Quiz

Correct answer to the quiz. Check your diagnosis

Case report

Squash smear cytology and histopathology findings of angiocentric glioma

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We herein report a case of a 12-year-old girl who presented with a superficial mass in the right temporal lobe and a 7-month history of seizures. Intraoperative consultation with squash smear cytology was done. It showed low-grade glioma with slender, bipolar cells with angiocentric features. The surgical resection specimen revealed features of angiocentric glioma with extensive schwannoma-like areas and typical EMA "dot-like" positivity.

Key words: angiocentric glioma, low-grade glioma, cytology, squash smear.

Introduction

Angiocentric glioma (AG) is one of the least common central nervous system tumors. It was firstly described in 2005 [1, 2] and its distinct clinical and pathological features led lead to inclusion in the World Health Organization (WHO) classification system in 2007 [3]. This tumor mainly involves affects children and young adults, without gender predilection. Clinically it is a slow-growing tumor, usually located superficially in the cerebral hemispheres and associated with long-standing and drug-resistant epilepsy [1, 2]. Angiocentric glioma generally shows an indolent course but single cases with recurrence and even dissemination have been reported [4]. To date histological characteristics of AG have been quite well described but only a few reports describing its cytological features have been published.

We herein present an AG case with extensive schwannoma-like areas and put special emphasis on squash smear cytomorphologic findings. We also analyze the AG reports previously published in the literature and morphological features of tumors which need to be included in the differential diagnosis.

Case report

A 12-year-old girl presented with a 7-month history of seizures which occurred approximately twice per month. The physical examination was unremarkable but magnetic resonance (MR) imaging revealed a non-enhancing, superficial mass in the right temporal lobe (size: 2.5 × 1.8 × 2.6 cm). The lesion was hypointense in T1 images, and hyperintense in T2 and FLAIR images (Fig. 1). It had a slightly blurred margin on the white matter side and heterogenous structure with solid and small cyst components.

