VOLUME - 12, ISSUE - 05, MAY - 2023 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Pathology

# ROSETTE FORMING GLIONEURONAL TUMOR: A CASE REPORT AND REVIEW OF THE LITERATURE

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**ABSTRACT** Rosette-forming glioneuronal tumor (RGNT) is a rare, slow-growing, mixed neuroglial neoplasm of the central nervous system with a predilection to the fourth ventricle region and occurring primarily in young adults. We present here a case of 45-year old male who presented with giddiness and headache from 1.5 months. Neurological examination revealed no abnormalities. On radiological evaluation, a large hypodense posterior fossa mass lesion was seen in relation to the fourth ventricle, accompanying a large cystic component along with obstructive hydrocephalus. Surgical resection of the tumor was carried out. Histopathological examination revealed a biphasic tumor with a uniform population of neurocytes arranged in rosettes forming the neurocytic component and spindle cells forming the glial component. On IHC synaptophysin and S-100 were positive in the neuropil-rich core of the rosettes. Based on these traits, a diagnosis of RGNT was made. RGNT of the fourth ventricle should be taken into consideration in the differential diagnosis of posterior fossa lesions, particularly involving the fourth ventricle and vermis in young adults.

**KEYWORDS :**

## INTRODUCTION

Rosette-forming glioneuronal tumor (RGNT) of the fourth ventricle is one of the newly described primary tumors of the central nervous system. It is a rare and novel neoplasm. RGNT was described by Kuchelmeister et al in 1995 as a dysembryoplastic neuroepithelial tumor (DNT) of the cerebellum. In 2002 despite the histological correspondence to DNT, Komori et al mounted the term RGNT of the fourth ventricle and described this tumor as a separate disease entity due to the morphology and biological behavior.[1] In 2007, the RGNT was named as a World Health Organization Grade I tumor and described as a slow-growing tumor typically localized to the fourth ventricle. It is composed of neurocytes that form neurocytic rosettes and glial components resembling to those of the pilocytic astrocytoma.[2]

In the 2016 WHO classification, the RGNT was again classified as a Grade I tumor and listed under the category of "neuronal and mixed neuronal-glial tumors.[3] According to this classification, RGNT is defined as "a slowly growing neoplasm that affects preferentially young adults, occurs predominantly in the fourth ventricle, can also affect other sites as pineal region, optic chiasma, spinal cord, and septum pellucidum and is composed of two distinct histologic components: one with uniform neurocytes forming rosettes and/or perivascular pseudorosettes, the other being astrocytic in nature and resembling pilocytic astrocytoma".[4]

### Case Report

A 45-year old male presented to OPD with chief complaints of giddiness and headache for one and half months and neck pain for one month. On examination, he was conscious and oriented with no focal neuro deficit. On radiological investigation, MRI Brain revealed a fourth ventricle SOL with obstructive hydrocephalus. On surgery brain tumor was excised and sent to the pathology department for histopathological examination. Intraoperative findings revealed greyish, soft to firm, moderately vascular mass at the fourth ventricular region.

Grossly multiple grey-brown to tan soft tissue pieces were there measuring together 3.0 x 3.8 x 0.4 cm. The microscopic examination revealed, a biphasic tumor with a uniform population of neurocytes arranged in rosettes forming the neurocytic component and spindle cells forming the glial component. (Figure 1). Immunohistochemical results revealed the following: GFAP – Positive, S-100 – Positive, Synaptophysin - Positive, Vimentin – Positive, NSE – Positive, EMA –Negative, CK- Negative, Ki67 - < 1%. (Figure 2). Based on microscopic findings and IHC, a diagnosis of rossete forming glioneuronal tumor was made.

## DISCUSSION

A comprehensive literature review using PubMed was performed in December 2022 using the search term "rosette-forming glioneuronal tumor". English, full-textual case reports, and series were included. Non-English, abstract-only text and review articles were excluded. To our information, about 150 cases have been described in the English literature to the duration. Based on this limited data, it has been determined that RGNT is a rare low-grade central nervous tumor usually localized within the fourth ventricle and occurring predominantly in young people with a mean age of 29.8 years.[5] There is a female preponderance (F: M ratio around 2:1).[6] Older patients may also be affected; two cases of patients with age over 65 years have been reported by Rosenblum et al.[7] A few cases have existed in the direction of association with neurofibromatosis type 1[5] as well as with Noonan syndrome[8] and with multiple sclerosis.[9]

