International Cancer Conference Journal
https://doi.org/10.1007/s13691-024-00726-x

CASE REPORT - PATHOLOGY

Intraventricular ganglioneuroblastoma: an uncommon location for a rare tumour in a young adult with review of literature

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Received: 3 July 2024 / Accepted: 10 September 2024

Abstract

Ganglioneuroblastoma (GNB) is a rare tumour of neuroectodermal origin consisting of a varying proportion of neuroblasts and ganglion cells. GNB arises from sympathoadrenal tissue usually affecting young children. Very few cases of brain GNB have been reported in the literature. To the best of our knowledge, this is the first-ever reported case of GNB at an intraventricular location in young adults. Because of the rarity of the neoplasm, it might be confused with other tumours of intraventricular location both in radiology and histopathology. We report a very rare case, which was surgically operated on and sent for a frozen section followed by a routine report. The final diagnosis was made by Immunohistochemistry (IHC) study. The patient was treated with further radiotherapy.

Keywords Intraventricular mass · Foramen of Monro · WHO grading · Embryonal tumours · Ganglioneuroblastoma · Synaptophysin · Radiotherapy

Introduction

Ganglioneuroblastoma (GNB) originates from primordial neural crest cells and may occur wherever sympathetic tissue prevails, including the adrenal gland, posterior mediastinum, neck and retroperitoneum. GNB affecting the brain are an uncommon tumour. Most cases are seen in young children (<2 years of age). Older children and young adults are rarely affected [1]. Very few cases of intracranial GNB have been reported to date. According to the World Health Organization (WHO) classification of Tumours of Central Nervous System (CNS), GNB is included in embryonal tumours. GNB is defined histologically by a combination of primitive small embryonal cells and large ganglion cells [2].

The signs and symptoms of cerebral neuroblastic tumours are associated with the location where they originate. These may include seizures, changes in awareness, elevated intracranial pressure, altered consciousness and impaired motor function. Typically, these tumours are found in the cerebral hemisphere, although there have been documented instances of them occurring in the pineal gland and the spinal cord [1].

At any uncommon site, diagnosis of GNB is possible only by microscopic examination. Here, we summarize the unique case of GNB located within the third ventricle in 22 years old male including clinical features, radiological findings on MRI (magnetic resonance imaging), histopathological diagnosis with immunohistochemistry (IHC) and treatment of intraventricular GNB along with a review of the literature.

Case report

A 22-year-old young adult male presented with a sudden change in consciousness with complaints of headache, diminished vision, and weakness in both arms and legs for 3 months. Significant past or family history was absent. On MRI, large T2 hypo to isointense, FLAIR isointense and T1 isointense lesion, measuring 28×28 mm is noted compressing on the foramen of Monro and situated in the body of left lateral ventricle causing obstructive hydrocephalus with

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Published online: 18 September 2024

dilatation of left lateral ventricle and compression of the right lateral ventricle. The mass shows diffuse restriction. A radiological diagnosis of central neurocytoma was suggested (Fig. 1, MRI findings).

The patient was operated on for frontal craniotomy with transcortical middle frontal gyrus approach and small tissue was sent for intraoperative frozen section examination. Squash smears showed diffusely arranged medium-sized cells having enlarged round nuclei with occasional nucleoli and many small-sized nuclei in the background. Intraoperative diagnosis of low-grade glioneuronal tumour was made. The patient underwent total surgical resection of the mass and the remaining tissue was sent for routine histopathological examination. Sections show predominantly diffuse proliferation of large ganglion-like cells. Few binucleated and multinucleated cells were also seen. Conspicuous thin-walled blood vessels were present throughout the lesion. Foci of small immature cells having round uniform nuclei with increased mitosis were seen. Necrosis or microvascular proliferation was not seen. Diagnosis of a high-grade glioneuronal tumour was made on formalin-fixed sections (Fig. 2).

Further, IHC showed positivity with chromogranin A, synaptophysin, CD34 and ATRX. Background reactive astrocytes show focal positivity with Olig-2 and GFAP. Ki67 stains 8–10% in small neuroblastic and large ganglion cells. Tumour cells are negative for BRAF, IDH-1, EMA and LIN-28. S100 stains for background neuropil (Fig. 3).

