ISSN: 2634 - 680X

Journal of Clinical Case Studies Reviews & Reports

SCIENTIFIC Research and Community

Case Report

Open Access

An Unusual Case of Anaplastic Oligodendroglioma with Extensive Calcifications and IDH1 R132H Mutation in a Young Male from Pakistan: A Comprehensive Clinicopathologic Report

Nouman Asad[1]*, Mir Muhammad Rai[2]*, Sarah Arif[3], Ismail Mazhar[4] and Hammad Akram[5]

[1]House Officer, CMH Lahore, Pakistan, Pakistan

[2]House Officer, Lahore General Hospital, Lahore, Pakistan

[3]House Officer, Services Hospital, Lahore, Pakistan

[4]Internal Medicine, CMH Lahore Medical College, Lahore, Pakistan

[5]CMH Lahore Medical College, Lahore, Pakistan

ABSTRACT

Oligodendrogliomas are diffuse gliomas defined by IDH mutation and 1p/19q codeletion, typically associated with favorable prognosis compared to astrocytic tumors. We report a unique case of a 37-year-old Pakistani male presenting with new-onset seizures, found to have an anaplastic oligodendroglioma with unusually extensive calcifications on neuroimaging. Diagnosis was confirmed by histopathology, immunohistochemistry, and molecular testing. This case underscores the importance of integrating radiologic, histologic, and molecular data, and highlights the need for documentation of such cases from South Asia, where published reports remain limited.

***Corresponding author's**

Nouman Asad, House Officer, CMH Lahore, Pakistan, Pakistan.

Mir Muhammad Rai, House Officer, Lahore General Hospital, Lahore, Pakistan.

Received: September 08, 2025; **Accepted:** September 14, 2025; **Published:** September 22, 2025

Introduction

Oligodendrogliomas are relatively uncommon primary brain tumors, accounting for approximately 5–10% of all gliomas and 20–25% of all diffuse gliomas [1-6, 7-9]. They are characterized by their predilection for the frontal lobes and a tendency to occur in middle-aged adults, with peak incidence in the fourth and fifth decades of life and a slight male predominance [7]. Historically, the diagnosis of oligodendroglioma was based on histological features such as uniform round nuclei surrounded by clear perinuclear halos, giving the characteristic "fried-egg" appearance, and a delicate "chicken-wire" vascular network [4, 5]. However, reliance solely on histology often resulted in considerable interobserver variability and misclassification, particularly when differentiating oligodendrogliomas from astrocytomas or mixed oligoastrocytomas.

The introduction of molecular diagnostics revolutionized the classification and understanding of these tumors. The 2016 WHO classification first mandated the integration of molecular alterations—IDH1/2 mutation and 1p/19q codeletion-into the diagnosis of oligodendroglioma, a requirement that has been carried forward and emphasized in the 2021 WHO CNS5 classification [1, 3, 4]. This molecular definition distinguishes oligodendrogliomas from diffuse astrocytomas, which typically harbor IDH mutations without 1p/19q codeletion, and glioblastomas, which often lack IDH mutations and carry poorer prognoses [1, 2].

Molecularly defined oligodendrogliomas tend to exhibit a relatively favorable prognosis compared with other diffuse gliomas, with median overall survival frequently exceeding 15 years in low-grade cases, particularly when treated with combined chemoradiotherapy [2, 10, 11]. The presence of 1p/19q codeletion has also been strongly associated with enhanced chemosensitivity to the procarbazine, lomustine (CCNU), and vincristine (PCV) regimen, as demonstrated in pivotal randomized trials such as RTOG 9402 and EORTC 26951 [10, 11].

Radiologically, oligodendrogliomas often display distinct features. T2-weighted MRI sequences typically reveal hyperintense cortical or subcortical masses, while calcifications-best detected on CT or susceptibility-weighted MRI-are a hallmark imaging characteristic seen in up to 90% of cases [7, 8]. Extensive calcification, however, is uncommon and when present may mimic other pathologies such as cavernomas or oligometastatic lesions, complicating radiologic interpretation [9].

In South Asia, and particularly Pakistan, published data on oligodendrogliomas remain sparse, with most reports limited to histological diagnoses without full molecular profiling [10]. Limited access to advanced neuropathology and molecular diagnostic facilities has contributed to this underreporting. As such, molecularly integrated case reports from this region are crucial to highlight the clinical and pathological spectrum of these tumors and to align local practice with global standards of diagnosis and treatment.

Case Presentation

History and Examination

A 37-year-old right-handed male from Lahore, Pakistan, with no significant personal or family history of neurological or oncological disorders, presented to our neurology clinic with two generalized tonic–clonic seizures over the preceding two weeks. He also reported dull, intermittent bifrontal headaches for approximately three months, most pronounced in the early mornings, without associated nausea or visual disturbances. Subtle word-finding difficulty had been noted by his family about a week before the presentation.

Neurologic examination revealed mild expressive dysphasia, with otherwise normal cranial nerves, motor strength, reflexes, and sensory modalities. Fundoscopic exam showed no papilledema.

Imaging Studies

Given the new-onset seizures and language involvement, an MRI of the brain was performed:

T2-weighted and FLAIR axial images (Figure 1A) demonstrated a heterogeneous hyperintense mass centered in the right inferior frontal gyrus with extension into the insular cortex, showing poorly defined margins and mild mass effect.

Post-contrast T1 sequences revealed patchy, non-ring enhancement without necrosis.

Susceptibility-weighted imaging (SWI) identified multiple punctate blooming foci suggestive of mineralization.

To better characterize these, a non-contrast CT scan (Figure 1B) was performed, which revealed extensive coarse calcifications throughout the lesion, an unusual but known feature of oligodendrogliomas [12].

