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LETTER TO THE EDITOR

Polymorphous low-grade neuroepithelial tumor of the young: case report of a newly described histopathological entity

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Introduction

Polymorphous low-grade neuroepithelial tumor of the young (PLNTY) is a recently described pathological entity featured by a specific histological, immunohistochemical and molecular profile combining an oligodendroglial-like component, a diffuse CD34 expression, and an alteration of the MAP-kinase signalling pathway. That entity was so far rarely described. We would like to report an additional case.

Case report

A healthy 33-year-old woman came to our hospital with a history of seizures of 18 months duration. The initial episode was a generalized tonic–clonic seizure during her first pregnancy. She thereafter suffered from repeated short episodes of partial seizures with hand automatisms, speech disorders and urine loss, lasting about 3–4 s. Frequency of such episodes worsened after delivery and she presented with a second generalized seizure one year after the initial episode. Neurological work-up was done including a brain magnetic resonance (MR) imaging revealing a right-sided cystic cortical lesion in the temporal lobe. The tumor appeared hypointense on T1-weighted images without enhancement after intravenous perfusion of contrast agent and hyperintense on T2/FLAIR images, mainly in cystic areas of the lesion. Positron emission tomography (PET) using labelled methionine as tracer highlighted increased uptake within the tumor (Fig. 1). Neuroradiological hypotheses were dysembryoplastic neuroepithelial tumor (DNET) versus ganglioglioma or gangliocytoma. Surgical excision was complete and uncomplicated. The histological examination showed a glial tumor of mainly cortical location displaying an infiltrative pattern. The tumor was heterogeneous with some oligodendroglial-like components, but also with astrocytic and more piloid (pilocytic) sub-areas. Some vague perivascular rosettes were observed at some places. Mitosis, necrosis, vascular proliferation, eosinophilic granular bodies, Rosenthal fibers, calcification, inflammation, and prominent cytonuclear atypia were all absent. The cortical architecture surrounding the lesion was preserved. The tumor was positive for the glial markers GFAP and Olig2. Nuclear expression of p53 and preserved nuclear staining for ATRX were observed, but no staining for IDH1 (R132H). Noteworthily there was an unusual intense and diffuse positivity for CD34 within the tumor, associated with a focally more ramified pattern of neuronal cells in the peritumoral cortex. Proliferation, as quantified by nuclear expression of the marker Ki67, was very low (Fig. 2).

Molecular analysis by Next Generation Sequencing (NGS) revealed a BRAF V600E mutation. All other genes of the panel were not mutated including IDH1 and IDH2. No 1p19q codeletion was detected at FISH test. The combination of theses findings strongly supported the diagnosis of polymorphous low-grade neuroepithelial tumor of the young (PLNTY).

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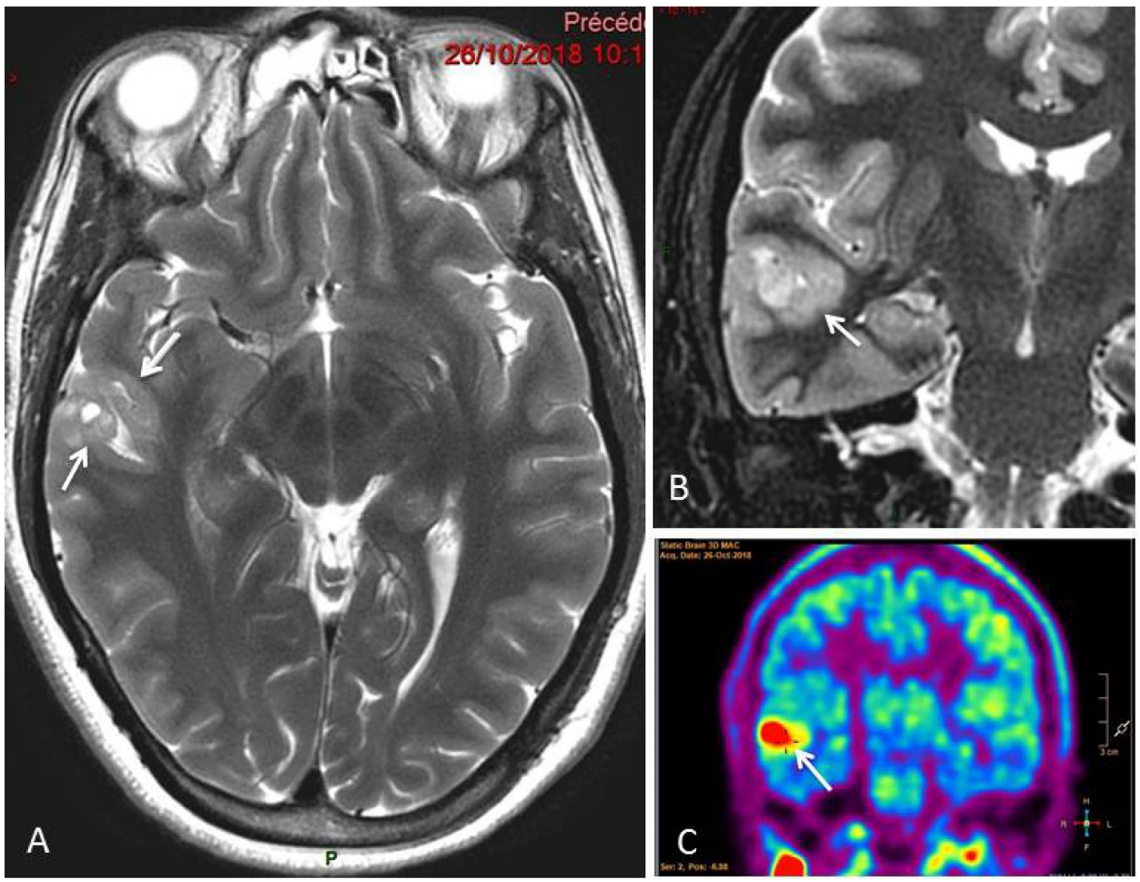