Based on morphological, radiological and IHC findings, the tumour was diagnosed as Ganglioneuroblastoma, WHO Grade 4. On follow-up, postoperative MRI revealed no residual tumour. Post-resection radiotherapy treatment was given.

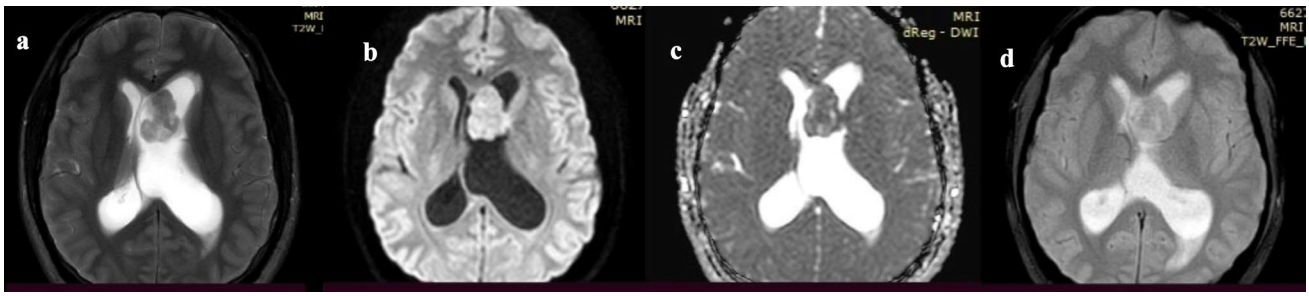

Fig. 1 MRI findings: mass lesion in the left-sided foramen of Monro and appears isointense on T2 sequence **a**, with diffusion restriction **b**, and significant drop on ADC map **c**. No evidence of any blooming on GRE sequence **d**

