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Case Report

Cortically based cystic supratentorial RELA fusion-positive ependymoma: a case report with unusual presentation and appearance and review of literature ☆,☆☆

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ABSTRACT

Ependymomas are rare central nervous system tumors that can arise anywhere in the neuroaxis. Supratentorial and posterior fossa ependymomas were identified as distinct diseases after extensive molecular analysis. The 2016 World Health Organization update further introduced RELA fusion-positive ependymoma as a novel entity as a subset of supratentorial ependymomas indicating the presence of C11orf95-RELA fusion genes. RELA fusion-positive ependymomas are commonly intraventricular, though they may rarely manifest as extraventricular, cortically-based tumors. They are commonly large solid, mixed solid/cystic tumors or rarely cystic. In this paper, we report a case of RELA fusion positive cortically based-cystic ependymoma and review the existing literature. Our patient is a 9-year-old boy who presented with an unusual presentation of right facial droop. He underwent gross total resection of the ependymoma, following resection, his facial droop resolved and there was no neurologic deficit.

☆ Consent: The consent was waived as the data were collected retrospectively. There was no contact with the patient and hence no risk related to the process. The data were collected from charts and databases which did not require any interviews. All data were deidentified and hence will not be tracked back by general audience. Hence, we do not anticipate any adverse effect to result from this paper and given that the data will be deidentified, the alteration of consent requirement in unlikely to adversely affect welfare of the patient.

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Introduction

Ependymal tumors are a group of neoplasms that can arise anywhere in the neuroaxis. They are of neuroectodermal origin. Supratentorial (ST) and posterior fossa (PF) ependymomas (EPNs) are distinct diseases with distinct genetic, transcriptional and epigenetic alterations [1]. Ependymomas are rare central nervous system tumors [2]. Almost 90% of pediatric ependymomas are intracranial and the remaining 10% are spinal. One third of intracranial ependymomas are supratentorial, while two-third are infratentorial [3].

In 2016, the World Health Organization (WHO) described 3 molecular subgroups of ependymoma according to DNA methylation profiling. These are Ependymomas with RELA (v-rel avian reticuloendotheliosis viral oncogene homolog A) fusion "EPN, RELA" including all cases that are RELA fusions positive (72%), "EPN-YAP" include cases which harbor YAP fusions (11%), and supratentorial subependymomas "SUBEPN, ST" that have not identified gene fusions or other driver genes yet. Ependymomas with RELA fusion positive represent two-third of the supratentorial ependymomas (ST-EPN) in children [4] and they have a relatively worse clinical course [4,7,8].

Classic imaging findings of RELA–positive ependymomas include large, complex-appearing mixed solid/cystic hemispheric mass that is either ventricular, extraventricular or rarely cortically based. The extraventricular ependymomas are usually in close proximity to the ventricles and contacting them, but the cortically based ependymomas do not contact the ependymal margin at all. However, definitive diagnosis cannot be made with conventional imaging alone [9–11].

Here we report an unusual presentation of a large cortically-based, cystic supratentorial RELA fusion-positive ependymoma with a rare presentation.

Case report

A 9-year-old boy presented to the emergency department (ED) with persistent neck and shoulder pain for 2 days after falling from a trampoline. Spinal radiography was reported as unremarkable and he was discharged home. The pain persisted and he went on to develop a right facial droop, prompting a return to hospital 2 days later. The boy underwent head computed tomography (CT) that showed a left frontal intracranial cystic mass with a small peripheral coarse calcification (Fig. 1).

The patient was referred to neurosurgery for evaluation, he was noted to have significant right-sided facial droop (House-Brackmann grade III) but was otherwise neurologically intact.

Subsequent magnetic resonance imaging (MRI) performed 2 days later revealed (Fig. 2), a cortically based left frontal cystic mass (5.6 × 5.3 cm) with a small enhancing mural nodule. FLAIR imaging showed small hyperintense rim indicating minimal surrounding edema. There was no midline shift or hydrocephalus. Differential consideration following the MRI included primitive neuroectodermal tumor, pleomorphic xanthoastrocytoma, oligodendroglioma, and cystic ependymoma.

