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International Journal of Pediatrics and Adolescent Medicine

journal homepage: <http://www.elsevier.com/locate/ijpam>

Case report

A rare cerebellar vermis high-grade neuroepithelial tumor: Radiological-pathological correlation

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ARTICLE INFO

Article history:

Received 17 July 2020

Received in revised form

19 October 2020

Accepted 16 December 2020

Available online 19 December 2020

Keywords:

Embryonal tumor

High-grade neuroepithelial tumor

Magnetic resonance imaging

ABSTRACT

Neuroepithelial tumors, formerly known as primitive neuroectodermal tumors of the central nervous system, are reclassified under embryonal tumors in the 2016 WHO Classification of Tumors of the Central Nervous System. The tumor has two known genetic alterations: HGNET-MN1 and HGNET-BCOR. Previously, radiological features of the tumor have been reported as large, intra-axial lesions in the cerebral or cerebellar hemisphere, which presents mild adjacent edema. Here, we report the first case of high-grade neuroepithelial tumor not elsewhere classified (HGNET-NEC) arising from the cerebellar vermis, demonstrating good outcomes in clinical follow-up when compared with previously known types.

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1. Introduction

High-grade neuroepithelial tumors (HGNET) are newly described entities with two known genetic alterations: HGNET-MN1 and HGNET-BCOR [1,2].

The previously reported tumors presented intra-axial, large and well-demarcated solid lesions, demonstrating necrosis, with minimal or no perilesional edema in the cerebrum or cerebellar hemisphere [1,2].

In our current case, the location of the tumor at the craniocervical junction was peculiar as well as the pathological findings of HGNET-not elsewhere classified (HGNET-NEC).

2. Case report

A 4-year-old female presented to our emergency department

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Peer review under responsibility of King Faisal Specialist Hospital & Research Centre (General Organization), Saudi Arabia.

<https://doi.org/10.1016/j.ijpam.2020.12.004>

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complaining of progressive unsteady gait for one month along with frequent falls. Clinically, she presented left-sided upper and lower limb weakness 4/5 with hyperreflexia and a positive Babinski sign on the ipsilateral side.

Unenhanced computed tomography performed overnight showed a midline hyperdense mass in the posterior fossa, with a mass effect on the brain stem. However, no hydrocephalus was observed.

On the following day, magnetic resonance imaging (MRI) of the brain and whole spine, with and without contrast, was performed according to our department protocol, revealing a well-circumscribed midline lesion arising from the inferior vermis, extending into the craniocervical junction.

The lesion showed intermediate signal intensity on T1WI (Fig. 1A), with markedly dark peripheral signal intensity on T2WI and central necrosis (Fig. 1B). The lesion showed a solid pattern of peripheral enhancement (Fig. 1C) and minimal restricted diffusion (Fig. 1D and E). Extensive edema was observed in the adjacent part of the medulla, which extended to the cervical spine. No spinal drop metastasis was observed.

The extremely low signal on T2WI was assumed to be related to high cellular impaction or high collagen/fiber contents; the tumor differed from desmoplastic medulloblastoma as it showed minimal diffusion restriction. Our differential diagnosis included high-grade glioma or anaplastic ependymomas.