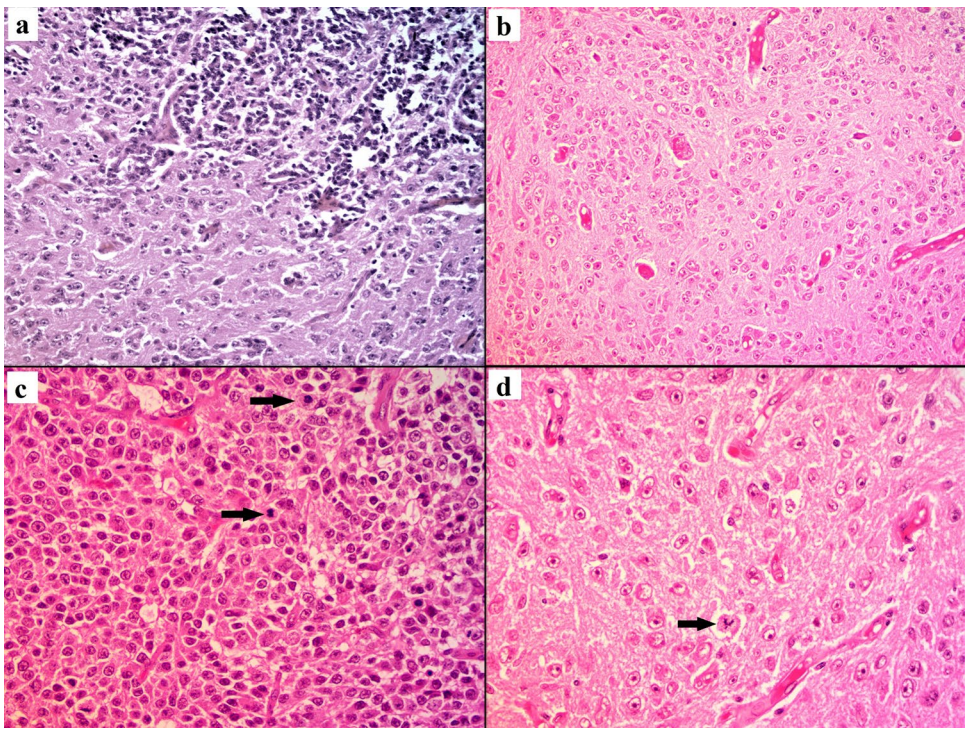

Fig. 2 Histopathology of Ganglioneuroblastoma: **a** Biphasic pattern is revealed- upper part showing small neuroblastic cells and lower part showing large ganglionic cells. (HE, 20x) **b** Diffusely spread large ganglion cells against the neuropil background with intervening blood vessels. (HE, 20x) **c** Neuroblastic area shows closely packed cells with round to oval hyperchromatic nuclei and increased mitosis. (arrow) (HE, 40x) **d** Ganglion cells having large round eccentric vesicular nuclei, central prominent nucleoli and eosinophilic cytoplasm. Moderate pleomorphism is seen with many binucleated cells. The background is fibrillary with occasional mitosis (arrow). (HE, 40x)