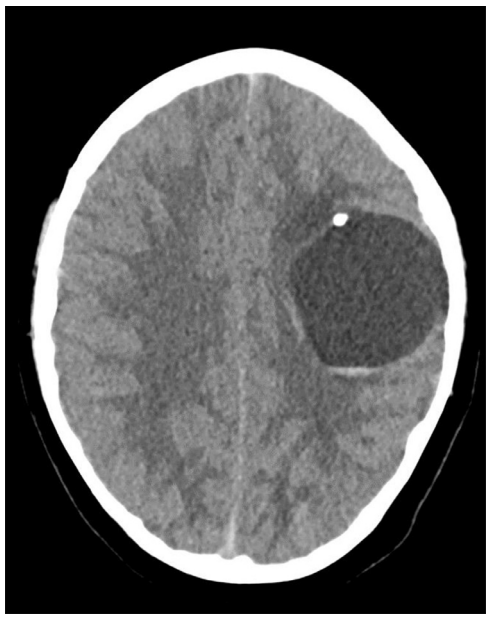

Fig. 1 – Axial unenhanced CT head showing a large, cortically based, cystic lesion with a dystrophic calcification and a small layer of dependent hemorrhage.

A left frontoparietal craniotomy for gross total resection of the tumor was performed. Pathology indicated a WHO grade II ependymoma, C11 or f95-RELA fusion transcript positive (Fig. 3).

Immunohistochemistry showed tumor cells that are diffusely and strongly positive for glial fibrillary acidic protein. Scattered tumor cells showed perinuclear dot-like immunopositivity for D2-40, epithelial membrane antigen staining and CD99, confirming the diagnosis. It not anaplastic and shows low Ki-67 index.

The reverse transcription PCR and Sanger sequencing techniques were used to test for and confirm the presence of C11orf95-RELA fusion transcripts in the patient's specimen.

The patient underwent gross total resection (treatment of choice).

Few days postoperatively, the patient recovered well and showed improvement of his facial droop. He had no new neurological deficit.

Discussion

Ependymomas are neuroepithelial tumors that most likely arise from radial glial precursor cells lining the walls of the ventricles in the brain and central canal of the spinal cord. Supratentorial ependymoma (STE) may occur inside the ventricles or in the brain parenchyma. Most of the STE are extraventricular, and are in close proximity to the ventricles, having some connection to its margins. However, cortical ependymomas where described as STE with no connection to ventricular lining [24]. These are very rare with a limited number of cases being reported in the literature. It has been hypothesized

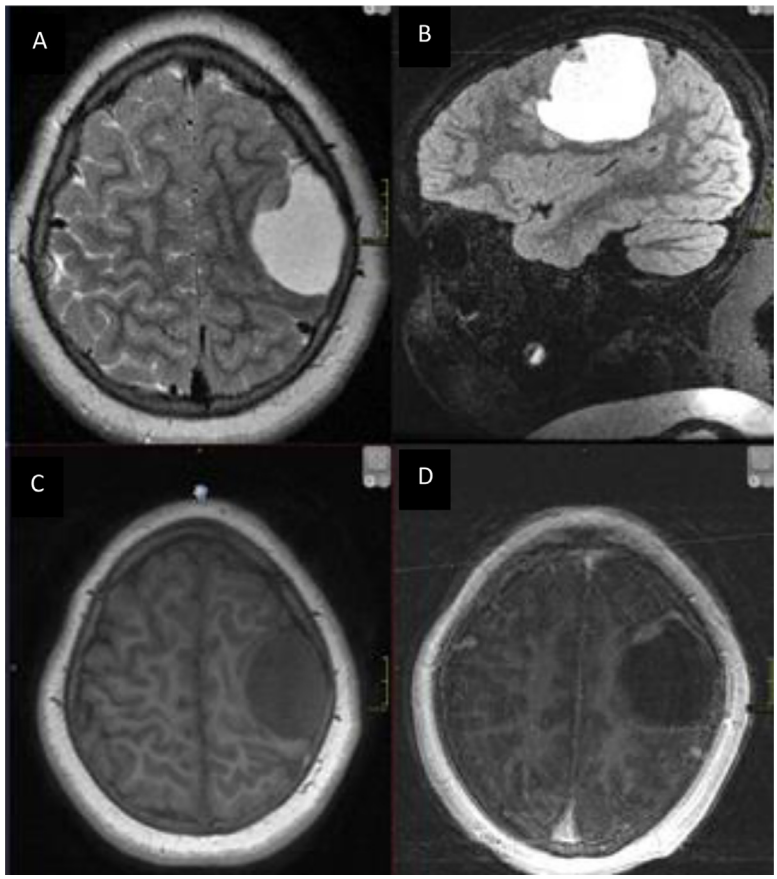

Fig. 2 – (A) Axial T2WI and (B) sagittal FLAIR images showing a large left frontoparietal cystic lesion with a small mural nodule (arrow). (C) Precontrast T1WI and (D) postcontrast T1WI showing enhancement of the small mural nodule.

