American Journal of Case Reports

e-ISSN 1941-5923
© Am J Case Rep, 2026; 27: e953049
DOI: 10.12659/AJCR.953049

Received: 2026.02.05
Accepted: 2026.04.29
Available online: 2026.05.28
Published: 2026.XX.XX

Adult-Onset Central Nervous System Embryonal Tumor With Neuronal Differentiation: A Diagnostic Challenge

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

BCDEF 1,2 Anh Quynh Pham
AC 3 Tuyen Van Pham
A 1,2 Thong Minh Pham

1 Department of Radiology, Bach Mai Hospital, Hanoi, Vietnam
2 Hanoi Medical University, Hanoi, Vietnam
3 Department of Pathology, Bach Mai Hospital, Hanoi, Vietnam

Corresponding Author: Anh Quynh Pham, Department of Radiology, Bach Mai Hospital, 78 Giai Phong Street, Phuong Mai Ward, Dong Da District, Hanoi, Vietnam, Phone: +8462900502, e-mail: phamquynhanh@hmu.edu.vn

Financial support: None declared
Conflict of interest: None declared

Patient: Female, 32-year-old
Final Diagnosis: Embryonal tumor • NOS, with neuronal differentiation
Symptoms: Severe holocranial headache that had been intensifying for three weeks
Clinical Procedure: —
Specialty: Radiology

Objective: Rare disease

Background: Neuroblastoma is the most prevalent extracranial solid tumor in children. Primary central nervous system (CNS) neuroblastoma represents an exceedingly rare histological subtype. Adult-onset CNS embryonal tumors, including neuroblastoma, are particularly uncommon and remain poorly characterized in the medical literature. We present a case of suspected primary CNS neuroblastoma in an adult patient to highlight the diagnostic challenges and aggressive nature associated with this rare condition, particularly in resource-limited settings.

Case Report: A 32-year-old woman presented with severe, progressively worsening headaches over several weeks that were unresponsive to over-the-counter analgesics. Due to symptom progression, she underwent urgent diagnostic evaluation. Initial non-contrast computed tomography of the brain identified a hyperdense lesion in the right temporal region suggesting acute intratumoral hemorrhage, accompanied by mass effect. Magnetic resonance imaging revealed a complex, heterogeneous, contrast-enhancing mass with internal hemorrhagic components and extensive surrounding vasogenic edema. Accordingly, the patient underwent neurosurgical resection. Histological examination of the resected specimen indicated an embryonal tumor, not otherwise specified, with neuronal differentiation. In the absence of advanced molecular profiling due to institutional resource limitations, primary CNS neuroblastoma remained a strongly suspected diagnosis rather than a definitive conclusion.

Conclusions: Primary CNS neuroblastoma in adults is an uncommon clinical entity that presents considerable diagnostic challenges and frequently mimics high-grade gliomas or metastatic lesions on radiographic imaging. This case underscores the aggressive nature of the tumor, the importance of including rare embryonal malignancies in the differential diagnosis, and the diagnostic challenges encountered when molecular confirmation is unavailable.

Keywords: Adult • Case Reports • Central Nervous System Neoplasms • Magnetic Resonance Imaging • Neuroblastoma • Neurosurgery

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/953049

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

Introduction

Neuroblastoma—a highly aggressive malignant neoplasm arising from the sympathetic nervous system—is recognized as the most prevalent extracranial solid tumor in the pediatric population. The tumor originates from neural crest cells, which are embryonic precursor cells responsible for development of the peripheral nervous system and adrenal medulla. Consequently, nearly 95% of cases occur in the retroperitoneum; the adrenal gland is the most common site, involved in 40% to 60% of cases. Additional sites include the paravertebral sympathetic chain in the abdomen, chest, neck, and pelvis [1,2].

Neuroblastoma is characterized by substantial clinical and genetic heterogeneity, ranging from low-risk tumors that may regress spontaneously to high-risk, extensively metastatic disease requiring comprehensive multimodal treatment. Recent studies have elucidated the biological mechanisms underlying disease progression. For example, aminoacylase 1 has been identified as a critical mediator of neuroblastoma cell proliferation and migration through the extracellular signal-regulated kinase (ERK)/transforming growth factor (TGF)-β signaling pathways. Understanding these molecular drivers provides broader insight into neuroblastoma biology and highlights potential therapeutic targets that may ultimately inform the management of rare variants, including those that arise within the central nervous system (CNS) [3].