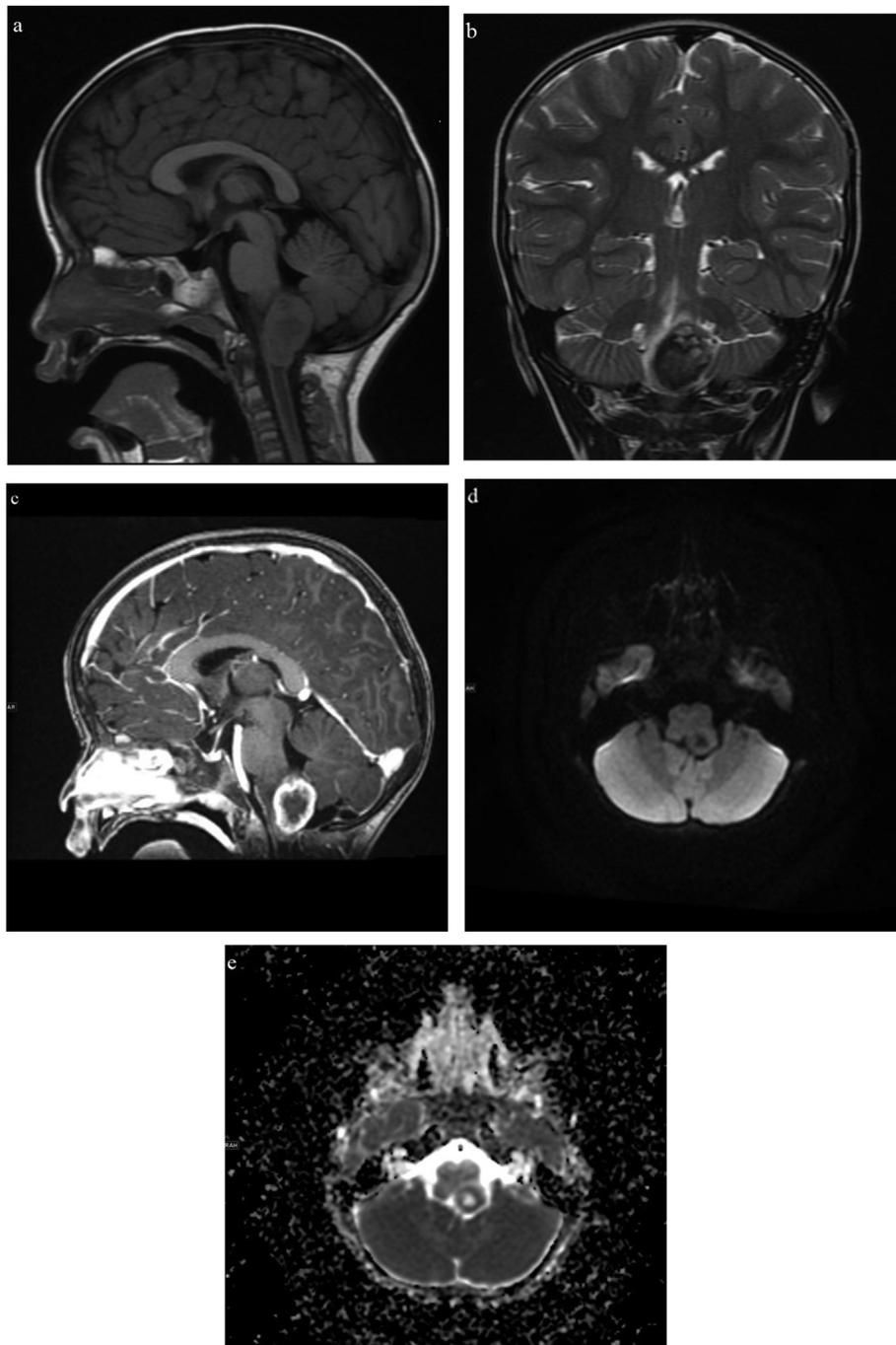


Fig. 1. A. Sagittal T1WI demonstrated a lesion in the inferior vermis with intermediate signal intensity on T1WI B. Axial T2WI demonstrated the lesion with markedly dark peripheral signal intensity and central necrosis and extensive edema C. Sagittal T1WI post contrast image showed a solid pattern of peripheral enhancement D. Axial DWI, and E. ADC the lesion exhibited minimal restricted diffusion.

Histopathological sections stained using hematoxylin & eosin were examined, revealing collagen-rich, low to moderately cellular neuroepithelial tumors. The tumor cells were arranged in a linear profile with small nests. Necrosis and focal endothelial proliferation were observed. The tumor cells were round/oval and hyperchromatic, with a fair amount of amphophilic cytoplasm. Additionally, some tumor cells with nuclear grooves were noted. The tumor cell nucleoli were not prominent. Frequent mitosis was observed in cellular areas, with a few entrapped neurons within the tumor (Fig. 2A, B, and 2C).

Additionally, we performed reticulin staining, and reticulin fibers were found to encircle individual cells and small tumor nests (Fig. 2D).

The tumor cells were immunopositive for synaptophysin (weak and perinuclear), vimentin, S100, EMA (rare dot-like staining), and immunonegative for glial fibrillary acidic protein (GFAP), Neu-N, neurofilament protein (NFP), chromogranin, cytokeratin CAM5.2, HMB45, Melan A, CD34, and CD68. INI-1 immunostaining was normal (retained). Ki-67 immunolabeling was estimated to be high (up to 40%) (Fig. 2E).

Given the unusual morphology, the case was transferred to St. Jude Children's Research Hospital for a second expert opinion. Additional immunostaining and molecular studies were performed.