that they originate from nests of ependymal cells that have migrated from the periventricular areas deep into the adjacent white matter or the embryonic cell rests in these sites [18,24].

Supratentorial ependymomas are relatively rare and have a bimodal age distribution in children aged 1-5 years and smaller peak in young adults 20-30 years [12]. It has male predominance as compared with previous case reports [24].

Histologically, RELA-positive ependymomas possess clear cell morphology and prominent vascularity, but definitive pathological features are absent [5,6]. Genomic classification has supported the distinction of RELA–positive ependymomas from other tumor types along with a worse clinical course [4,7,8].

STE predominantly involve the brain parenchyma and at presentation usually tend to be large [14–16]. Common presenting symptoms include raised intracranial pressure such as a headache and vomiting, diplopia, limb weakness, and/or seizures [23].

Less than 50 cases of cortically based ependymomas have been previously reported, largely as individual case reports [13,22]. These tumors were found more frequently among younger patient population. Of these rare cases, the majority are predominantly solid or mixed solid-cystic. Predominantly cystic lesions are extremely rare [17–21].

In 2019, Matsumoto et al published a case series with review of literature of all cortical ependymomas including those with solid, mixed, and predominantly cystic appearance. They published 8 cases from their institute, of which 5 were RELA-fusion positive, and had predominantly cystic appearance. This report also summarized 57 previously published cases of cortical ependymomas, of which 37 had at least some cystic component. The report did not document RELA-fusion status.

Radiologically, the imaging characterization of STE relays preliminary on MRI [26]. Cortical ependymomas generally appear as large, well-demarcated mass located away from the margins of the ventricles and are cortically based. They are mostly located in frontal and to a lesser extent in parietal lobes. It is either solid, solid cystic or rarely predominantly cystic and usually associated with minimal vasogenic edema. Some may enhance following gadolinium administration [26]. Imaging appearance however, does not show high specificity. In our case, the differential considerations were broad and cystic ependymoma was not on top of the list due to its rarity.

Our patient presented with a rare presentation that was not previously reported, namely unilateral facial droop and notably with no emesis, limb weakness, or seizures. Moreover, its radiologic appearance was not reported earlier. It appears as a cystic lesion with a small solid nodule.

Histopathologic evaluation was performed on hematoxylin and eosin stained slides. We also performed immunohisto-