Primary central nervous system neuroblastoma (PCNSNB) represents an exceptionally rare form of embryonal malignancy [4]. Unlike conventional neuroblastoma, PCNSNB originates in the brain parenchyma or spinal cord, rather than in the peripheral nervous system. Distinguishing between these entities is essential for accurate diagnosis, classification, and treatment planning. The World Health Organization (WHO) classifies PCNSNB as a high-grade neuroepithelial tumor. Earlier literature occasionally grouped these tumors under primitive neuroectodermal tumors; however, more recent classifications recognize CNS neuroblastoma, particularly the forkhead box R2 (FOXR2)-activated subtype, as described in the 5th edition of the WHO Classification of CNS Tumors (2021) [2].

The incidence of primary CNS neuroblastoma in adults is extremely low, representing only a small proportion of neuroblastoma cases and adult brain tumors [4]. Although neuroblastoma comprises less than 5% of all tumors diagnosed after 10 years of age, PCNSNB in individuals older than 18 years remains a complex and poorly understood clinical entity [5]. Due to its rarity, no standardized treatment guidelines currently exist for adult PCNSNB. Management strategies are generally based on a limited number of case reports and adapted from pediatric high-risk treatment protocols [4]. By presenting a suspected case of primary CNS neuroblastoma in an adult, we aim to contribute to the limited literature and emphasize the importance of integrated diagnostic approaches.

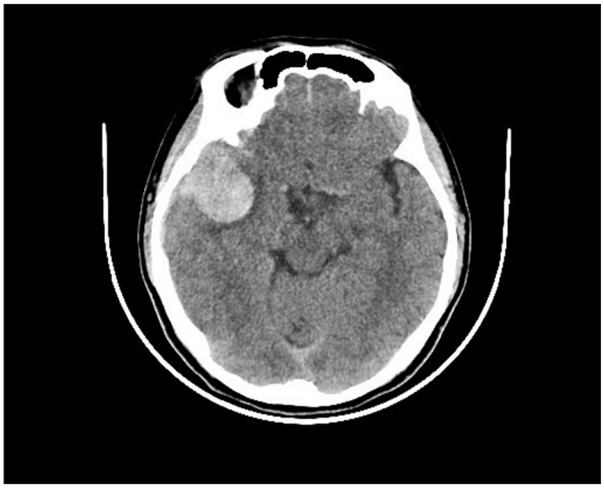

Figure 1. Non-contrast brain computed tomography showed a hemorrhagic mass in the right temporal lobe.

Case Report

A 32-year-old woman with an unremarkable medical history presented to the emergency department for management of a severe holocranial headache that had progressively worsened over the preceding 3 weeks. She described the pain as constant, severe, and unresponsive to conventional over-the-counter analgesics, although she had taken maximum recommended doses of paracetamol. She reported no recent trauma, fever, visual disturbances, or notable changes in personality or cognitive function at symptom onset. The patient was alert and oriented during physical and neurological examination. Fundoscopic examination showed no evidence of papilledema, and motor and sensory functions were intact. Initial laboratory investigations, including a complete blood count, comprehensive metabolic panel, coagulation profile, and basic inflammatory markers (erythrocyte sedimentation rate and C-reactive protein), were all within normal limits. The patient subsequently underwent non-contrast brain computed tomography, which revealed a hemorrhagic mass in the right temporal lobe (**Figure 1**).

Next, the patient underwent magnetic resonance imaging (MRI) of the brain with gadolinium contrast enhancement, which revealed a large right temporal lobe mass measuring 31×35×38 mm. The lesion demonstrated substantial internal heterogeneity. Extensive intratumoral hemorrhage was identified as regions of mixed signal intensity on T1- and T2-weighted sequences, accompanied by distinct blooming artifacts on T2*-weighted images suggestive of subacute hemorrhage. The solid components of the mass showed heterogeneous enhancement