Kuchelmeister et al in 1995 reported a case of dysembryoplastic neuroepithelial tumor (DNT) of the cerebellum in 28-year-old women presenting with complaints of rotatory vertigo, blurred vision, unsteady gait, pressure sensation in the head along with fatigue, forgetfulness and diminished power of concentration.[10] Kamori et al in 2002 reported a series of 11 cases of the posterior fossa tumor, with patient ages ranged from 12 to 59 years, accompanying a mean age of 31.5 years, out of which 7 were female and 4 were male with common presenting symptoms of headache and cerebellar ataxia however, few of them also presented with blurred vision, neck pain, confusion, brain stem dysfunction,

and dysarthria.[11] Hakan et al in 2016 reported a case of RGNT in a 29-year male who presented with acute neurological deterioration and somnolence with a past record of mild head injury three years before.[2] Verbančič et al in 2021 reported a case of RGNT in a 34-year-old Caucasian male accompanied by an experience of progressively worsening morning headaches followed by nausea and vomiting and pain acted not vanish entirely after analgesic use and was followed by numbness, tingling sensations, and muscle power loss in his upper extremities, while occasionally, the patient also experienced foggy or double vision, vertigo, and clumsy gait.[12]

By reviewing various literature, it has been found that the clinical symptoms and signs lack specificity and depends on the size and the exact location of the lesion. It includes headache, ataxia/gait disturbance, vomiting, nausea, visual disturbance, vertigo, and dysarthria. Headache was the most common presenting symptom in the series of Komori et al.[11] Several cases were likewise raise incidentally or with rare manifestations such as brain stem dysfunction.

Anan et al suggested that the lesion might arise from the gray matter or the middle motor nuclei in the spinal cord, so RGNT may not be limited in distribution.[13] Scheithauer et al reported that periventricular germinal matrix is the likely origin of RGNTs and accordingly, can be happening in "ectopic" sites.[14] Various other anatomical sites of origin have been reported including pineal region, optic chiasma, spinal cord, and septum pellucidum.

The histogenesis of RGNT is still unclear. The origin of RGNT has still expected elucidated on account of rarity of the tumor and its indolent course. It has been hypothesized that the neoplasm originates from pluripotent cells of the subependymal plate[15], and Chakraborti et al. showed evidence of differentiation of stem cells in their case series on RGNT.[16] Many genetic mutations have also been found in association with RGNT. The most common genetic marker associated with RGNT is the PIK3CA mutation.[17] FGFR1 mutations have also been implicated in tumor pathogenesis as well as IDH1, KIAA1549/BRAF gene fusion, PPP1R1A and RNF21.[6] Sievers et al reported the possibility of FGFR1 and PIK3CA co-mutations in RGNT.[18]

Radiologically, on CT scan, the solid parts of the tumor are usually hypo-intense, and the cystic parts present with lower intensity. Dense calcification may be visualized infrequenty and may be extensive. On MR evaluation, T1- iso/hypo-intensity and T2-hyper-intensity are the rule. RGNTs are relatively circumscribed, may be solid, cystic-solid, or multi-cystic, and usually display at least focal contrast-enhancement that may be nodular, linear, ring or spot-like, which is relatively specific. Satellite lesions could be detected. There may be part of edema or hydrocephalus, which is generally minimal.[19]

On pathological examination, grossly these tumors have been described to be soft, gelatinous, and generally well-demarcated. Histologically, the striking feature is that the tumors exhibit two major components. The first consists of uniform neurocytes engaged in the formation of neurocytic rosettes as well as perivascular pseudorosettes, while the second component consists of spindle-to-stellate astrocytes with elongation to oval nuclei and moderately dense chromatin in a dense background of fibrillary processes. Occasional Rosenthal fibers, eosinophilic granular bodies, microcalcifications and dysmorphic neurons of ganglion cell dimension may be found in glial areas.

