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Case Report

Spinal rosette-forming glioneuronal tumor: First case in a young child ☆

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Introduction

Rosette-forming glioneuronal tumor (RGNT) is a rare tumor composed of a glial component and a neurocytic component forming neurocytic rosettes and/or perivascular pseudorosettes [1,2]. It was originally classified as a "rosette-forming glioneuronal tumor of the fourth ventricle" by the World Health Organization (WHO) in 2007. However, RGNTs have since been found elsewhere in the central nervous system (CNS) [2]. Therefore, in the 2016 WHO classification system, "of the fourth ventricle" was removed from the description. RGNTs in the spinal cord are especially rare, with only 7 prior cases documented. We encountered a young child with a spinal RGNT. To the best of our knowledge, this is the first case of a spinal RGNT in a young child.

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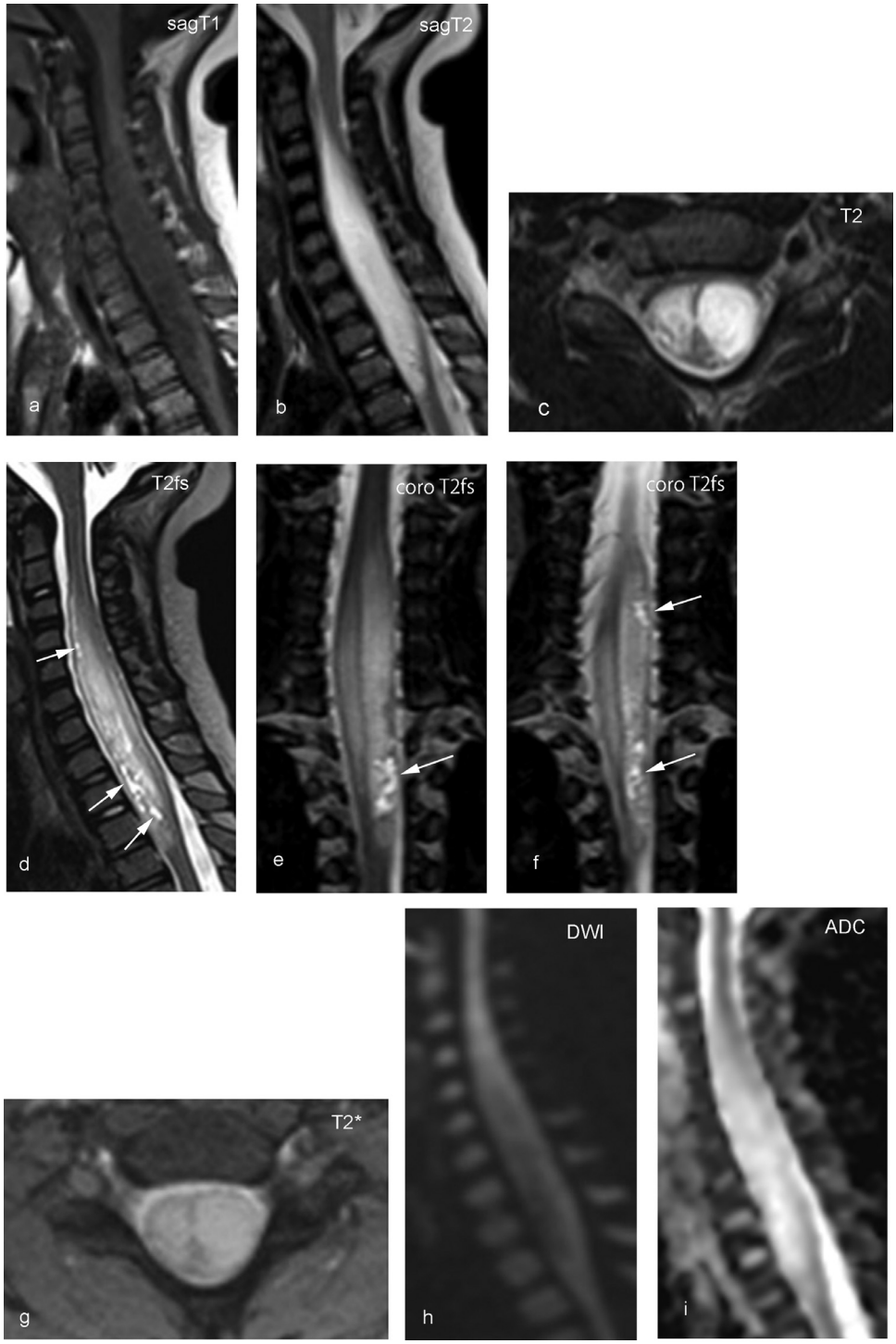

Fig. 1 – MRI revealed a mass lesion in the gray matter from C3–T4 with enlargement of the spinal canal. (a) Sagittal images showing low intensity on T1WI and (b) high intensity on T2WI. (c) Axial T2WI showed the mass had a poor margin on the right side at the vertical end of the left side of the mass. A cystic lesion showing high intensity on fat-suppressed T2WI was present at the vertical end of the left side of the mass (d,e,f, arrow). (g) There was no hemosiderin deposition on axial T2-star-weighted images. (h,i) No significant diffusion restriction on DWI and ADC map.