Fig. 1 Imaging work-up. **a** Axial transverse T2-weighted MR (magnetic resonance) image showing focally abnormal cortex (between arrows) in the right temporal lobe displaying disrupted sulcation and increased cortical thickness. **b** Coronal STIR (Short Tau Inversion-Recovery) MR image (magnified view) showing the thickened cortex in the depth of the superior temporal sulcus bridging the superior and the middle temporal gyri (arrow). **c** Coronal reformat of the PET (Positron Emission Tomography) imaging using labelled methionin (MET-PET) showing avid uptake of the tracer by the lesion (arrow)

Discussion

Polymorphous low-grade neuroepithalial tumor of the young (PLNTY) is a recently described epileptogenic histopathological entity with specific histological, immunohistochemical and molecular characteristics. The original description of the condition was made by Huse et al. on a series of 10 patients in 2017 [1]. Since, four others cases have been reported (Table 1) [2–4]. Similar lesions displaying extensive positivity for CD34 had been presviously described by Blumcke et al. in 2014 and termed "long-term epilepsy associated brain tumor" (LEAT) [5].

PLNTY more frequently affects children and young adults (range 4–57 years, mean age of 20,6), with a slightly female predominance (8F and 6 M reported so far). The majority of the lesions are localized in the temporal lobe (65%) [1–4]. FLAIR-hyperintensity and heterogeneous T2-hyperintensity are seen at MR examination. There is no mass effect or edema. Calcifications are frequently seen on computed tomography (CT) images. The neuroradiological differential diagnosis commonly includes oligodendroglioma, dysembryoplasic neuroepithelial tumor and focal cortical dysplasia [1].

Histological examination reveals a tumor with infiltrative appearance with intra- and inter-tumoral heterogeneity. The presence of an oligodendroglial-like population with typical perinuclear clear halo is a constant finding. It is associated with other components, such as astrocytic, fibrillary, fusiform cells and sometimes pleomorphic cells. Variable degrees of calcification are observed in the majority of the cases demonstrate. Some vague perivascular rosettes are occasionally described. There is no gemistocytic component and Rosenthal fibers are absent. Eosinophil granular bodies, endothelial proliferation, necrosis and prominent mitosis are all absent as well [1–5].

The tumoral cells show diffuse expression of Olig2 at immunochemistry and a more variable expression of GFAP. A strong and diffuse positivity for CD34 is typically present throughout the lesion and some neuronal cells with

