CASE REPORT

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# A 19-year-old man with headaches and a first epileptic seizure and diagnosis of composite pleomorphic xanthoastrocytoma-ganglioglioma of the right temporal lobe

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## Abstract

Composite pleomorphic xanthoastrocytoma (PXA)–gangliocytoma (GC) is an exceptionally rare biphasic CNS tumour, often associated with epilepsy in young adults. The case report involves a 19-year-old male presenting with a first seizure and severe headaches. Neuro-imaging showed a heterogeneous, solid-cystic lesion with calcifications and vivid contrast enhancement in the right medial temporal lobe. Slight progression on follow-up MRI led to complete surgical resection. Histopathology confirmed a composite tumour with GC features (dysmorphic neurons, NeuN+, synaptophysin+, CD34+) and PXA components (pleomorphic astrocytes, GFAP+, Rosenthal fibres, eosinophilic granular bodies, foam cells, desmoplasia). Ki-67 was <1%, and p53 expression was limited to PXA. This case underscores the diagnostic challenges of mixed glioneuronal–astrocytic tumours and the importance of multimodal evaluation, including imaging, histopathology, and molecular profiling.

## Key words

pleomorphic xanthoastrocytoma, glioneuronal tumour, gangliocytoma, epilepsy in young adults

## INTRODUCTION

Gangliocytoma (GC) and pleomorphic xanthoastrocytoma (PXA) are rare tumours of the central nervous system, often associated with long-term epilepsy, and commonly found in the temporal lobe of young patients [1]. GC consists of mature ganglion cells and is classified as a World Health Organization (WHO) grade I neoplasm, with surgical resection as the preferred treatment [2]. PXA is a WHO grade II astrocytic neoplasm characterized by pleomorphic cells, eosinophilic granular bodies, and reticulin fibres [2]. Although PXA generally has a favourable prognosis, it has a higher recurrence rate than other paediatric gliomas, necessitating long-term monitoring [2]. The diagnosis of mixed tumours relies on histopathological examination, significantly influencing treatment strategies.

This report describes a 19-year-old man who presented with headaches and a first epileptic seizure associated with a solid and cystic mass in the right temporal lobe, diagnosed as a composite PXA-GC.

While both GC and PXA have been individually described, composite tumours containing both components are exceptionally rare. Their clinical behaviour, prognostic implications, and management remain poorly understood. This report adds to the limited literature by providing detailed clinical, radiological, histopathological, and molecular findings.

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## CASE REPORT

A 19-year-old male presented to the emergency department following his first epileptic seizure. On neurological examination, no abnormalities were detected; however, the patient complained of severe headaches. Routine laboratory tests were conducted, including a complete blood count, coagulation profile, and electrolyte analysis, all of which yielded normal results. Toxicology screening was negative, ruling out the influence of substances.

As the next diagnostic step, neuroimaging was performed. Computed tomography revealed a hypodense structure, likely of fluid density, in the medial part of the right temporal lobe, specifically within the hippocampal gyrus. Amorphous calcifications were observed near the lesion (Fig. 1A). Magnetic resonance imaging (MRI) demonstrated a heterogeneous, solid-cystic tumour in the same region (Fig. 1B). Post-contrast T1-weighted sequences showed intense enhancement in the solid portion of the lesion (Fig. 1C). The maximum tumour dimensions were approximately 33 × 12 × 10 mm. The lesion closely abutted the right internal carotid artery, involving approximately 50% of its circumference. Magnetic resonance angiography did not reveal any vascular pathology (Fig. 1D).