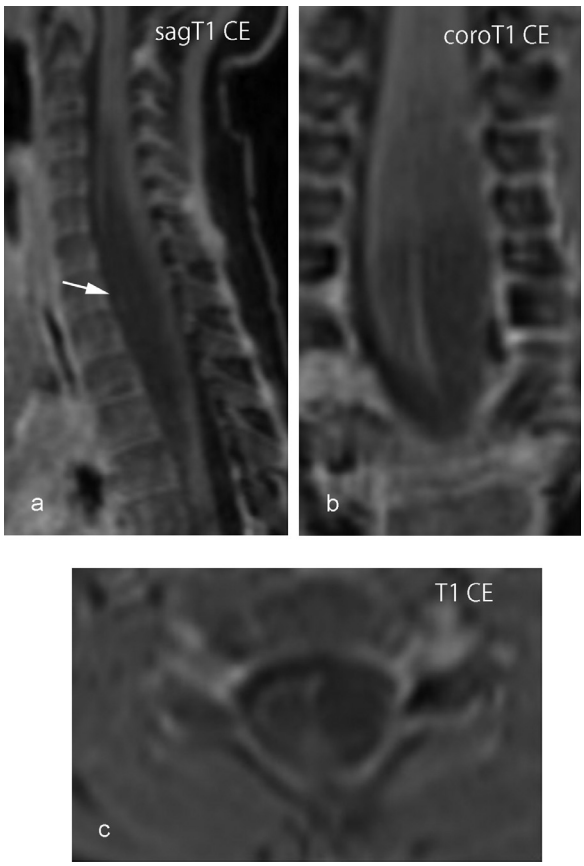

Fig. 2 – (a) Sagittal contrast-enhanced T1WI. (b) Coronal contrast-enhanced T1WI. (c) Axial contrast-enhanced T1WI. Contrast-enhanced T1WI showing very slight enhancement at the C7/Th1 level (a, arrow).

Case report

The parents of a four-year-old Japanese girl noticed that she had stopped using her left hand. She had no significant birth, family, or medical history. A neurological examination indicated left dominant upper flaccid paralysis and left lower spastic paralysis.

Magnetic resonance imaging (MRI) revealed a mass lesion in the gray matter from the cervical to thoracic spinal cord (C3–T4) with enlargement of the spinal canal (Figs. 1 and 2). The mass was left-sided dominant but was continuous to the right side through the central canal, showing low intensity on T1-weighted images (T1WI) (Fig. 1a) and high intensity on T2-weighted images (T2WI) (Figs. 1b and c). A cystic lesion showing high intensity on fat-suppressed T2WI was present at the vertical end of the left side of the mass (Figs. 1d, e, and f). There was no hemosiderin cap on the T2-star-weighted images of the adjacent spinal cord (Fig. 1g). There was no significant finding on diffusion-weighted imaging (DWI, ADC map) (Figs. 1h and i), and gadolinium (Gd) contrast showed only slight enhancement (Figs. 2a, b, and c). Computed tomography revealed homogeneous hypodensity with no calcification in the mass. There was no lesion in the other sites including the fourth ventricle.

Preoperative diagnostic imaging suggested a low-grade glioma, such as a pilocytic astrocytoma.

A biopsy was conducted, and the histopathologic examination demonstrated that the tumor consisted of two distinctive components: a glial component resembling pilocytic astrocytoma (Fig. 3a) and a neurocytic component with small, round nuclei with neurocytic rosettes (Fig. 3b). The centers of the rosettes showed positive immunostaining for synaptophysin (Fig. 3c). Glial fibrillary acidic protein (GFAP), S-100, Olig2, NeuN, and neurofilament were positive, and very little abnormal mitosis was detected (MIB-1 labeling index: approx. 1%) (Fig. 3d). No necrotic lesion or microvessel proliferation was detected. The DNA sequence showed no mutation including *FGFR1* and *PIK3CA*. As a result, the diagnosis was RGNT as a WHO grade I tumor.

Based on this diagnosis and considering the risk of nerve injury, a subtotal resection was performed on the left side of the lesion under motor-evoked potential monitoring. The intraoperative gross appearance of the tumor was gray and soft, well-demarcated at the left side but not at the right side. The tumor could not be gripped by forceps, and it was therefore resected by suction at the level of C7–T3. The histopathologic findings of the resected sample were similar to those observed in the previous biopsy.