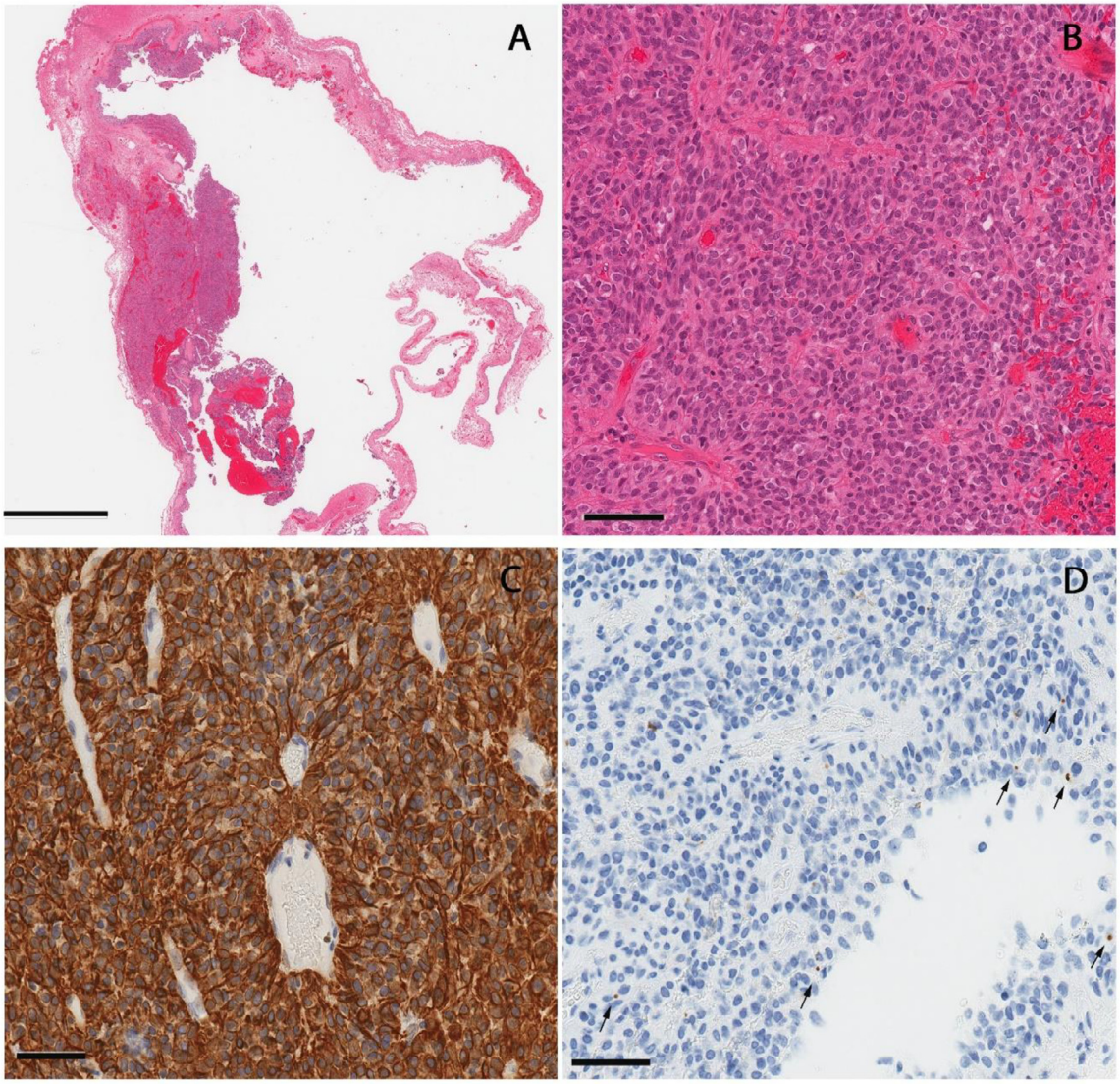

Fig. 3 – Neuropathology. (A) A cystic lesion is seen under low power view. There are areas with hypocellular dense fibrotic tissue and areas of increased cellular density. (B) The cells in the hypercellular component are arranged in solid sheets or pseudopapillae. They have moderate amount of eosinophilic to clear cytoplasm. The nuclei demonstrate moderate pleomorphism, with irregular nuclear contour and occasional nuclear grooves. The chromatin is finely granular. Inconspicuous nucleoli are present in some tumor cells. (C) The tumor cells are diffusely and strongly positive for GFAP. (D) Scattered tumor cells show perinuclear dot-like immunopositivity for EMA (arrows). Scale bars: 2 mm in A; 50 μm in B-D.

chemical stains for glial fibrillary acidic protein and epithelial membrane antigen. The C11orf95-RELA fusion genes were tested using reverse transcription PCR and confirmed with Sanger sequencing. This is a finding that was reported only in 5 patients having cystic ependymomas in the study by Matsumoto et al (2019), and our patient is the sixth [25].

The treatment of choice for ependymoma is gross total surgical resection [13]. There is no significant role of adjuvant radiotherapy, which is usually saved to manage anaplastic ependymomas showing disseminating, residual or recurrent disease [27,28]. Recurrence is not uncommon; our patient had a small solid enhancing nodule, denoting recurrence on the 5 months follow-up scan. The patient underwent successive MRI follow ups which confirmed stability of the nodule.

Conclusion

This case represents an unusual location, image morphology, and clinical manifestation of a WHO grade II ependymoma. Namely, the combination of a cortical location, cystic morphology, and unusual clinical presentation represent the first such description in a RELA-fusion positive ependymoma.

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