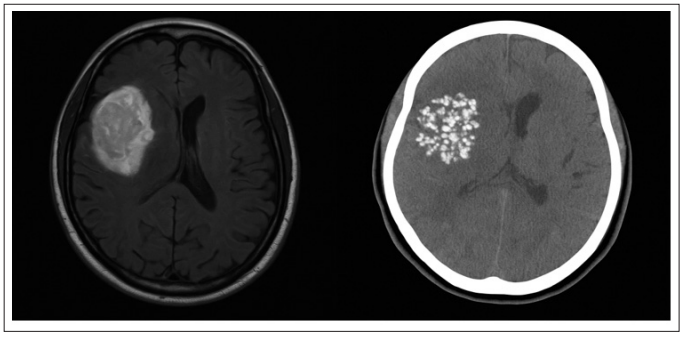

Figure 1A: Axial T2-Weighted MRI Showing Hyperintense Mass in Right Frontal Lobe.
Figure 1B: Non-contrast CT scan Showing Coarse Calcifications Scattered Throughout the Right Frontal Lobe Tumor-An Unusually Extensive Feature for Oligodendrogliomas

Surgery and Pathologic Evaluation

Given the imaging features and progressive symptoms, the patient underwent right frontal craniotomy with gross total tumor resection. Intraoperatively, the mass was firm, grayish, and notably gritty due to intratumoral calcifications.

Histopathology (H&E, Figure 2A)

Microscopic sections showed a highly cellular neoplasm composed of monomorphic round nuclei with clear perinuclear halos (fried-egg appearance) and a delicate chicken-wire capillary network.

There was brisk mitotic activity (>8 mitoses/10 HPF), focal microvascular proliferation, and multiple foci of dystrophic calcification.

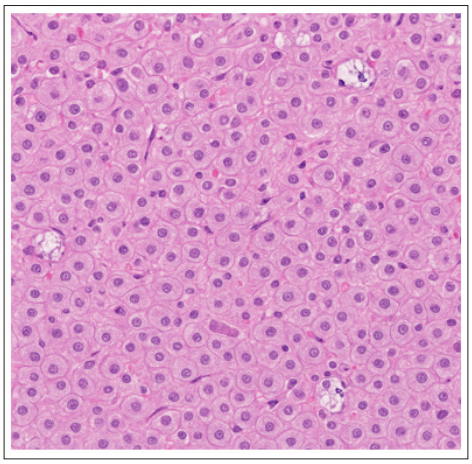

Figure 2A: H&E section (400x) Displaying Monomorphic Cells with Clear Halos and Delicate Vasculature.

Immunohistochemistry (Figure 2B)

Marker	Finding
IDH1 R132H	Strong diffuse nuclear positivity
ATRX	Retained nuclear expression
p53	Low (<5%) positivity
Ki-67	Elevated (~20% hot spots)
Olig2	Diffuse nuclear positivity
GFAP	Patchy positivity

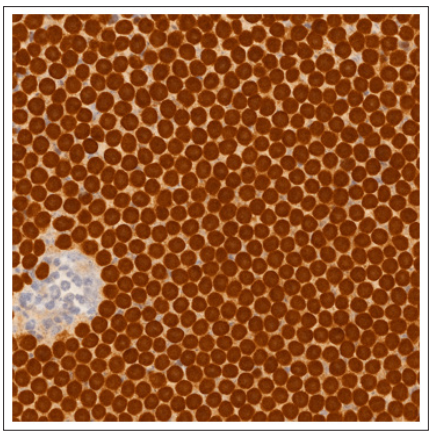

Figure 2B: IDH1 R132H Immunostain Demonstrating Strong Nuclear Positivity

Immunohistochemistry (Fig. 2B): IDH1 R132H was strongly positive[4]. ATRX was retained, p53 was low, and Ki-67 ~20%.

Molecular studies: 1p/19q codeletion confirmed by FISH, fulfilling WHO 2021 criteria[1,3,5]. MGMT promoter unmethylated[6].

Discussion

This case highlights an anaplastic oligodendroglioma (WHO grade III) with classic histology and molecular confirmation, but an unusually high degree of calcification [1, 3-5, 7-9].

Extensive calcification is characteristic of oligodendrogliomas but rarely this is pronounced, even in high-grade tumors [7-9]. Radiologically, such calcifications may help distinguish them from astrocytomas [12, 13, 14].

Histopathologically, the fried-egg morphology, delicate vasculature, and calcifications are well-documented diagnostic hallmarks [4, 5]. IDH1 mutation and 1p/19q codeletion remain indispensable for diagnosis and prognosis [1, 3, 4]. The retention of ATRX expression and absence of significant p53 accumulation further differentiate oligodendrogliomas from astrocytomas. Therapeutically, combined PCV chemotherapy with radiotherapy improves outcomes in anaplastic oligodendrogliomas [10, 11]. However, MGMT unmethylated status may reduce temozolomide responsiveness[6]. Novel approaches like IDH inhibitors (vorasidenib) show promise [13].

Prognostically, oligodendrogliomas represent one of the most favorable subtypes of diffuse gliomas, with survival often measured in decades [2]. Nonetheless, WHO grade, mitotic activity, necrosis, and Ki-67 index remain important modifiers of outcome [5, 6]. In our case, high mitotic activity and Ki-67 index (~20%) signaled aggressive potential despite extensive calcification. From a regional perspective, reports of molecularly confirmed oligodendrogliomas from South Asia are limited. This case underscores the importance of integrating advanced diagnostic modalities in Pakistan to align with international standards and improve patient care. Importantly, such detailed molecularly confirmed cases remain underreported in South Asia, underscoring the need for expanded diagnostic infrastructure and documentation in the region.

Acknowledgments

The authors would like to thank the patient and family

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest

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