Over twelve months have passed since the operation. The patient's neurological symptoms remain but have not become worse, and no evidence of remnant tumor growth has been observed on repeat MRI.

Discussion

RGNT was first described in 2002 by Komori et al. as occurring in the fourth ventricle [3]. However, over the years, several cases of RGNTs have been described in the cerebellum, supratentorial ventricular system, spinal cord, temporal lobe, thalamus, brain stem, frontal lobe, pineal region, suprasellar region, and basal ganglia [2]. This newly recognized tumor entity is little known, and spinal manifestations of RGNT are especially rare. There have been only seven cases of spinal RGNT reported so far: two males, five females, ages 14-44 years (average, thirty-two years) [4–9]. All but two of the spinal RGNT cases originated from the cervical region; the others involved the thoracic to lumbar regions. Our case is the youngest patient among the spinal RGNT cases up to this point.

The etiology of this tumor remains uncertain. Several research groups have suggested that RGNT might be derived from the subependymal plate that belongs to the second germinal layer [3,4,10]. Yang et al. demonstrated that most cases of RGNT were located adjacent to the midline with a few counterparts in the lateral parenchyma, supporting their hypothesis [2]. Duan et al. reported two cases of spinal RGNT that were observed to have originated in the central canal of the spinal cord [7]. In our case, the central canal seems the most likely point of origin, as this tumor showed a butterfly-like spread out of the central canal on MRI axial imaging.

It is said that RGNTs can be categorized by the following three patterns on MRI: cystic pattern (35%), solid pattern (47%), and mixed cystic-solid pattern (18%). The cystic com-

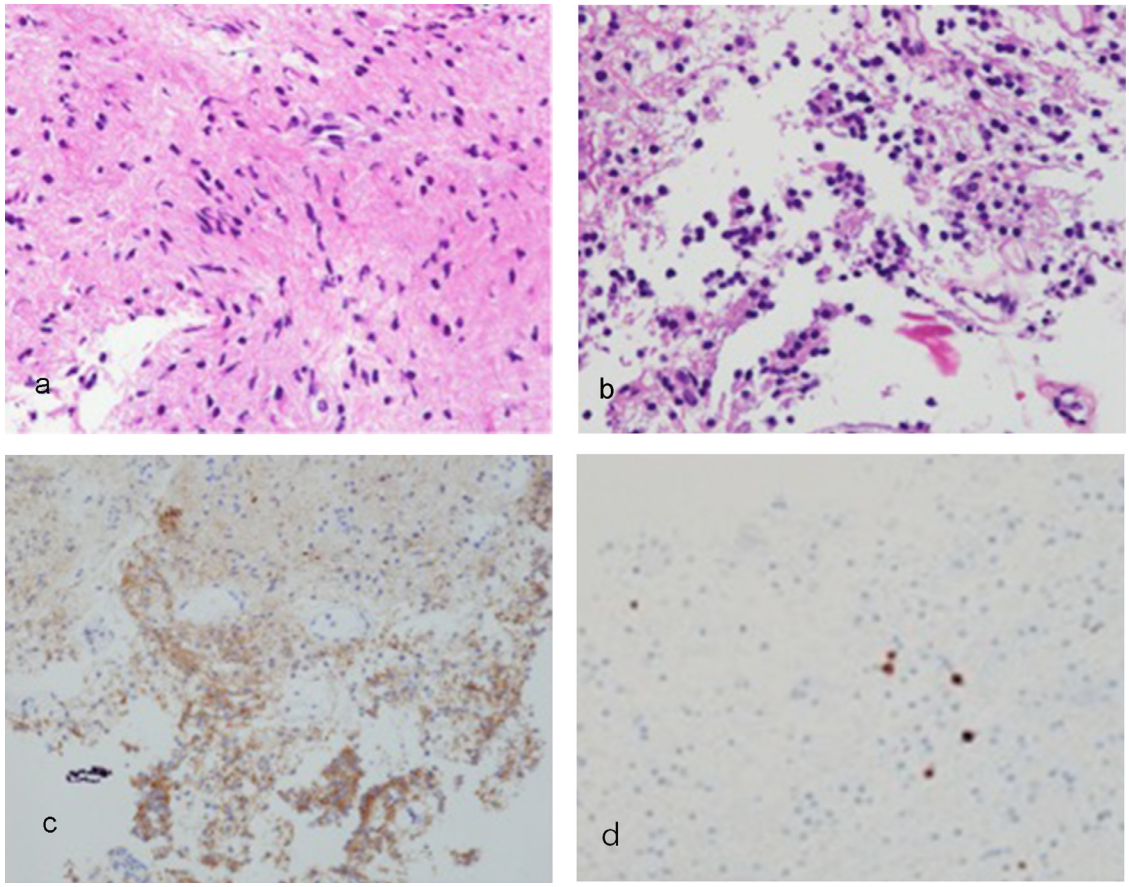

Fig. 3 – Histological analysis of this case. (a,b) Hematoxylin and eosin (HE) staining. (a) Low-power view showing the glial component resembling pilocytic astrocytoma. (b) High-power microscopic view showing the neurocytic component having small, round nuclei with neurocytic rosettes. (c) In immunohistochemistry, the center of the rosettes showed positive immunostaining staining for synaptophysin. (d) The MIB-1 antibody stained approximately 1% of the tumor nuclei.