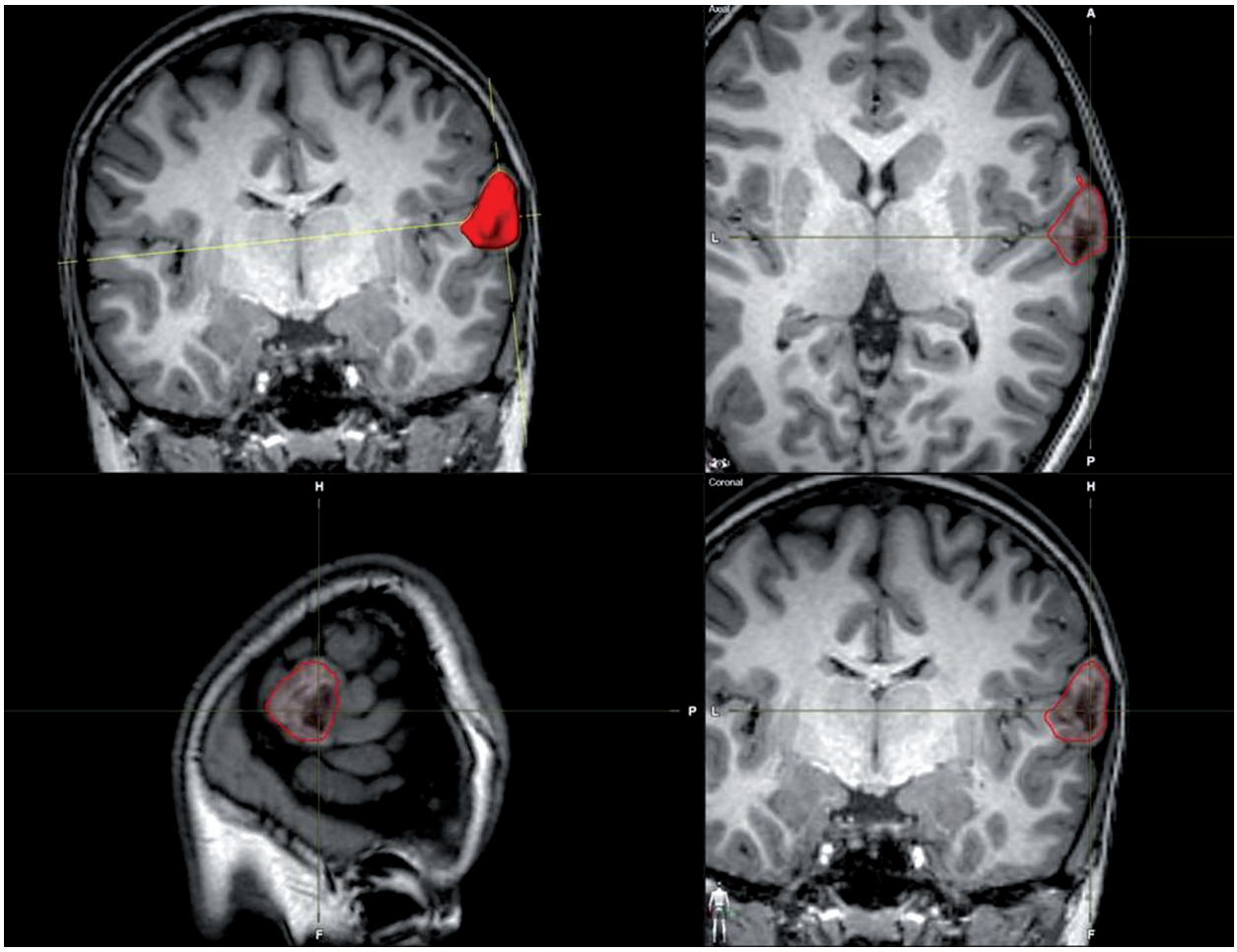

Fig. 1. MRI T1-weighted image showing the tumor located in the posterior part of the right superior temporal gyrus which had a volume of 3 cm^3 (red area). Tumor visualization was performed in the SmartBrush station program (Brainlab, Germany)

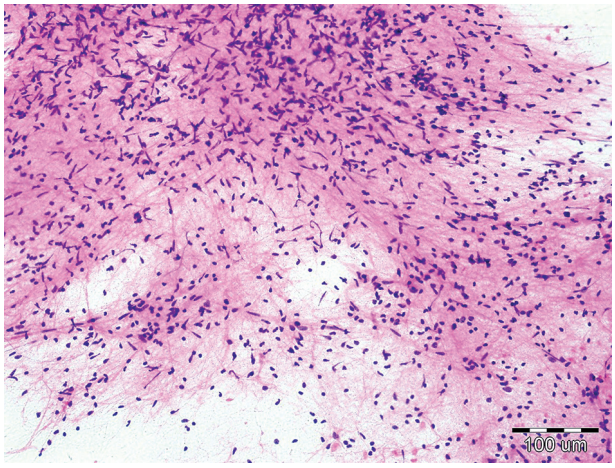

Fig. 2. Smear showing monomorphic neoplastic cells with spindle-shaped and oval nuclei and elongated projections (HE, 100×)

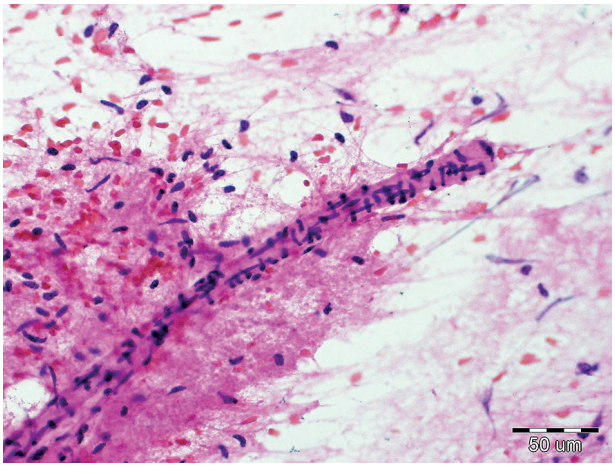

Fig. 3. Smear showing angiocentric arrangement of tumor cells with perpendicular alignments to blood vessel (HE, 200×)

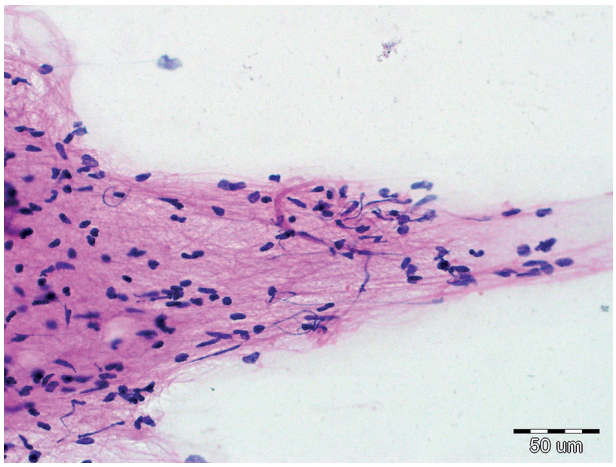

Fig. 4. Smear showing Rosenthal fiber (HE, magnification 200×)