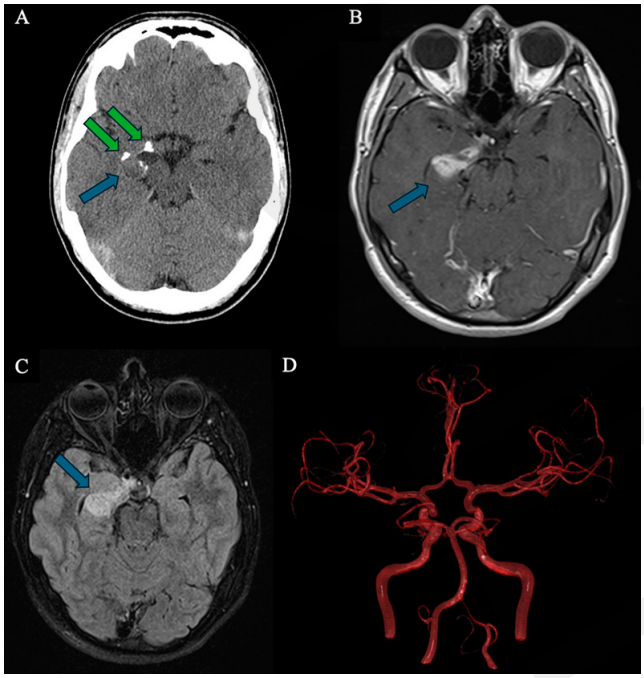


**Figure 1.** A) Computed Tomography (CT) – axial view of hypodense tumour with calcifications. Axial CT image showing a hypodense, solid-cystic lesion (blue arrow) with amorphous calcifications (green arrows) located in the medial portion of the right temporal lobe, adjacent to the hippocampal bend.
B) Magnetic Resonance Imaging (MRI) – axial T1-weighted image of heterogeneous lesion. Axial T1-weighted MRI reveals a heterogeneous solid-cystic mass (blue arrow) in the right temporal lobe, measuring approximately 33 × 12 × 10 mm.
C) MRI – Axial post-contrast T1-weighted image demonstrating enhancement. Axial post-contrast T1-weighted MRI shows marked enhancement of the solid portion (blue arrow) of the lesion in the right temporal lobe.
D) Magnetic Resonance Angiography (MRA) – evaluation of tumour vascularity. MRA image shows no evidence of abnormal or pathological vessels surrounding the lesion

Two months later, a follow-up MRI was performed, revealing a slight increase in lesion size to 33 × 14 × 20 mm. At the same time, magnetic resonance spectroscopy was carried out, which showed a slightly elevated choline peak, a decreased N-acetylaspartate peak, and a stable myo-inositol level.

Based on the imaging features, the differential diagnosis included dysembryoplastic neuroepithelial tumour (DNET) and GC. Given the tumour's characteristics and potential for progression, an elective surgical resection was performed, achieving complete tumour excision.

Histopathological examination of the resected tumour revealed the presence of two distinct components (Tab. 1). The first component was characterized by dysmorphic neurons (NeuN+, synaptophysin+) with numerous calcifications and a reactive glial component containing CD34+ projective neural precursors. The second component consisted of a mixture of neuro-like cells (NeuN+, synaptophysin+) with strongly reactive GFAP+ astroglial projections, numerous foam cells, eosinophilic granular bodies, and Rosenthal fibres. Scattered lymphocytic infiltrates and prominent desmoplasia were also present, along with increased Olig2 expression compared to the first component.

Molecular analysis for the BRAF V600E mutation was performed on formalin-fixed paraffin-embedded tumour tissue by the pathology department using immunohistochemistry with a mutation-specific monoclonal antibody, followed by confirmation with polymerase chain reaction. Both PXA and GC components tested positive for the BRAF V600E mutation. IDH1 was negative, and the Ki-67 labeling index was low (under 1%). Tumour protein p53 expression was present in the second component but absent in the first. Numerous CD68+ cells were observed, while ATRX expression was uncertain. Based on the histopathological and molecular findings, the first component was diagnosed as classic GC, and the second as PXA.

Following gross total resection, the patient has remained seizure-free and without neurological deficits and is under regular follow-up at the neurology outpatient clinic.

**Table 1.** Histological comparison of both tumour components

| First component – gangliocytoma | Second component – PXA |
|---|---|
| NeuN+ | NeuN+ |
| synaptofiz+ | synaptofiz+ |
| Olig2+ | Olig2+ |
| CD68+ | CD68+ |
| BRAF V600E | BRAF V600E |
| CD34+ | GFAP+ |
| LI Ki-67 <1% | LI Ki-67 <1% |
| | foam cells |
| | granular eosinophilic bodies |
| | Rosenthal fibers |
| | lymphocytic infiltrates |
| | desmoplasia |
| | p53+ |

## DISCUSSION

This case provides valuable insight into the diagnostic and clinical complexity of rare, composite tumours composed of PXA and GC, highlighting the importance of a multimodal diagnostic approach that includes imaging, histopathology, immunohistochemistry, and molecular analysis. The coexistence of two distinct tumour components in a single lesion poses significant diagnostic challenges, particularly when presenting with non-specific symptoms such as seizures and headaches in young patients. Due to the rarity of composite GC-PXA tumours, data on their clinical course, molecular characteristics, and optimal management are extremely limited.

In the presented patient, the seizure disorder was associated with a biphasic lesion consisting of PXA and classic GC, making diagnosis particularly challenging. Temporal lobe lesions causing epilepsy should be considered in the differential diagnosis, particularly long-term epilepsy-associated tumours (LEATs), including GG, DNET, angiocentric glioma, and isomorphic astrocytoma [1]. These slow-growing WHO grade I tumours often contain mixed glial and neuronal components, necessitating histopathological examination and immunohistochemistry for precise classification [2].

GC is a rare, low-grade glioneuronal tumour typically occurring in young individuals, with a predilection for the temporal lobe and strong contrast enhancement on imaging [3, 4]. Unlike GG, GC lacks neoplastic glial cells and GFAP expression. Differentiating GG from GC can be difficult due to overlapping features, but key markers, including CD34 and BRAF V600E mutation, aid in distinguishing them [5].

DNETs, another LEAT subtype, share similarities with GC but exhibit different molecular alterations, such as FGFR1 and PIK3CA mutations, rather than BRAF V600E [6, 7]. Compared to GC, GG exhibits less pleomorphism, lacks lipidized astrocytes, and has a more prominent neuronal component, often confirmed by the presence of eosinophilic granular bodies and Rosenthal fibres [8].