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

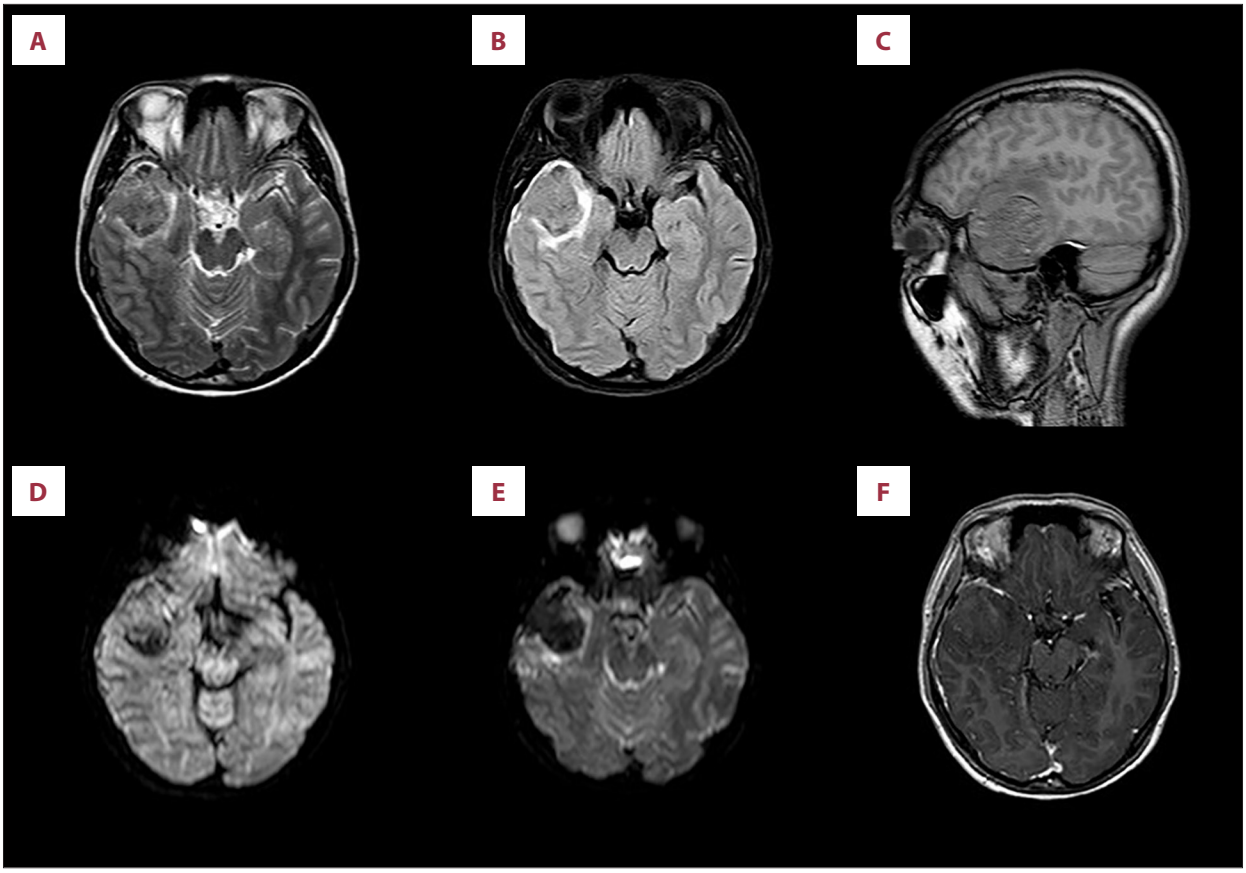

Figure 2. A large heterogeneous mass measuring 31×35×38 mm was centered in the right temporal lobe. The lesion demonstrated mixed signal intensity with extensive surrounding vasogenic edema extending into the adjacent white matter on T2-weighted imaging (**A**) and fluid-attenuated inversion recovery (FLAIR) (**B**) sequences. T1-weighted imaging (**C**) demonstrated mixed signal intensity and mass effect. Areas of restricted diffusion were evident within the solid component, characterized by high signal intensity on diffusion-weighted imaging (**D**) and low apparent diffusion coefficient signal values (**E**). After contrast administration, the solid components demonstrated heterogeneous enhancement on T1-weighted imaging (**F**).

after intravenous gadolinium administration. Extensive vasogenic edema extended into the surrounding white matter, contributing to a pronounced local mass effect and mild leftward midline shift (**Figure 2**).