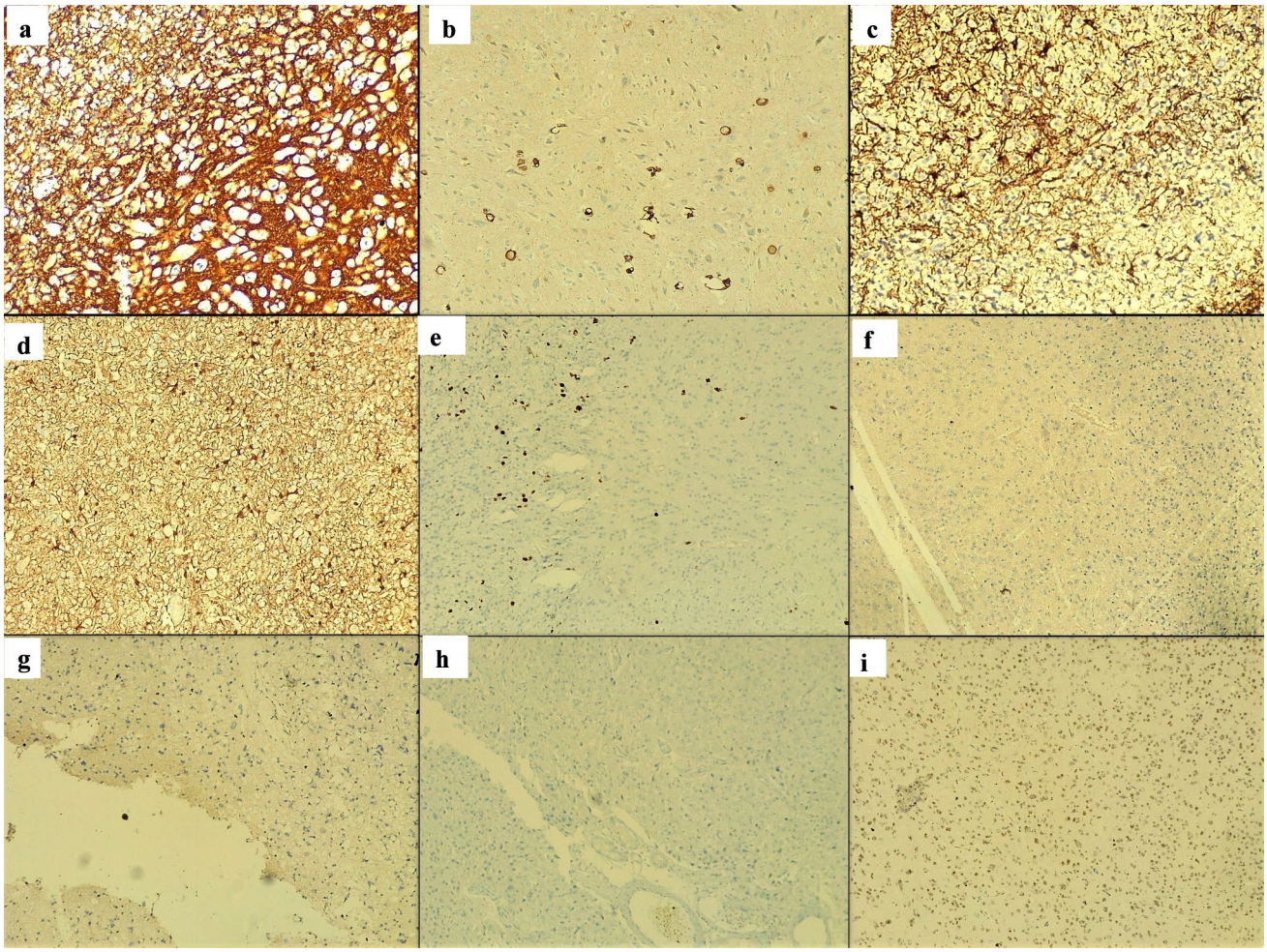

Fig. 3 Immunohistochemistry. **a** Diffuse positive Synaptophysin staining in large ganglion cells and small neuroblastic cells. (40x). **b** Strong Positive Chromogranin in large ganglion cells and small cells. (40x). **c** GFAP positive background reactive astrocytes. (20x) **d** S100 positive background neuropil. (10x) **e** Tumour cells showing 8–10% MIB-1 index. (10x) Tumour cells Non-immunoreactive for **f** IDH-1, **g** BRAF, and **h** LIN28. **i** ATRX is retained showing nuclear positivity in about 80% of cells. (10x)

Discussion

GNB arises due to developmental malformation of neuroblasts or neural crest cells. GNB is identified by the International Neuroblastoma Pathology Committee as a part of neuroblastoma subgroups. A GNB contains both mature ganglion cells and malignant neuroblastoma in the same tumour. The degree of differentiation of GNB lies between that of highly malignant neuroblastoma and benign ganglioneuroma. GNB is usually seen in infants and young children but, is very rarely seen in older children and young adults [3].

Through the search of the literature using NLM (National Library of Medicine) and PubMed database, only a few cases of intracranial GNB have been reported. The earliest reported case of intracranial GNB by Durity et al. in 1968 shows cerebellum involvement [4]. Pizzolato et al. studied the largest case series of 12 cases on intracranial GNB [5]. Schipper et al. reported two cases of adult-onset cerebral GNB [6]. Rest of the cases were reported as a case report. A case of paediatric cerebral GNB in a 4-year-old girl, presented with acute onset headache and transient blindness and was treated by surgical resection followed by chemo-radiation [7]. A rare case report of GNB of the brain with spinal fluid metastasis was recorded [8]. Other intracranial sites reported were each case of cerebellum, hippocampus, and cerebellopontine angle [1, 3, 9]. Mirza et al. reported a case of paediatric supratentorial GNB in a 4-year-old male present with declining mental status [10]. A rare case of suprasellar GNB mimicking craniopharyngioma was documented in a 9 year-old female child showing partially calcifying solid-cystic mass treated with subtotal surgical resection and intensive chemo-radiotherapy [11]. De Frutos et al. described a case of leptomeningeal GNB in a 5-year-old-boy

showing a posterior fossa lesion on CT (computed tomography) scan with focal intraventricular lesions suggestive of metastasis [12] (Table 1).

GNB is a rare tumour usually confirmed on microscopic examination. So, on MRI, it is not easy to differentiate intraventricular GNB from other intraventricular neoplasms. MRI findings of ventricular neoplasm are diverse because of the variability of tissue in the brain, which gives rise to such tumours. Differential diagnoses of ventricular mass on imaging are ependymoma, subependymoma, central neurocytoma, low-grade astrocytoma, subependymal giant cell astrocytoma (SEGA), choroid plexus papilloma, meningioma, primitive neuroectodermal tumour and rarely other embryonal tumours [1, 13].

In the case of GNB, MRI often reveals features of low-grade glioma with clearly defined margins and exhibiting hyper-signal lesions on diffusion-weighted imaging (DWI) and poor apparent diffusion coefficient (ADC) value [3]. Our case presented with a mass lesion at the left foramen of Monroe on MRI with an isointense lesion on T2 and significantly low ADC value.