ponents, when present, may have a relatively benign nature based on statistical analyses [2]. In the majority of RGNTs, the solid portion shows homogeneous hypointensity on T1WI, homogeneous hyperintensity on T2WI, and no evidence of restricted diffusion on DWI [2,3,11]. The gadolinium (Gd)-enhancement patterns of the reported RGNTs vary: in one study, 25% of RGNTs demonstrated no enhancement while the others showed heterogeneous, rim, or focal enhancement [2]. On CT imaging, RGNTs commonly show hypodensity and <25% have calcification [2,3,11].

These features apply to almost all past spinal cases. The distributions and boundaries of the tumors have varied. Syringomyelia adjacent to the tumor has often been observed in the past spinal cases. Spinal RGNTs differ from intracranial RGNT in their lack of both satellite lesions on MRI and calcification on CT. Hemosiderin deposition (as is often the case with ependymoma) has been reported in only one spinal RGNT case [2,4–9].

In our patient, although the enhancement seemed to be weaker than in previous spinal cases and syringomyelia was not observed. Before the surgery we suspected a low-grade astrocytoma and thought ependymoma was not likely because of the tumor heterogeneity, partially unclear margin, and poor enhancement on Gd-contrast MRI. Considering the patient's age, we thought that pilocytic astrocytoma was the most likely entity and considered subependymoma as a differential diagnosis. As spinal RGNTs are so rare and their neuroimaging features resemble those of other intramedullary tumors such as astrocytoma to some degree, the preoperative diagnosis was challenging. We hope this paper will remind clinicians to consider RGNT as a differential diagnosis for intramedullary spinal cord tumors if there is a particular imaging finding that might be suspicious.

A genetic analysis of RGNT was recently reported. Sievers et al. reviewed 30 patients with RGNTs and revealed *FGFR* mutations in all tumors, with co-occurrence of *PIK3CA* mutations in 63%. They suggested that, in contrast to most other low-grade gliomas, RGNTs are characterized by highly recurrent combined genetic alterations. [12]. Among the previous seven cases of spinal RGNTs, only two underwent this genetic analysis and were both negative, as was the present case. It remains uncertain how these genetic mutations affect spinal RGNT, and further genetic analyses are thus required. Such efforts might lead to the identification of subsets of the tumor that are more aggressive, or differences between intracranial and spinal cases.

Progressive events are uncommon in RGNT. However, there are cases with presumable drop metastases [13–16]. Several authors have wondered whether some RGNT cases might belong to a higher WHO tumor grade, with a more aggressive behavior, unlike the classical benign evolution usually ascribed to this type of tumor [13,15,16]. Cabezas et al. described one case with an intraspinal lesion having leptomeningeal spread. Such cases that are not as benign have all been multifocal and have also had marked atypical microvascular proliferation and a focus of necrosis, with a high MIB-1 proliferation index (reaching about 20% in some cases) in the areas of vascular proliferation [16].

Surgical resection is reported to be the first-choice treatment for spinal RGNT, with no adjuvant therapy [4]. In previous spinal cases, patients underwent a total resection when feasible, without recurrence. Although most of the reported RGNTs were located at midline sites, a complete resection (which can pose a high risk of neurologic injury) is not always possible, as in the present case. We speculate that aggressive surgery with a complete resection might be not necessary in cases with a greater risk of neurological injury, because RGNTs have shown no significant difference in progression between cases of gross total resection and cases of subtotal resection [2]. In our case, no satellite lesions or aggressive behavior were seen. Hence, we chose surgical resection with no adjuvant therapy at first.

The efficacies of postoperative radiation and chemotherapy have not yet been determined for RGNT because of the limited number of cases involving adjuvant therapy [2,16,17]. Outcomes after radiation therapy for several intracranial RGNT cases have been described, with clinical and radiographic stability after treatment in the short term [16,17]. The optimal treatment strategy for patients with dissemination from an RGNT (especially for spinal cases) is not yet known. Thorough follow-up should be conducted in all cases, as the accumulation of this evidence, along with further spinal RGNT cases, is necessary in order to elucidate this newly recognized tumor entity and estimate the long-term prognosis.

Patient consent

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

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