Subsequent chest and abdominal radiographs, as well as abdominal ultrasonography, showed no evidence of intrathoracic or intra-abdominal lesions. The patient then underwent gross total resection. Histopathological examination revealed a highly cellular tumor composed of sheets and clusters of small, uniform, round cells with dark hyperchromatic nuclei, scant cytoplasm, and a high nuclear-to-cytoplasmic ratio. Notably, the tumor exhibited embryonal features with evidence of neuronal differentiation, including rosette-like structures; no histological evidence of glial differentiation was identified.

Immunohistochemistry was performed to differentiate PCNSNB from other small round blue cell tumors. The tumor cells lacked several key markers, including synaptophysin, cytokeratin (CK), glial fibrillary acidic protein (GFAP), CD20, and Sal-like protein 4 (SALL4). Although the absence of synaptophysin expression is atypical, the presence of well-defined rosette-like structures provided strong morphological evidence supporting a primitive neuronal lineage. In this context, the presumptive classification heavily relied on structural morphology because the immunophenotype alone was insufficient to establish a definitive lineage. Due to institutional resource limitations, advanced molecular testing, including DNA methylation profiling and FOXR2 status evaluation, could not be conducted. Consequently, the tumor was cautiously classified as an embryonal tumor, not otherwise specified (NOS), with neuronal differentiation; PCNSNB remained the leading differential diagnosis (**Figure 3**).

The patient experienced an uneventful postoperative recovery. On postoperative day 7, a follow-up MRI performed prior to discharge showed no evidence of residual tumor and demonstrated fluid collection within the surgical bed (**Figure 4**). Due

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

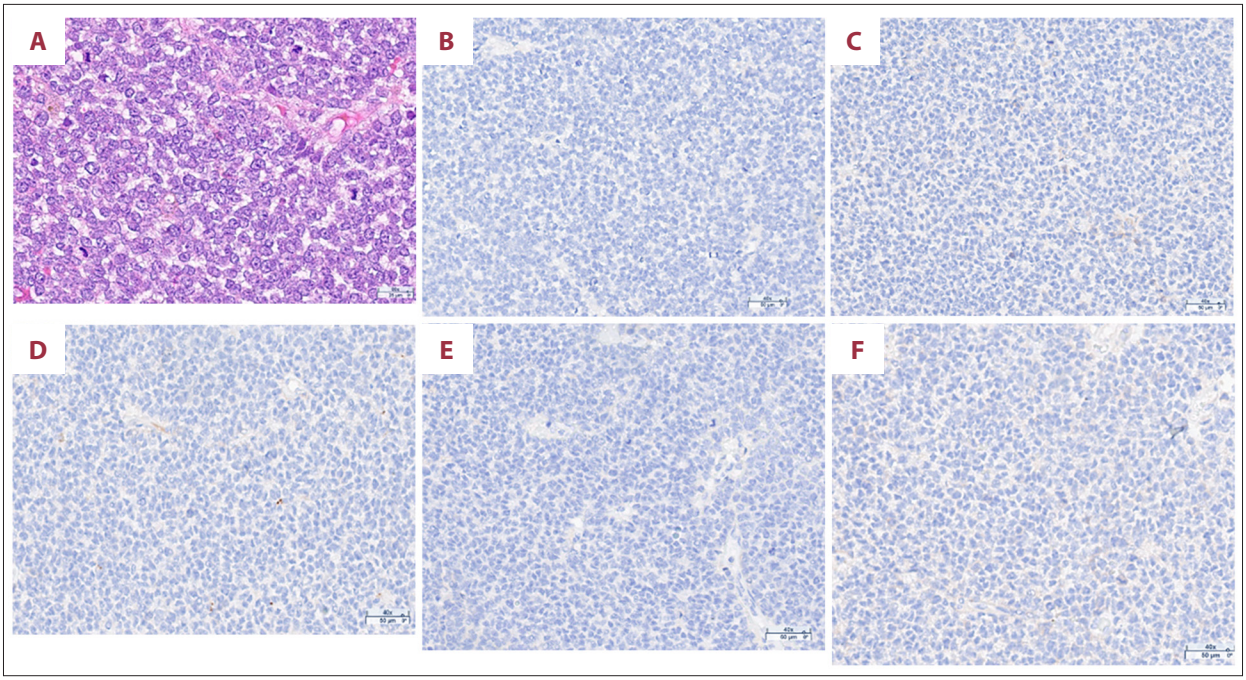

Figure 3. Histopathological findings demonstrated a highly cellular tumor composed of sheets and clusters of small round blue cells characterized by hyperchromatic nuclei, scant cytoplasm, and a high nuclear-to-cytoplasmic ratio, along with rosette-like structures (**A**). Immunohistochemical staining showed the absence of CD20 (**B**), cytokeratin (**C**), glial fibrillary acidic protein (**D**), Sal-like protein 4 (SALL4) (**E**), and synaptophysin (**F**).

