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Letter to the Editor

Myxoid glioneuronal tumor with PDGFRA p.K385 mutation in the periventricular white matter: a rare case and literature insights

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Dear Editor,

We report the case of a 29-year-old man who presented with severe headache. MRI revealed an oval, well-defined lesion (12×18 mm) in the left periventricular white matter, hyperintense on T2-weighted imaging without contrast enhancement or edema. Gross total resection was performed.

Brain and brainstem MRI revealed, in the left frontal region, an ovoid-shaped lesion measuring approximately 12×18 mm in axial dimensions, exhibiting a 'target-like' appearance. On FLAIR sequences, the lesion showed peripheral hyperintensity with a centrally hypointense area. The lesion margins appeared well-defined, and the core demonstrated high signal intensity on T2-weighted images (Fig. 1A) and hypointensity on FLAIR sequences.

Histologically, the lesion showed rounded, oligodendroglioma-like cells in a myxoid stroma, with focal perivascular arrangements. Immunohistochemistry demonstrated positivity for GFAP, OLIG2, and synaptophysin, while IDH1 (R132H), BRAF V600E, CD34, and EMA were negative. Ki-67 index was approximately 1%. Molecular analysis detected a PDGFRA mutation at codon p.K385 (p.K385L), confirming the diagnosis of myxoid glioneuronal tumor (MGT), CNS WHO grade 1 (Fig. 1B-F).

MGT is a rare tumor newly defined in the 2021 WHO classification [1]. Its diagnosis may be challenging, especially on small biopsy specimens showing an oligo-like cellularity with a variably myxoid stroma; in this scenario, the distinction with diffuse low-grade glial tumors, e.g., diffuse low-grade glioma, MAPK pathway-altered, may be challenging as well. Although the septum pellucidum is the most frequent site, other locations such as corpus callosum, midbrain, and periventricular white matter are increasingly described [1].

In our review of 37 previously reported cases [1-11] (Tab. I), 65.8% were located in the septum pellucidum, while 15.8% – including our case – arose in the periventricular region. Gross total resection was the preferred treatment. The PDGFRA mutation at codon K385 (either p.K385L or p.K385I) is a diagnostic hallmark, helping distinguish MGT from dysembryoplastic neuroepithelial tumor (DNT), rosette-forming glioneu-

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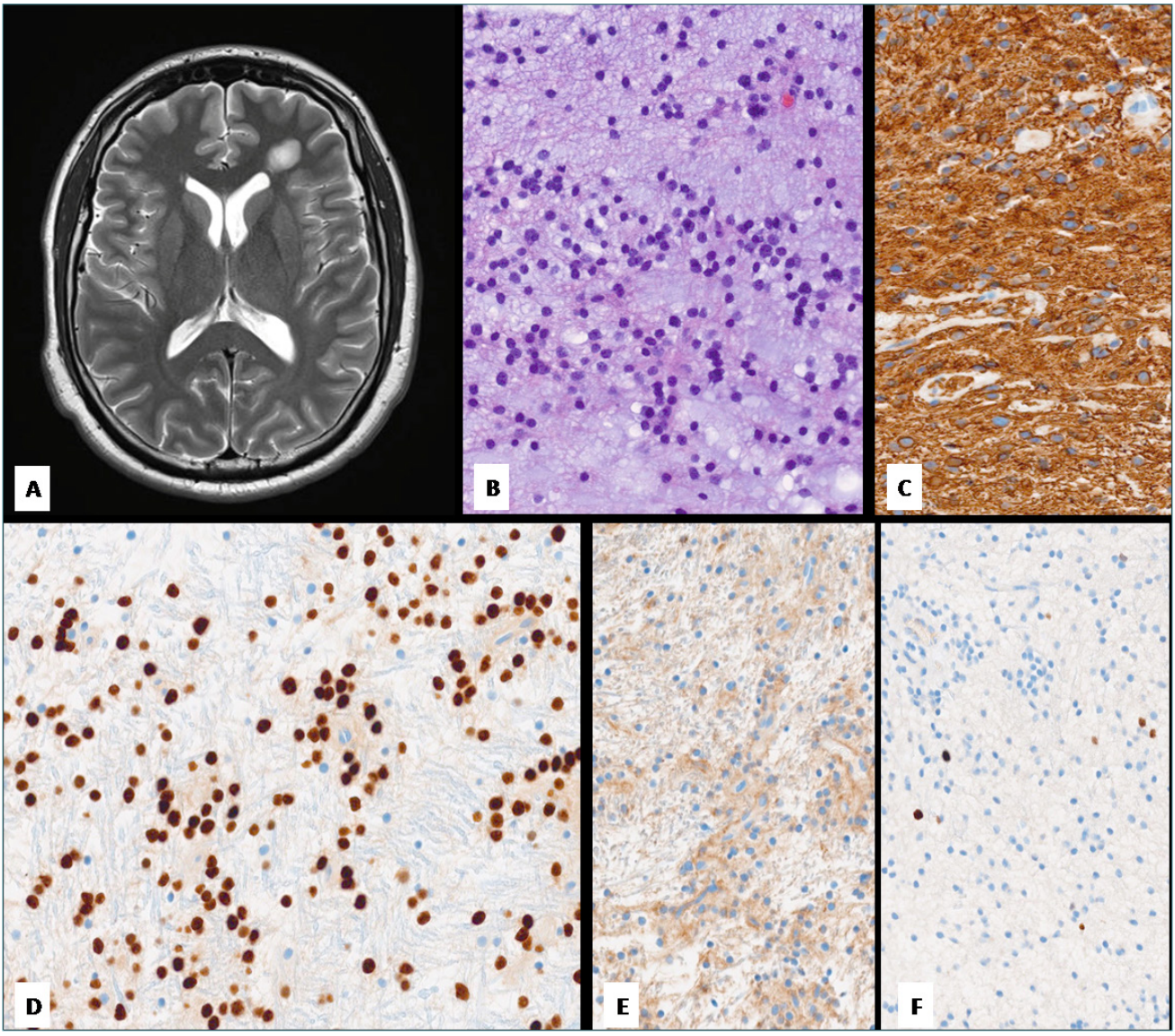