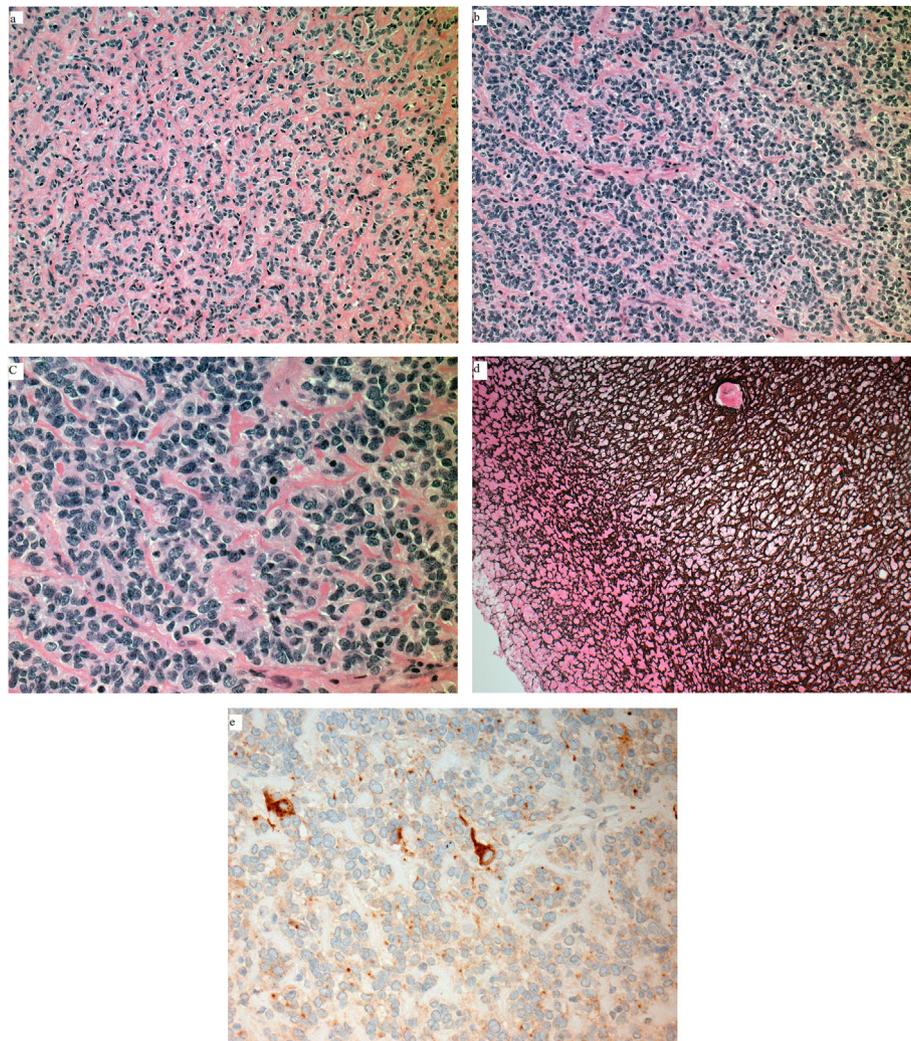


Fig. 2. Hematoxylin and eosin stains 100× **A.** H&E 200× **B.** and H&E 400× **C.** showed that frequent mitosis was observed in cellular areas, with a few entrapped neurons within the tumor. **D.** Reticulin stain showed reticulin fibers were found to encircle individual cells and small tumor nests. **E.** Immunohistochemistry of the tumor cells Ki-67 immunolabeling was positive and estimated to be as high as 40%.

Immunoreactivity (IR) for CD99 characterized all tumor cells, with some demonstrating IR for GFAP and/or OLIG2, and rare cells expressing microtubule-associated protein-2 (MAP-2). Furthermore, a variable, but generally weak, IR for BCOR was observed. No IR for NFP, CD34, NUTM1, or cytokeratins was documented.

Based on immunofluorescence in situ hybridization (immunofISH), no rearrangement of EWSR1, CIC, or MN1 was observed.

Targeted next-generation sequencing (NGS) was performed on DNA extracted from tissue containing neoplastic cells to evaluate a panel of genes relevant to pediatric CNS tumors. No pathogenic or likely pathological variants were detected.

This unusual neuroepithelial tumor presented challenging morphology with dense hyalinization, reminiscent of that observed in some astroblastomas. Although retained in the 2016 WHO classification, astroblastoma is a diagnosis now aligned with the CNS HGNETs containing MN1 alterations or extremely rarely, BCOR alterations. Molecular testing (iFISH and NGS) results failed to indicate MN1, BCOR, or any other alterations. The tumor considered as HGNET-NEC.

The patient underwent a gross total excision within a few days of presentation, using an occipital craniotomy approach. Total tumor resection was performed, and the tissue was observed on an

immediate postoperative MRI scan. The patient developed respiratory symptoms and weakness. Therefore, the patient did not receive any chemotherapy or radiation therapy. Follow-up with serial MRI was performed every 2–3 months, demonstrating no evidence of recurrence.

The patient showed excellent respiratory and neurological recovery and was discharged in stable condition, with normal breathing and almost normal neurological status. The total duration of follow-up was 15 months with no adjuvant treatment.

3. Discussion

The previously known primitive neuroectodermal tumors of the central nervous system (CNS-PNET) terminology was replaced by embryonal tumors in the 2016 World Health Organization Classification of Tumors of the Central Nervous System [3–5]. It has been reclassified into four new, molecularly defined subgroups: CNS neuroblastoma with FOXR2 activation, CNS Ewing sarcoma family tumor with CIC alteration, CNS HGNET with MN1 alteration, and CNS HGNET-BCOR. However, a minority of CNS-PNETs fail to be classified and are currently considered as CNS embryonal tumors, not otherwise specified (NOS) [4].