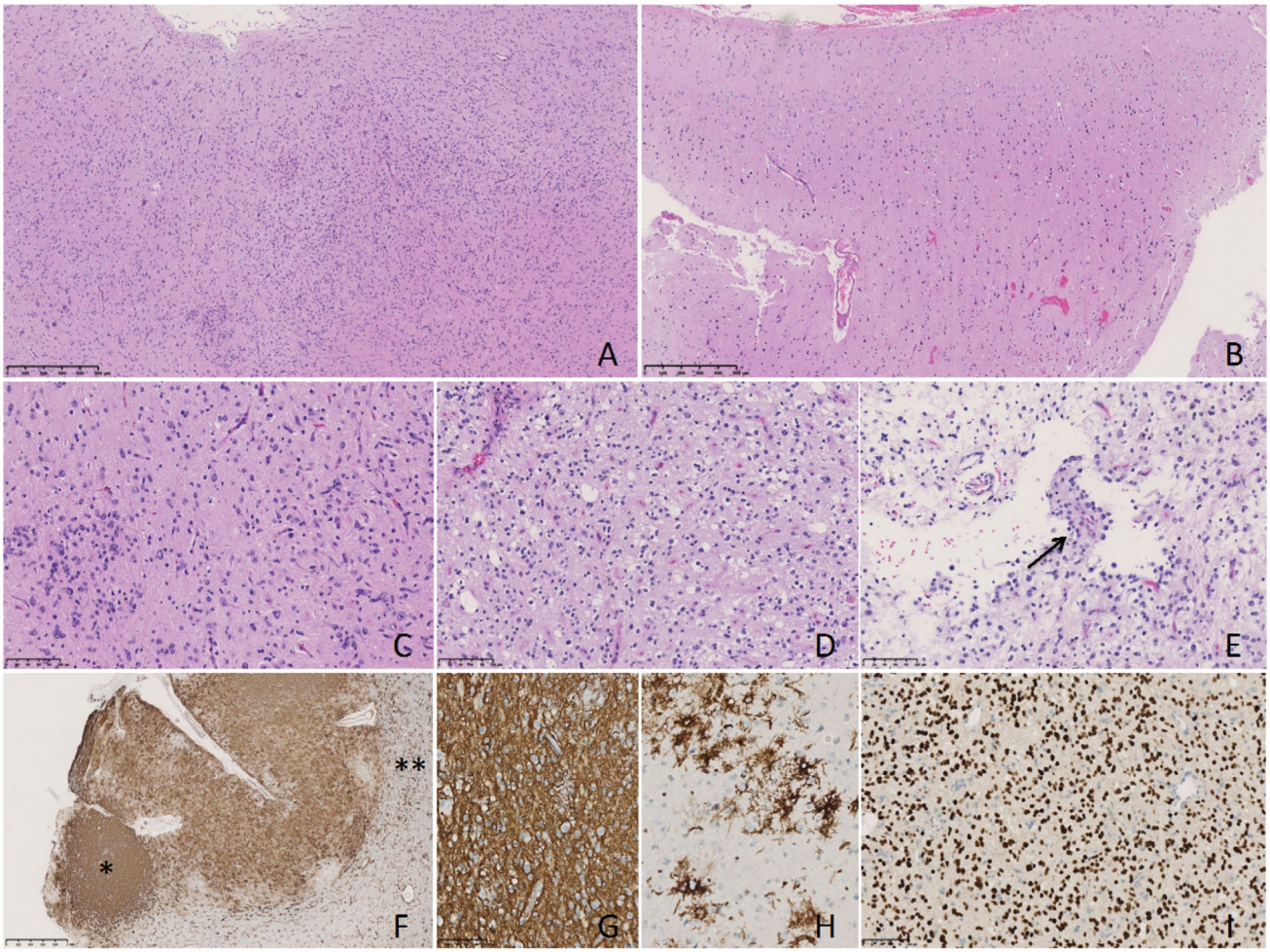

Fig. 2 Histological examination. The cortex is diffusely infiltrated by the tumor cells of the lesion (**a** HE×50) but the architecture is preserved in the surrounding parenchyma (**b** HE×50). At high magnification, the infiltrative pattern of the lesion is confirmed (**c** HE×200) by a heterogeneous population of cells, frequently showing an oligodendroglial-like pattern (**d** HE×200). Some vague perivascular rosettes are seen (black arrow, **e** HE×200). Immunochemistry shows an unusual positivity for CD34 (**f**×25), which is intense and diffuse within the tumor (*, **g**×200), with a ramified pattern of neuronal cells in the peritumoral cortex (**, **h**×200). Olig2 confirms the glial nature of the tumor cells (**i**×200)

ramifying CD34 staining are seen in the peripheral cortex. There is no staining of neuronal markers, like NeuN and chromogranin. Immunohistochemistry for IDH1 (R132H) is negative as well. The proliferation rate as quantified by Ki67 is very low [1–5]. No 1p19q codeletion is seen. From a genetic point of view, PLNTY shows alterations of the MAP kinase pathway, mainly with BRAF V600E mutation or FGFR fusion (mainly FGFR2-KIAA1598 and FGFR3-TACC3 fusions). These molecular aberrations occur in a mutually exclusive way. Up to now, about 45% of the genetically investigated lesions had a BRAF V600E mutation which was prominently found in young adults (16–33 years, mean = 24.2), whereas FGFR2 fusions are more likely to be observed in younger patients (4–12 years, mean = 8.5) [1–4].

Because of the very low proliferation rate, PLNTY is currently classified as grade 1 according to the WHO criteria. However, long-term follow-up is warranted to validate this classification [1].

In conclusion, PLNTY is a newly described variant of epileptogenic tumor with specific histological, immunohistochemical and genetic features occurring mainly in children and young adults.

Table 1 Main characteristics of patients with polymorphous low-grade neuroepithelial tumors of the young (PLNTY)

Case	Author	Age (years)	Gender	Location	Genetic
1	Huse	16	M	Temporal	BRAF V600E
2	Huse	18	F	Temporal	BRAF V600E
3	Huse	23	F	Temporal	BRAF V600E
4	Huse	17	F	Temporal	FGFR3-TACC3
5	Huse	4	M	Temporal	FGFR2-CTNNA3
6	Huse	9	M	Frontal	FGFR2-KIAA1598
7	Huse	10	M	Occipital	FGFR2-KIAA1598
8	Huse	23	F	Temporal	Non performed
9	Huse	32	F	Temporal	Non performed
10	Huse	24	F	Occipital	Non performed
11	Riva	57	M	Frontal	FGFR3-TACC3
12	Zhang	12	F	Temporal	FGFR2 fusion (?)
13	Zhang	12	F	Parietal	FGFR2 fusion (?)
14	Bitar	31	M	Temporal	BRAF V600E
15	Lelotte	33	F	Temporal	BRAF V600E

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments.

Informed consent Participant gave informed consent.

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