5 years.⁵ Lower overall survival in transplant patients has been associated with multicentricity and intracranial involvement.^{4,6}

The optimal management of EBV-SMT remains unclear. Surgical resection is the most common therapy.^{1,5,9} Other strategies have included involved field radiation therapy, stereotactic radiosurgery, systemic chemotherapy, mTOR inhibitors, and modification of post-transplant immunosuppression therapy.^{1,4,5} However, there is no evidence supporting superiority of one modality over another.

In the appropriate clinical context, awareness of this rare entity is important to avoid delayed or missed diagnosis. EBV-SMT may occur in a range of unusual sites with variable histological appearance, as illustrated in the present case. Differential diagnoses may include other spindle cell neoplasms such as Kaposi sarcoma, leiomyoma, and leiomyosarcoma, as well as other poorly differentiated malignancies. This case highlights the variable appearances and range of presentations seen in EBV-SMT.

Conflicts of interest and sources of funding: The authors state that there are no conflicts of interest to disclose.

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DOI: <https://doi.org/10.1016/j.pathol.2021.08.012>

Transformation of ganglioglioma to epithelioid glioblastoma, both with *BRAF* V600E mutation

To the Editor,

Ganglioglioma is a low-grade neuronal-glial tumour showing *BRAF* V600E mutation in 20–60% of cases. High-grade transformation of ganglioglioma is extremely rare, particularly in the absence of chemotherapy or radiation. The molecular basis of progressive disease is not well understood. Previous literature has documented transformation of *BRAF* mutant pleomorphic xanthoastrocytoma to *BRAF* mutant epithelioid glioblastoma, but such a link has not been well established in ganglioglioma.

The patient was a 19-year-old woman who presented in 2018 with a history of refractory epilepsy since the age of 11. Magnetic resonance imaging (MRI) showed a structural lesion within the left parahippocampal gyrus, considered most likely to be a developmental neoplasm such as a ganglioglioma. Surgical resection was performed. Histology showed a World Health Organization (WHO) grade I ganglioglioma, comprising a low-grade proliferation of astrocytes admixed with mildly dysmorphic neurons including rare binucleate forms (Fig. 1). Immunohistochemistry for GFAP highlighted astrocytic cells, while dysmorphic neurons were positive for chromogranin and NeuN. *BRAF* VE1 and CD34 showed patchy positivity in lesional cells. IDH1-R132H immunohistochemistry was negative and ATRX was retained. Ki-67 was 5%. Features were consistent with a ganglioglioma, WHO grade I. Molecular testing was not performed. Resection was favoured to be near complete on post-operative imaging.

The patient re-presented in 2020 with left-sided headache. MRI showed a 25 mm mass associated with the posterior margin of the resection cavity, compatible with recurrent tumour and highly suggestive of a high-grade glial neoplasm. Surgical resection was performed, with histology showing a markedly cellular lesion comprising sheets of malignant epithelioid cells with extensive necrosis and microvascular proliferation (Fig. 2). The cells showed hyperchromatic nuclei with coarse chromatin and eosinophilic cytoplasm. No low-grade component was identified. Tumour cells were positive for S100 and OLIG2, but negative for GFAP, SOX10 and AE1/3. *BRAF* VE1 stain was positive, with *BRAF* codon 600 mutation confirmed on polymerase chain reaction (PCR) analysis. Ki-67 was up to 40%. Features were consistent with an epithelioid glioblastoma, WHO grade IV. Next generation sequencing performed at Royal Prince Alfred Hospital Department of Neuropathology (Sydney) confirmed a *BRAF* V600E mutation, also detecting chromosome 7p gain and heterozygous CDKN2A/B deletion. No other pathogenic variants were detected (1p/19q co-deletion,

Fig. 1 Imaging and biopsy from 2018. (A) MRI showing cystic lesion within the left parahippocampal gyrus. (B) Dysmorphic neurons with low-grade astrocytic proliferation, consistent with ganglioglioma (H&E). (C) BRAF VE1 positivity. (D) CD34 positivity. (E) GFAP positivity in astrocytic component. (F) Ki-67 in 5% of the lesion.

EGFR amplification, IDH1 codon 132, IDH2 codon 172, H3F3A codons 27 and 34, TERT promoter). MGMT promoter was unmethylated.

Ganglioglioma, WHO grade I, represents around 1.3% of all brain tumours, with the median age of presentation between 8.5–25 years.¹ It is considered a benign tumour, with

97% recurrence-free survival rate at 7.5 years. Features such as high Ki-67 proliferation index and anaplastic changes in the glial component have been suggested to correlate with worse prognosis, but findings are inconsistent.

