diagnoses for primary intracranial pPNETs include CNS embryonal tumors (such as medulloblastoma, neuroblastoma, and atypical teratoid/rhabdoid tumors), malignant meningioma, lymphoma, rhabdomyosarcoma, and melanoma.^{1,3} However, it is necessary to correctly identify intracranial pPNET and differentiate it from other CNS embryonal tumors due to different treatment and prognosis (intracranial pPNETs require 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 pPNETs and has been detected in almost all patients.^{1,3,5} Molecular cytogenetics representing EWSR1 gene rearrangement is the gold standard for diagnosis of intracranial pPNETs. Since chromosomal translocations are not unique to these tumors, diagnosis of intracranial pPNETs is 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 also negative for EWSR1 gene rearrangement.⁵

Jiang et al.¹ presented a case of intracranial pPNET 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. There are differences between our case and their case in terms of age, symptoms, and adjuvant treatment; there is similarity between both cases in terms of tumor location.

Chen et al.² reported a case of intracranial pPNET located in the right parietal lobe of a 43-year-old male patient who presented with the chief complaint of epilepsy and treated by GTR with adjuvant chemoradiotherapy; the patient died after 48 months post-surgery.

VandenHeuvel et al.³ reported a case of intracranial pPNET located in the right temporal lobe of a 61-year-old male patient who presented with left hemiparesis and left-side facial drooping. He underwent just biopsy. There are no agreements between our case and their case in terms of age, tumor location, symptoms, and treatment.

A standard treatment plan for primary intracranial pPNETs has not yet been established. Surgical resection (that is GTR) is the main therapeutic option.¹ Radiotherapy plays a significant role in improving the survival of patients with intracranial pPNETs. Chemotherapy can also significantly improve the survival rate. GTR with adjuvant radiotherapy and chemotherapy is probably the best treatment plan for these tumors.^{2,5}

The site of origin of pPNETs is quite varied and has significant influence on the prognosis. Intracranial pPNETs are aggressive malignancies with a poor prognosis. The overall 5-year survival rate is estimated to be 19%.² Wide surgical resection margins can 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 pPNETs in patients over 33 years are extremely rare. Since clinical characteristics, imaging features, treatment, and prognosis of these tumors remain unclear, further reports are necessary to fully understand them.

3.4 | Clinical significance

The clinical significance of this case is to pay attention to the diagnosis of pPNET in patients over 33 years of age and the correct differentiation of pPNET from cPNET and to the rare clinical manifestations such as aphasia for the diagnosis of pPNET.

3.5 | Message from article

Correct diagnosis of the pPNET tumor in this patient helped to proper treatment of the patient and possibly her better prognosis.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

AUTHOR CONTRIBUTIONS

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

ETHICAL 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.

CONSENT

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

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Hamid Abbaszadeh  <https://orcid.org/0000-0002-7443-0607>

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