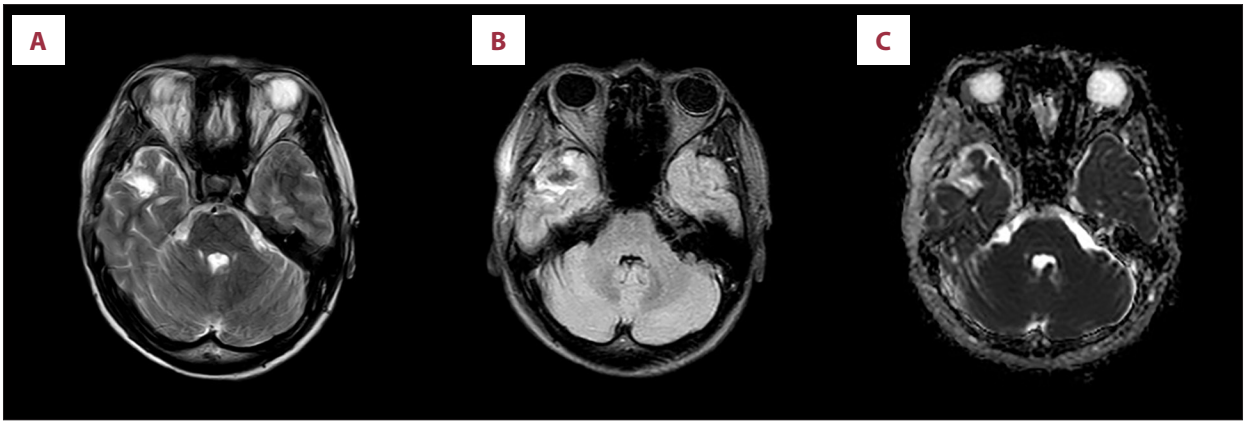

Figure 4. Postoperative scans showed no evidence of residual tumor and fluid collection within the surgical bed on T2-weighted imaging (**A**), fluid-attenuated inversion recovery (FLAIR) (**B**), and diffusion-weighted imaging/apparent diffusion coefficient sequences (**C**).

to the high-grade nature of the tumor, standard adjuvant therapy consisting of chemotherapy and radiotherapy was strongly recommended after gross total resection. Despite extensive counseling regarding the substantial risk of recurrence, the patient declined all recommended adjuvant treatment.

Three months after surgery, the patient returned for a scheduled follow-up visit and reported recurrent mild headaches. Repeat brain MRI confirmed local tumor recurrence at the right temporal surgical bed, measuring 39×22×28 mm. The recurrent lesion appeared isointense on fluid-attenuated inversion recovery (FLAIR) and T2-weighted sequences, whereas it was hypointense on T1-weighted images; homogeneous enhancement was noted, with well-defined margins. Mild restricted diffusion was observed on diffusion-weighted imaging/apparent diffusion coefficient sequences, and no evidence of hemorrhage was identified via T2*-weighted imaging (**Figure 5**). Based on the clinical history, MRI findings, and histopathological features, a provisional diagnosis of recurrent embryonal tumor, NOS, with features highly suspicious for PCNSNB was established.