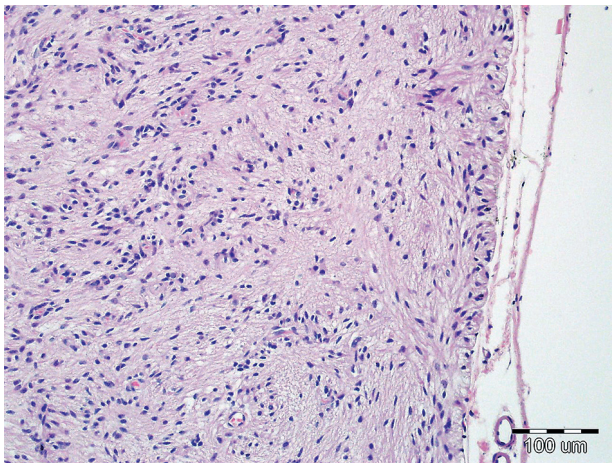

Fig. 5. Histological section showing angiocentric arrangements of monomorphic cells and perpendicular orientation of neoplastic cells to the pia (HE, magnification 100×)

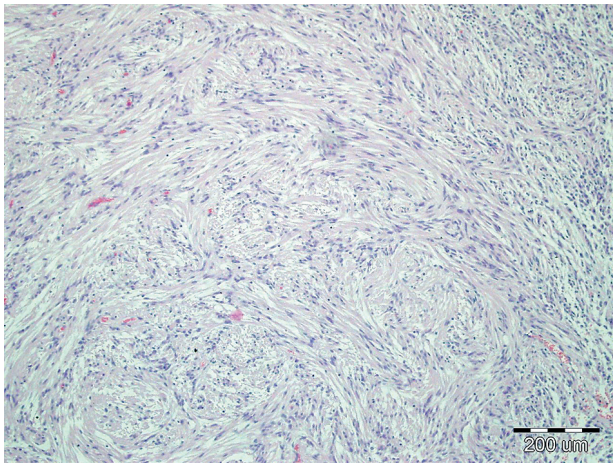

Fig. 6. Histological section showing fibrillary areas resembling schwannoma (HE, magnification 40×)

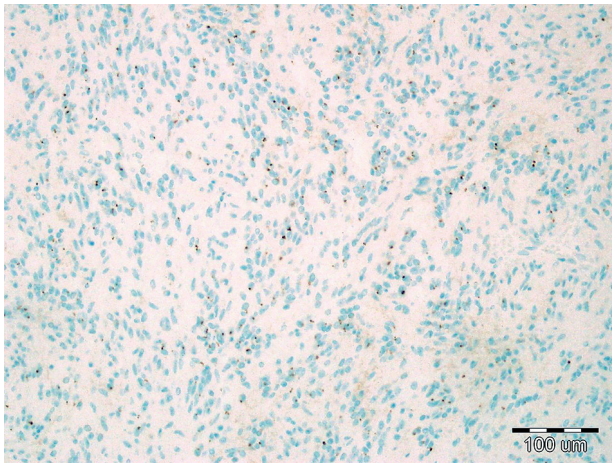

Fig. 7. Tumor cells showing "dot-like" EMA positivity (magnification 100×)

The patient was admitted to our hospital for resection of the tumor. During surgery intraoperative consultation with squash cytology was performed.

The surgical specimen for intraoperative consultation was obtained from the superficial portion of the tumor. It was whitish, soft, and quite easily smeared. The slides were fixed in 95% alcohol and HE stained. The smears showed a moderately cellular tumor consisting of monomorphic cells within fibrillary stroma. The neoplastic cells were bipolar in shape and showed delicate, elongated projections which focally suggested "hair-like" processes in pilocytic astrocytoma (Fig. 2). Spindle-shaped, slender nuclei consisted of fine or speckled chromatin. In the fibrillary stroma there were quite numerous thin-walled vessels. Tumor cells were radially oriented to some blood vessels which resembled ependymal pseudorosettes and a few poorly formed rosettes were also seen (Fig. 3). In the fibrillary stroma there were single Rosenthal fibers (Fig. 4). No mitotic activity, nuclear atypia or necrosis was observed. Also, no myxoid matrix in the background was noted. The cytological diagnosis of low-grade glioma was made.