Microscopically, GNB shows primitive embryonal cells and ganglion cells present in varying proportions [2]. Differential diagnosis with other tumours originating within the ventricle and showing such large ganglionic cells includes central neurocytoma (CN) with extensive ganglionic differentiation, ganglioglioma, anaplastic ganglioglioma, gangliocytoma and SEGA. The central neurocytoma with ganglionic differentiation may be easily confused because of its intraventricular location, but it usually shows a low ki-67 index (< 2%), whereas the present case shows high ki-67 (8–10%). Attachment to septum pellucidum seems to be a feature of CN, which was absent in this case. Ganglioglioma usually occurs in the temporal lobe, showing neuronal and glial elements with dysplastic neurons. IHC further confirms the dual component. Other features are eosinophilic granular bodies, dystrophic calcification and perivascular lymphoid aggregates. The submitted case lacks dual glio-neuronal elements. Gangliocytoma displays groups of dysplastic ganglion cells with low density. Unlike gangliocytoma, present GNB shows ganglion cells in a diffuse pattern without dysplasia. SEGA is a WHO Grade 1 tumour usually associated with tuberous sclerosis with origin near the foramen of Monro, as in the present case. Albeit, this case did show neither subependymal nodules nor signs related to tuberous sclerosis. Histopathology of SEGA shows large cells resembling gemistocytic astrocytes or ganglion cells with focal streaming. Unlike GNB, SEGA on IHC demonstrates mixed glioneuronal phenotype with GFAP, S100, synaptophysin positivity and low MIB1 index [2].

Extra ventricular GNB is usually treated with subtotal resection followed by chemotherapy and radiotherapy [11]. This patient of intraventricular GNB underwent total surgical resection. After the final pathological diagnosis, the patient was treated with radiation therapy (60 Gy in 30 fractions).

Conclusion

This is the first-ever case of GNB of the lateral ventricle in a young adult, to be reported in global literature. This rare tumour should be kept in mind at unusual locations of the brain including the intraventricular site, particularly when it shows a biphasic population of small embryonal and large ganglion cells. Definite diagnosis as GNB, Grade 4 using IHC is of vital importance as it rules out low-grade tumours with morphologic similarities and helps in further management using radiotherapy treatment.

Table 1 A literature review of published cases of ganglioneuroblastoma (GNB)

Sr No	Author	Year	Article details	Patient Age (Years)	Location
1	Durity et al. [4]	1968	A case report involving cerebellum	3 years	Cerebellar
2	Pizzolato et al. [5]	1982	Case series of 12 cases of intracranial GNB	Infants and young adults	Intracranial
3	Schipper et al. [6]	2012	Two cases of cerebral GNB of adult-onset	28 and 42 years	Cerebral
4	Steenberge et al. [7]	2014	A case report of cerebral GNB in 4-year-old girl	4 years	Cerebral
5	Nikonov et al. [8]	1981	A case report of GNB brain with spinal fluid metastasis	–	Brain
6	Soham et al. [9]	1992	A case report of cerebellopontine angle GNB	–	Cerebellopontine Angle
7	Gasparetto et al. [1]	2007	A case report of cerebellar GNB with neuroimaging and pathology findings	1 year, 8 months old	Cerebellar
8	Yao et al. [3]	2017	A case report of hippocampal GNB	16 years	Hippocampal
9	Mirza et al. [10]	2018	A case report of paediatric supratentorial GNB	4 years	Supratentorial
10	Mrowczynski et al. [11]	2020	A case report of suprasellar GNB mimicking craniopharyngioma	9 years	Suprasellar
12	De Frutos et al. [12]	2023	A case report of intracranial leptomeningeal GNB	5 years	Leptomeningeal

Acknowledgements The authors wish to thank the other members of the Pathology Department, Radiology Department and Neurosurgeons for their support and contribution.

Author contributions All authors have been personally and actively involved in substantial work leading to the paper, and will take public responsibility for its content.

Data availability The data that support the findings of this study are not openly available due to reasons of sensitivity and are available from the corresponding author upon reasonable request.

Declarations

Conflict of interest There are no conflicts of interest.

Ethical approval All procedures performed were following the ethical standards of the institutional ethical committee.

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