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

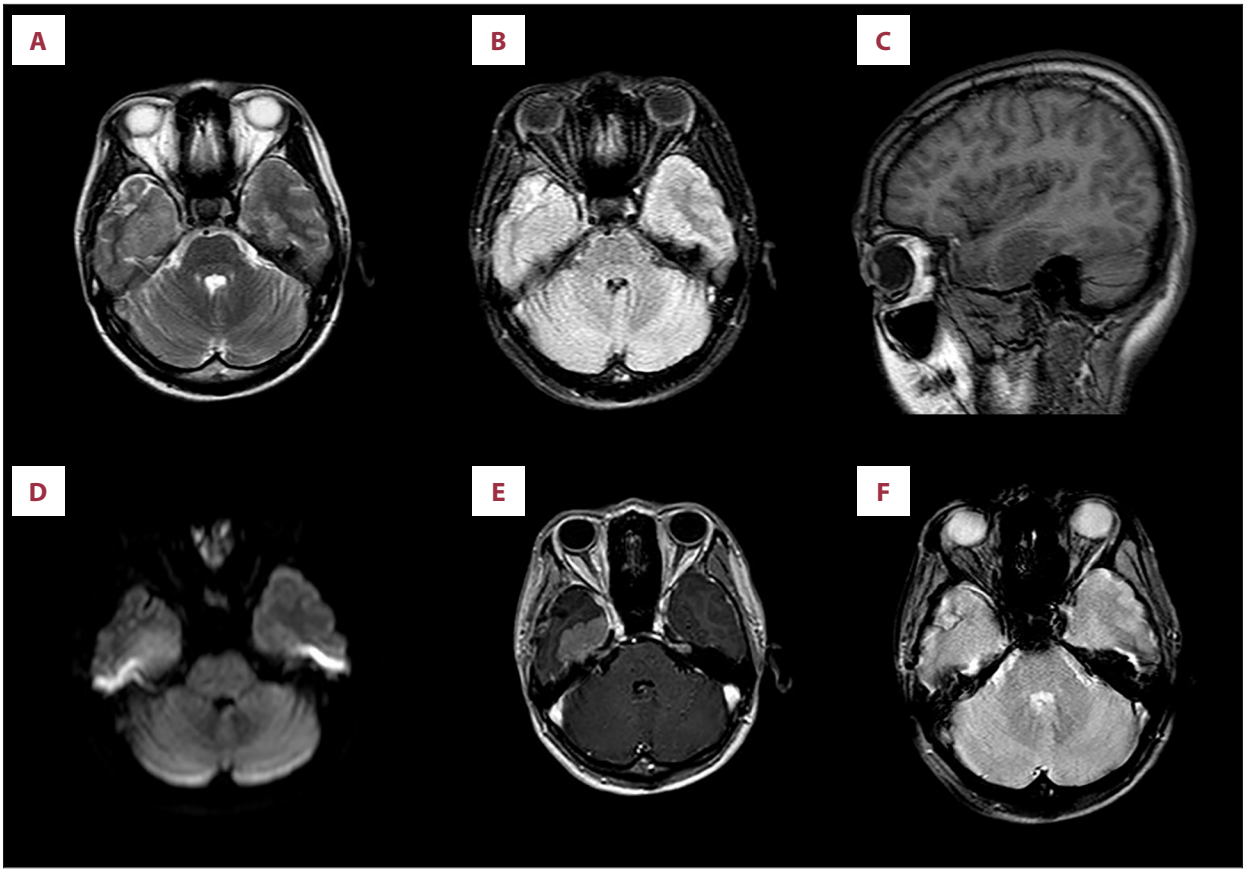

Figure 5. The recurrent lesion appeared isointense on T2-weighted imaging (**A**) and fluid-attenuated inversion recovery (FLAIR) (**B**), whereas it was hypointense on T1-weighted imaging (**C**); mild restricted diffusion was noted on diffusion-weighted imaging/apparent diffusion coefficient sequences (**D**). The lesion exhibited homogeneous enhancement after contrast administration (**E**). No evidence of hemorrhage was observed on T2*-weighted imaging (**F**).

During this visit, the patient received symptomatic treatment with a combination of vitamins B1, B6, and B12 (Neutri Fore 250 mg), as well as paracetamol 500 mg.

Discussion

PCNSNB is an exceptionally rare malignancy, particularly in adults, representing a very small proportion of primary brain tumors [5]. Neuroblastoma in adults is itself exceedingly uncommon, with an estimated incidence of fewer than 1 per 10 million adults annually, making PCNSNB in this population an exceptionally rare clinical entity. Primary cerebral neuroblastoma occurs sporadically in adults; a limited number of cases have been reported in the literature, underscoring its rarity. In 1990, Davis et al conducted a comprehensive study of 12 cases, including 7 adult patients, thereby establishing an early clinicopathological and imaging framework for PCNSNB [6]. Berger et al later performed a retrospective analysis involving patients up to 26 years of age and highlighted the tumor's variable yet aggressive clinical behavior [7].