Genetic alterations in ganglioglioma most commonly involve genes activating the MAP kinase signalling pathway,

Fig. 2 Imaging and biopsy from 2020. (A) MRI showing irregular nodular heterogeneous enhancing mass in the left parahippocampal gyrus. (B) Sheets of malignant epithelioid cells with microvascular proliferation, consistent with epithelioid glioblastoma (H&E). (C) BRAF VE1 positivity. (D) S100 positivity. (E) Focal OLIG2 positivity. (F) Ki-67 in up to 40%.

which plays a role in the regulation of cellular proliferation. The most common genetic alteration found in ganglioglioma is *BRAF* V600E mutation, occurring in 20–60% of cases;¹ this mutation is also frequently observed in other low-grade neoplasms, including pleomorphic xanthoastrocytoma and pilocytic astrocytoma. Gain of chromosome 7 is also commonly seen.¹ Other mutations found in a cohort of 40 gangliogliomas using next-generation sequencing included alternative *BRAF* mutations, *BRAF* fusion, *KRAS* mutations, and *FGFR1/2* alterations.² The various alterations did not show significant association with disease progression, but analysis was limited by small case numbers.

High-grade transformation of ganglioglioma in the absence of radiation therapy is extremely rare. A review of the literature found 17 cases of malignant transformation of grade I ganglioglioma, with 14 of these describing transformation to anaplastic ganglioglioma (WHO grade III).³ Two of the remaining cases described transformation to glioblastoma without additional detail, with the final case showing transformation to anaplastic ganglioglioma, designated as WHO grade IV, with glioblastomatous change of the astrocytic component. Molecular testing in two cases showed *BRAF* V600E mutation in both the initial and transformed lesions by immunohistochemistry and sequencing.^{3,4} Epithelioid morphology in the transformed lesion was not described in either case. Two cases showed *H3F3A* (*p.K27M*) mutations in both lesions, with one case having both *BRAF* V600E and *H3F3A* mutations.^{4,5} Prognosis amongst the transformed tumours was universally poor with survival ranging from 4 to 42 months. A case series of 54 midline paediatric grade I gangliogliomas found *H3 K27M* and *BRAF* V600E mutations in five cases, with one showing progressive disease after 8 years.⁶ Although *H3K27M* alterations are required for the diagnosis of diffuse midline glioma WHO grade IV, this case series shows that they are not pathognomonic for, or invariably associated with, poor outcomes in glioneuronal tumours. Mutations in *H3F3A* have also been reported in high-grade neuroepithelial neoplasms with glial and dysplastic ganglion cell components.⁷ However, histone H3 alteration was not demonstrated in our case.

High-grade transformation of *BRAF*-mutant pleomorphic xanthoastrocytoma to *BRAF*-mutant epithelioid glioblastoma has been previously reported, but this has not been documented for *BRAF*-mutant ganglioglioma.⁸ One case report has described an anaplastic ganglioglioma with focal epithelioid cells at diagnosis, with *BRAF* V600E mutation demonstrated by immunohistochemistry in both components. The authors suggest that the lesion may have eventually evolved into epithelioid glioblastoma, but a temporal relationship was not clearly demonstrated.⁹

The pathogenesis of high-grade transformation of ganglioglioma remains poorly understood due to the paucity of cases in the literature, and relatively few cases detailing molecular associations. Identification of molecular alterations that may be associated with potential high-grade transformation could allow for closer clinical supervision or targeted therapy. This case highlights the potential for malignant transformation of ganglioglioma, in particular to epithelioid glioblastoma, and the need for clinical follow up.

Conflicts of interest and sources of funding: The authors state that there are no conflicts of interest to disclose.

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DOI: <https://doi.org/10.1016/j.pathol.2021.09.017>

Ovarian mesonephric-like adenocarcinoma: morphological diversity and histogenetic considerations of an unusual tumour

To the Editor,

Pathologists are familiar with various vestiges of the female apparatus. One of these vestiges, the mesonephric remnants, are frequently encountered in the cervix or the vagina and lesions developing from these remnants, such as mesonephric hyperplasia or adenocarcinoma, are rare but well-recognised. In 2016, McFarland *et al.*¹ described a similar type of adenocarcinoma arising in the ovary, and called it mesonephric-like adenocarcinoma (MLA). Since their description, only a few similar cases have been reported, but given the addition of a new chapter in the latest World Health Organization (WHO) classification, more studies are expected to arise, and more information is needed for this rare histological subtype.

A 74-year-old patient was incidentally found to harbour a left ovarian mass. The patient had a family history (daughter) of an ovarian low grade serous carcinoma. Total non-conservative hysterectomy with omentectomy, and peritoneal lesions and lymph node excision was decided. Macroscopic examination revealed a partly solid partly cystic (large cystic space) ovarian left mass measuring 19×14.5×11 cm,