PXA is a rare circumscribed astrocytic glioma (WHO grade II or III) primarily affecting young patients and commonly presenting with long-standing seizures [2]. Imaging typically reveals cystic lesions with contrast-enhancing mural nodules [2]. Histologically, PXA contains pleomorphic astrocytic and mesenchymal-like cells, Rosenthal fibres, and eosinophilic granular bodies, distinguishing it from gangliogliomas [9]. BRAF V600E and CDKN2A/B mutations are key molecular markers, aiding in diagnosis. PXA has a higher recurrence rate than other paediatric gliomas, necessitating long-term monitoring even after complete resection [9]. The differential diagnosis of PXA includes GG, glioblastoma, pleomorphic sarcoma, and pilocytic astrocytoma [10].

Multinodular and vacuolating neuronal tumour (MVNT) is another glioneuronal tumour associated with epilepsy, classified as WHO grade I in 2016 [9]. MVNT typically appears as T2-hyperintense lesions with minimal enhancement and remains stable over time, usually not requiring surgical intervention. Despite similarities in disease course, the presented case lacked histopathological features consistent with MVNT. Overall, the case underscores the diagnostic complexity of mixed PXA-GC lesions, and highlights the importance of integrating imaging, histopathology, and molecular diagnostics for accurate classification and management [9]. It should be noted that the presented case of a composite glial tumour with PXA and GC components, represented a challenge both in diagnosis and treatment. Similar cases have been described in the literature as being exceedingly rare, such as in the report, where was analyzed uncommon glioneuronal tumours in adults [11].

The case report detailed the disease progression, from the initial epileptic seizure and MRI imaging (highlighting the solid-cystic nature of the lesion), through to the histopathological findings, including key markers such as GFAP, NeuN, synaptophysin, and CD34. A key diagnostic insight was the use of a proliferative Ki-67 index below 1%, which may indicate low malignancy potential in certain PXA variants [12]. Additionally, limited p53 expression in the PXA component may carry prognostic implications, such as variable disease progression depending on the presence of pTERT mutations [13].

The COVID-19 pandemic, especially long COVID consequences, may cause significant challenges to neuro-oncological care. [14, 15, 16] Numerous studies suggest that SARS-CoV-2 may directly or indirectly influence glioma biology. Viral spike proteins can bind to overexpressed receptors in glioblastoma cells, potentially activating oncogenic pathways and increasing tumour aggressiveness [17]. Furthermore, structural damage to the blood–brain barrier in brain tumours may facilitate viral neuroinvasion, complicating disease progression. Clinical observations also indicate that patients with gliomas who have contracted COVID-19 may experience accelerated tumour progression, with hyperaggressive and multifocal disease developing within weeks of infection. This highlights the importance of vigilant monitoring and prompt intervention, particularly in young patients presenting with atypical or rapidly evolving lesions. In this context, the case discussed gains particular significance: the early onset of epileptic seizures, rapid radiological progression, and low Ki-67 index may point toward a unique disease trajectory, potentially influenced by pandemic-related factors – such as delayed access to medical care or altered immune responses. The patient in the presented case did not report a history of COVID-19 infection, but the broader implications of SARS-CoV-2 on gliomas and glioneuronal tumours warrant further investigation.

Although this case does not directly address rural health disparities, it indirectly underscores the importance of access to specialized diagnostics and surgical care – particularly for rare central nervous system tumours. Accurate histological classification and timely intervention are critical to optimizing clinical outcomes [18]. In terms of imaging, the findings correspond with previously reported descriptions of the variable radiological characteristics of uncommon glioneuronal tumours [19]. The presented case aligns with these prior reports in terms of clinical presentation (first-time seizure and headaches), temporal lobe localization, and biphasic histological architecture. Notably, the presence of BRAF V600E mutation in both components supports a unified neoplastic origin, consistent with prior molecular findings in composite tumours. However, the absence of long-term epilepsy and the lesion's proximity to major vasculature represent distinctive features that contribute to the evolving understanding of the clinical spectrum of composite PXA-GC tumours.

## CONCLUSIONS

This case illustrates the diagnostic complexity of rare biphasic tumours such as composite pleomorphic xanthoastrocytoma – gangliocytoma. The integration of imaging, histopathology, and molecular testing – particularly the identification of the BRAF V600E mutation in both tumour components – was essential for accurate diagnosis. Although gross total resection was achieved, the risk of recurrence associated with the PXA component warrants long-term follow-up. The findings obtained highlight the importance of considering composite tumours in the differential diagnosis of temporal lobe epilepsy, and suggest that molecular profiling, including BRAF mutation status, may inform both prognosis and potential targeted therapies. This case report adds to the limited literature on mixed glioneuronal and astrocytic tumours and emphasizes the importance of a multimodal diagnostic approach in young patients presenting with seizures.

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