The surgical resection specimen showed a grey tumor with a brown, cystic area in the center. Histological sections showed glial tumor composed of uniform, bipolar cells with elongated nuclei. The cells showed angiocentric arrangements mainly with perpendicular but also with longitudinal alignments. Perpendicular orientation of tumor cells to the pia was also noted (Fig. 5). In the center of the tumor there were extensive schwannoma-like areas with small cystic spaces which were not seen in smears. In these areas there were numerous structures resembling Verocay bodies (Fig. 6). Mitotic activity, nuclear atypia or necrosis was not found.

Tumor cells demonstrated strong GFAP and S100 positivity, focal Olig2 positivity and cytoplasmic

dot-like EMA positivity as seen in ependymomas (Fig. 7). The Ki-67 proliferative index was low at 1% to 2%. The tumor was negative for *IDH1/IDH2* mutations (determined by Sanger sequencing), negative for *BRAF* V600 mutations (determined using Amoy-Dx BRAF V600 Mutations Detection Kit) and negative for *MGMT* promoter methylation (determined by methylation-specific PCR).

The final diagnosis of AG was made which was consistent with clinical and radiological features. The patient was free of seizures and there was no recurrent disease during 12 months of postoperative follow-up.

Discussion

Angiocentric glioma is a rare tumor of the central nervous system. It is a morphologically and genetically distinct entity with MYB-QKI rearrangements found to be quite specific [5]. Cerebrocortical location of the tumor is typical and long-term epilepsy is the main clinical presentation [6]. A few cases of brainstem AG presenting with symptoms other than refractory epilepsy have also been reported [7, 8, 9].

Histological findings of AG have been widely studied but there are only a few reports describing its cytological characteristics [8, 10, 11, 12]. Most cases investigated by intraoperative squash cytology showed monomorphic cells on a fibrillary background [8, 10, 12]. Mild pleomorphism was described only in one case [11]. Neoplastic cells usually had long astrocytic processes. Nuclei of neoplastic cells were elongated with finely granular chromatin. In all cases cells showed a tendency to form pseudorosettes or rosettes. No eosinophilic granular bodies or Rosenthal fibers were observed [8, 10, 11, 12]. LaCruz *et al.* [12] also observed in their cases a myxoid background, which can also be found in dysembryoplastic neuroepithelial tumor or pilocytic astrocytoma. Cytological features of our case were similar to the reports described earlier. Our smears showed monomorphic cells with elongated nuclei within fibrillary stroma and focal pseudorosette formation. Unlike LaCruz *et al.* [12], we did not observe a myxoid background, but we noted single Rosenthal fibers.

Cytological differential diagnosis should include mainly other low-grade gliomas. Ganglioglioma is composed of a low-grade glial component, which can be similar to AG but usually without obvious angiocentric arrangements. A significant feature of ganglioglioma is presence of neoplastic ganglion cells that are lacking in AG [13]. Smears in pilocytic astrocytoma are usually composed of bipolar neoplastic cells with long processes and with Rosenthal fibers as seen in our case. Neoplastic cells in pilocytic astrocytoma are usually more pleomorphic and angiocentrism is usually not observed. Diffuse astrocytoma shows more nuclear atypia, but obvious angiocentric features are also not seen. Ependymoma may have very similar cytomorphological findings as AG and the main differential features are clinical presentation and localization of the tumor [11]. In difficult cases molecular studies should be performed.

In histological sections in the deep portion of the tumor we observed an extensive schwannoma-like growth pattern, which was not seen in the intraoperative consultation specimen. Schwannoma-like areas are a well-recognized pattern of AG, but usually it is noted only focally. Histologically, AG is predominantly composed of elongated, slender astrocytes with marked longitudinal or radial vascular orientation. Subpial aggregation of tumoral cells is also a common feature [1, 2, 13, 14, 15]. Mitotic activity, necrosis and microvascular proliferation are not observed in typical AG, but may be seen in malignant transformation [1, 4].

Angiocentric glioma is a rare central nervous system tumor and more studies are needed to learn more about the morphology and biology of this neoplasm. Cytologically, AG is a low-grade, monomorphic glial tumor with some morphologic similarities to ependymoma and pilocytic astrocytoma such as presence of rosettes structures and long "hair-like" processes of the cells. In some cases, intraoperative squash cytology may be crucial for patient management, especially when the tumor is in structures that are not amenable to complete surgical resection and only small biopsy samples can be obtained. In such cases intraoperative cytology can be helpful to provide proper differential diagnostics and to save some fresh material for molecular studies if needed.

The authors declare no conflict of interest.

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