Recently, HGNETs of the CNS have been described in the pediatric age group. The tumor demonstrates no gender predilection and may arise from the cerebrum or cerebellum. The age group of the tumor varies; however, most patients are below 5 years of age [1,2,6]. Clinically, patients present with variable symptoms, including headaches, seizures, or focal neurological deficits.

Tauziède-Esparia et al. [1] have observed that CNS HGNET-MN1 was predominantly present in girls, mainly supratentorial tumors. Radiologically, all our tumors were large, well-demarcated solid lesions, demonstrating necrosis with minimal or no perilesional edema.

A study by Ferris S [2] has shown that CNS HGNET-BCOR is predominantly detected in girls, with tumors present in the cerebral or cerebellar hemisphere as a well-circumscribed, large mass with associated mass effect. Several tumors demonstrated central areas of necrosis or blood products, with variable contrast enhancement. Diffusion-weighted imaging frequently showed reduced diffusion, suggestive of neoplasms that demonstrated high cellularity.

Our case demonstrated CNS HGNET-NEC, with a peculiar location at the inferior vermis/cranio-cervical junction. The lesion was well-circumscribed with central necrosis; however, it showed a significant mass effect on the adjacent part of the brain stem. Additionally, reduced diffusion with contrast enhancement was noted.

In a previous study, all patients underwent gross total resection, similar to our patient, undergoing chemotherapy with or without radiotherapy, presenting poor overall prognosis in general, and limited follow-up data.

4. Conclusion

CNS HGNET is an embryonal tumor, recently classified into two groups with MN1 and BCOR, which presents a poor prognosis. However, our case showed HGNET-NEC, a new category that, to our knowledge, has not been previously reported. This tumor should be considered in our differential diagnosis for the cranio-cervical junction location. Furthermore, this tumor presented a superior prognosis during our short-term follow-up.

Ethical Statement

Hereby, I **Amna Kashgari, MD** consciously assure that for the manuscript “A rare cerebellar vermis high-grade neuroepithelial tumor: Radiological-pathological correlation” the following is fulfilled:

1) This material is the authors' own original work, which has not been previously published elsewhere.

2) The paper is not currently being considered for publication elsewhere.

3) The paper reflects the authors' own research and analysis in a truthful and complete manner.

4) The paper properly credits the meaningful contributions of co-authors and co-researchers.

5) The results are appropriately placed in the context of prior and existing research.

6) All sources used are properly disclosed (correct citation). Literally copying of text must be indicated as such by using quotation marks and giving proper reference.

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I agree with the above statements and declare that this submission follows the policies of Solid State Ionics as outlined in the Guide for Authors and in the Ethical Statement.

Date: July 17, 2020.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgment

We would like to thank Dr. David Ellison (Neuropathologist) at St. Jude Children's.

References

- [1] Tauziède-Esparia A, Pagès M, Roux A, Siegfried A, Uro-Coste E, Nicaise Y, et al. Pediatric methylation class HGNET-MN1: unresolved issues with terminology and grading. *Acta neuropathologica communications* 2019 Dec 1;7(1):176.
- [2] Ferris SP, Velazquez Vega J, Aboian M, Lee JC, Van Ziffle J, Onodera C, et al. High-grade neuroepithelial tumor with BCOR exon 15 internal tandem duplication—a comprehensive clinical, radiographic, pathologic, and genomic analysis. *Brain Pathol* 2020 Jan;30(1):46–62.
- [3] Sturm D, Orr BA, Toprak UH, Hovestadt V, Jones DT, Capper D, et al. New brain tumor entities emerge from molecular classification of CNS-PNETs. *Cell* 2016 Feb 25;164(5):1060–72.
- [4] Louis DN, Perry A, Reifenberger G, Von Deimling A, Figarella-Branger D, Cavenee WK, et al. The 2016 World Health Organization classification of tumors of the central nervous system: a summary. *Acta Neuropathol* 2016 Jun 1;131(6):803–20.
- [5] Johnson DR, Guerin JB, Giannini C, Morris JM, Eckel LJ, Kaufmann TJ. Updates to the WHO brain tumor classification system: what the radiologist needs to know. *Radiographics* 2016;37(7):2164–80. 2017 Nov.
- [6] Al-Battashi A, Al Hajri Z, Perry A, Al-Kindi H, Al-Ghathith I. A cerebellar high-grade neuroepithelial tumour with BCOR alteration in a five-year-old child, a case report. *Sultan Qaboos University Med J* 2019;19(2):e153–6. <https://doi.org/10.18295/squmj.2019.19.02.012>.