Recent case reports suggest that PCNSNB can mimic other intracranial tumors. For example, Huynh et al described an adult case of primary CNS neuroblastoma that radiographically resembled a trigeminal schwannoma [8]. Similarly, Singh et al reported an atypical presentation in a 25-year-old woman with a right frontal lesion initially suggestive of hemangiopericytoma [9]. The present case is consistent with previous reports describing supratentorial, intra-axial tumors in adults. This suspected adult-onset primary CNS neuroblastoma illustrates the substantial clinical and diagnostic differences from its more typical pediatric counterpart. Given the rarity of such cases, our report contributes valuable information to the limited literature, particularly regarding the diagnostic challenges and aggressive nature of embryonal tumors in adults.

Historical reports involving both pediatric and adult populations consistently indicate a predilection for supratentorial locations, particularly in large cerebral lobes such as the temporal and parietal regions, consistent with the right temporal lobe involvement observed in our patient [8]. This presentation substantially differs from medulloblastoma, the most common

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

embryonal tumor of the CNS, which typically arises in the infratentorial posterior fossa.

Both computed tomography and MRI demonstrated a space-occupying lesion in the right temporal parenchyma with radiological features suggestive of a high-grade malignancy. The pronounced internal heterogeneity evident on T1- and T2-weighted imaging, along with blooming artifacts on T2*-weighted sequences, confirmed substantial intratumoral hemorrhage. These findings suggest rapid tumor growth and necrosis, features commonly associated with high-grade gliomas and embryonal tumors. Furthermore, the solid tumor components exhibited avid, heterogeneous post-contrast enhancement, indicating blood–brain barrier disruption and clinically significant tumor vascularity. Extensive vasogenic edema and midline shift further reflected the aggressive growth pattern and substantial mass effect of the lesion.

Given the above radiographic ambiguities, definitive classification heavily relied on comprehensive histopathological and molecular evaluation. Histopathological examination demonstrated small round blue cells, a characteristic feature of neuroblastoma. Immunohistochemistry was subsequently performed to differentiate PCNSNB from other small round blue cell tumors. The tumor cells lacked several key markers, such as CK, ruling out metastatic carcinoma; GFAP, ruling out glial differentiation such as glioblastoma; CD20, ruling out B-cell lymphoma; and SALL4, ruling out germ cell tumor components.

Although the histological findings strongly suggested neuronal differentiation through the presence of rosette-like structures, the absence of synaptophysin expression presented a diagnostic challenge. However, this finding does not entirely exclude neuroblastoma within an appropriate morphological context. Integration of the clinical, radiological, and histopathological findings was essential to establish a coherent diagnostic pathway. Whereas the rapidly enlarging hemorrhagic temporal mass initially suggested a high-grade glioma or metastatic lesion, histopathology revealed small round blue cells with rosette-like structures, thereby excluding typical gliomas. Furthermore, the absence of GFAP, CK, CD20, and SALL4 expression systematically ruled out glioblastoma, metastatic carcinoma, lymphoma, and germ cell tumors. Despite the lack of synaptophysin expression and molecular confirmation, this process of exclusion strongly supported a provisional classification of embryonal tumor, NOS, with PCNSNB as the leading differential diagnosis.

A major limitation of the present case is the absence of molecular testing. The 2021 WHO Classification of CNS Tumors increasingly incorporates molecular characteristics, including FOXR2 activation, for the definitive classification of CNS neuroblastomas. Because advanced testing methods such as DNA methylation profiling and FOXR2 status evaluation were unavailable at our institution due to resource limitations, the tumor was cautiously classified as an embryonal tumor, NOS, with neuronal differentiation. Therefore, PCNSNB remains a highly suspected entity rather than a definitively confirmed diagnosis.

Current medical literature emphasizes the critical importance of comprehensive neuropathological evaluation for rare CNS embryonal tumors. According to Tauziède-Espariat et al [10] and Gojo et al [11], an integrated diagnostic approach is now considered essential. This strategy combines extensive immunohistochemical profiling with targeted molecular testing, particularly DNA methylation profiling and FOXR2 activation assessment. Such a comprehensive approach is necessary for the definitive diagnosis of rare embryonal malignancies, including FOXR2-activated CNS neuroblastomas, and for accurately distinguishing them from a broad range of morphological mimics.