On Immuno histochemistry, synaptophysin labels the neurophil matrix of the neurocytic rosette, and the astrocytic component is labeled by GFAP and S-100. Focal immunoreactivity for neuron-specific enolase and neurofilament protein are observed. Epithelial membrane antigen (EMA) staining was negative in all cases reported. The proliferation indices according to Ki-67 expression are generally very low ranging from 0% to 5%.[2,11,12]

Based on the absence of specificity of clinical manifestations and radiographic features of RGNT, the diagnosis can typically be confirmed only by post-operative pathology. The main differential diagnosis of RGNT includes pilocytic astrocytoma (PA), dysembryoplastic neuroepithelial tumor (DNET), central neurocytoma, plexus papilloma, oligodendroglioma, ependymoma, primitive neuro ectodermal tumor (PNET), glioneuronal tumor with neuropil-like islands (rosette) glioneuronal tumor, papillary glioneuronal tumor and metastasis.

Pilocytic astrocytoma is the most troublesome tumor type for differential diagnosis with RGNT. Pilocytic astrocytoma has small round cells as well as astrocytic cells but rosette structures like those of RGNT are not found in PA. There is further no evidence of neural differentiation in the rounded cells of pilocytic astrocytoma.[11]

Dysembryoplastic neuroepithelial tumour has mature neurons in mucinous pools that help for differentiating from RGNT. Rosette-forming glioneuronal tumour does not have "floating neurons" as is the case for the "specific glioneuronal element" of DNET.[20]

Central neurocytoma is characterized by uniform round cells and has similar immunohistochemical features of neuronal differentiation as in RGNT, but it does not have biphasic architecture with a distinctly separate glial component and true neurocytic rosette formation. Central neurocytomas have no astrocytic components as RGNT.[21] Neurocytes or well-formed rosettes may be found in oligodendrogliomas, but oligodendroglial components are not seen in RGNT.[22] The distribution pattern of synaptophysin and GFAP staining in ependymomas are quite the opposite of that seen in RGNT.[20]

## CONCLUSION

RGNT is a rare low-grade central nervous tumor usually localized within the fourth ventricle. They can be seen outside the posterior fossa. Thus, RGNT of the fourth ventricle should always be considered in the differential diagnosis of a posterior fossa tumor and with other infratentorial lesions, especially in relation to fourth ventricle and vermis in a young adult and has to be differentiated from other lesions for its indolent course and favourable prognosis. RGNT should always be considered in differential diagnosis with other infratentorial lesions, especially in young adults. Despite mostly indolent course and favourable postoperative outcome, the experience with this tumor remains limited. Therefore, further pathologic and clinical subclassifications may be required for prognostication and treatment. Careful and long-term follow-up monitoring will be wise for these uncommon tumors.

### Conflict Of Interest

The author declares no conflict of interest.

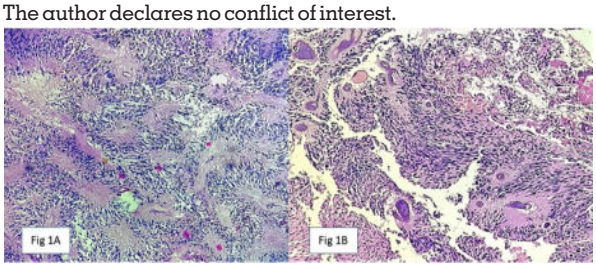


**Figure 1A and 1B: Tumor area shows perivascular pseudorosettes and true rosettes comprising neurocytic component dispersed in fibrillary background of astrocytic component. (H&E 200X, 400X)**

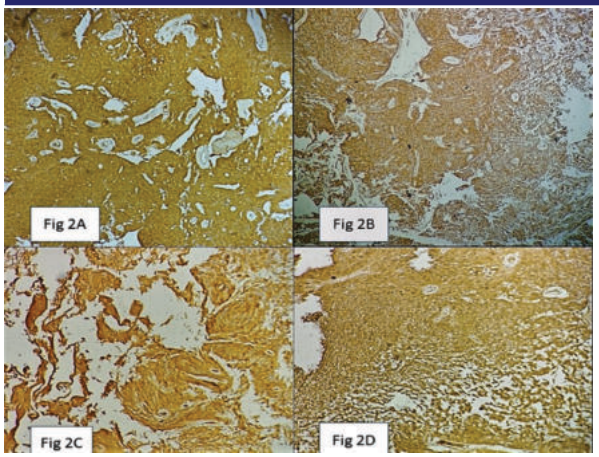


**Figure 2A: NSE positivity in neurocytic component. (200X) Figure 2B: Synaptophysin positivity in neurocytic componemnt (100X) Figure 2C: GFAP positivity in astrocytic component (200X) Figure 2D: S100 positivity in astrocytic component (200X)**

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