Figure 1. (A) T2-weighted axial MRI sequence demonstrating a non-enhancing, solid intra-axial lesion adjacent to the frontal horn of the left lateral ventricle, not inducing a significant mass effect and not associated with surrounding edema. Histopathological features of the tumor: (B) oligodendroglioma-like cells in myxoid stroma; (C) GFAP-positive cells; (D) OLIG2 immunoreactivity; (E) synaptophysin highlights perivascular arrangements; (F) Ki-67 index ~1%.

ronal tumor (RGNT), and pilocytic astrocytoma [3-7].

We acknowledge that the differential diagnosis includes a spectrum of low-grade tumors, both glioneuronal and glial. In our case, the absence of IDH, BRAF, and FGFR1 alterations, along with the identification of PDGFRA p.K385L, allowed for a definitive diagnosis. Given its rarity and potential for misclassification, increased awareness of MGT clinico-pathologic and molecular features is essential for neuropathologists and neuro-oncologists.

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Table I. Data selected in the literature review.

Author	Cases	Age	Gender	Anatomic site	Molecular profile	Treatment	Follow-up
Narvaez EO [8]	3	59 49 22	F M M	Septum pellucidum	N.A.	No treatment (1); total resection (1); partial resection (1)	3 months; uneventful
Chu J [6]	1	N.A.	M	Frontal lobe	PDGFRA p.K385L mutation	Surgery	8 months; uneventful
Gilani A [7]	1	37 days	M	Cerebral	PDGFRA p.K385L mutation	No treatment	N.A.
Stasenko A [5]	1	30	F	Septum pellucidum	PDGFRA p.K385L mutation	Subtotal resection	10 months; uneventful
Solomon DA [2]	4	Range 8-31	1 F 3 M	Septum pellucidum (3); corpus callosum (1)	3 cases: PDGFRA p.K385L mutation; 1 cases: PDGFRA p.K385I mutation	Total resection	N.A.
Gilani A [9]	1	10	F	Temporal lobe	PDGFRA p.K385L mutation	Total resection	N.A.
Kleinschmidt-DeMasters BK [3]	1	41	F	Midbrain tectum	PDGFRA p.K385L mutation	Total resection	N.A.
Caporalini C [4]	6	Range 2-19	2 F 4 M	Periventricular white matter of lateral ventricle (4); Septum pellucidum (2)	PDGFRA p.K385L mutation	Total resection (5); subtotal resection (1)	uneventful
Oktay K [10]	1	10	M	Septum pellucidum	PDGFRA p.K385L mutation	Total resection	12 months; uneventful
Lucas CG [1]	8	Range 6-65	3 F 5 M	Septum pellucidum (4); corpus callosum (3); periventricular (1)	6 cases: PDGFRA p.K385L mutation; 2 cases: PDGFRA p.K385I mutation	Total resection (3); subtotal resection (3); no treatment (2)	uneventful
Baisden [11]	10	Range 6-35	5 F 5 M	Septum pellucidum	PDGFRA p.K385L mutation	Total resection (6); subtotal resection (2); no treatment (2)	follow-up (n = 6; median, 14 months); uneventful

Abbreviations: F, Female; M, Male; N.A., Not available.

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