Regardless of the specific molecular subgroup, adult CNS embryonal tumors generally exhibit an aggressive clinical course and poor prognosis [12]. The current standard of care typically consists of maximal safe gross total resection followed by intensive multimodal adjuvant therapy, including radiotherapy and chemotherapy [8]. Recurrence rates after gross total resection remain high, particularly in the absence of adjuvant treatment, as demonstrated by the rapid recurrence 3 months after surgery in the present case. Despite successful gross total resection and extensive counseling regarding the high-grade nature of the tumor, the patient declined all recommended adjuvant therapies. This outcome further supports the growing consensus that surgery alone is insufficient for managing high-grade CNS embryonal malignancies and underscores the critical need for prompt, comprehensive multimodal treatment to achieve meaningful disease control [13].

Conclusions

This report describes a highly uncommon case strongly suggestive of adult-onset primary CNS neuroblastoma presenting atypically as a rapidly progressive hemorrhagic temporal lobe lesion. This case emphasizes the critical role of comprehensive pathological and molecular analyses in achieving accurate classification of rare embryonal tumors. Furthermore, it highlights the serious diagnostic challenges encountered in resource-limited settings. In the absence of advanced molecular testing modalities, definitive diagnostic confirmation may not be achievable, warranting a cautious and systematic approach to tumor classification and therapeutic decision-making.

Acknowledgments

We thank the patient for her participation and contribution to advancing clinical knowledge. We also acknowledge the

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]

anonymous editorial reviewers for their expertise and valuable contributions to the final version of this manuscript.

Department and Institution Where Work Was Done

Department of Radiology and Department of Pathology, Bach Mai Hospital, Hanoi, Vietnam.

Patient Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

References:

1. Louis CU, Shohet JM. Neuroblastoma: Molecular pathogenesis and therapy. Annu Rev Med. 2015;66(1):49-63
2. Louis DN, Perry A, Wesseling P, et al. The 2021 WHO classification of tumors of the central nervous system: A summary. Neuro Oncol. 2021;23(8):1231-51
3. Chen Z, Gao J, Sun J, et al. Aminoacylase 1 (ACY-1) mediates the proliferation and migration of neuroblastoma cells in humans through the ERK/transforming growth factor β (TGF-β) signaling pathways. Med Sci Monit. 2020;27:e928813
4. Yadav K, Sharma P, Singh D, Mishra V. Primary central nervous system neuroblastoma mimicking a meningioma: A case report. J Postgrad Med. 2024;70(3):178-81
5. Mossé YP, Deyell RJ, Berthold F, et al. Neuroblastoma in older children, adolescents and young adults: A report from the International Neuroblastoma Risk Group project. Pediatr Blood Cancer. 2014;61(4):627-35
6. Davis PC, Wichman RD, Takei Y, Hoffman JC. Primary cerebral neuroblastoma: CT and MR findings in 12 cases. Am J Neuroradiol. 1990;11(1):115-20
7. Berger MS, Edwards MSB, Wara WM, et al. Primary cerebral neuroblastoma: Long-term follow-up review and therapeutic guidelines. J Neurosurg. 1983;59(3):418-23
8. Huynh BQ, Hung ND, Khuong NH, et al. A rare case of a primary central nervous system neuroblastoma mimicking a trigeminal schwannoma in an adult. Radiol Case Rep. 2023;18(8):2697-703
9. Singh S, Singh N, Baliyan J. A unique case of primary central nervous system neuroblastoma mimicking as hemangiopericytoma in an adult. Radiol Case Rep. 2025;20(4):2029-34
10. Tauziède-Espariat A, Figarella-Branger D, Métais A, et al. CNS neuroblastoma, FOXR2-activated and its mimics: A relevant panel approach for work-up and accurate diagnosis of this rare neoplasm. Acta Neuropathol Commun. 2023;11(1):43
11. Gojo J, Kjaersgaard M, Zezschwitz BV, et al. Rare embryonal and sarcomatous central nervous system tumours: State-of-the art and future directions. Eur J Med Genet. 2023;66(1):104660
12. Lu X, Zhang X, Deng X, et al. Incidence, treatment, and survival in primary central nervous system neuroblastoma. World Neurosurg. 2020;140:e61-72
13. Mishra R, Agrawal A. Primary central nervous system neuroblastoma: An enigmatic entity. In: Cianci P, Restini E, Agrawal A, editors. Pheochromocytoma, Paraganglioma and Neuroblastoma. IntechOpen; 2021

Indexed in: [PMC] [PubMed] [Emerging Sources Citation Index (ESCI)] [Web of Science by Clarivate]