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Case Report

High-grade astrocytoma with piloid features: MRI findings associated with a novel entity ☆,☆☆

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ABSTRACT

High-grade astrocytoma with piloid features is a newly defined brain tumor that requires DNA methylation profiling for diagnosis. Imaging features specific to this tumor have only recently been described in the radiological literature. We highlight the case of a 34-year-old man who presented with a 4-week history of headaches and light-headedness. Postresection, pathological analysis identified the tumor based on DNA methylation profiling, and the patient was started on adjuvant chemotherapy with Temozolomide. T2-weighted imaging showed a well-circumscribed cerebellar mass, which correlated with the pathology-reported glial tumor cells being elongated and piloid. T1-postgadolinium imaging showed heterogeneous enhancement of linear serpiginous areas, which correlated with regions of high microvascular density and vessels that showed thickening and hyalinization. Diffusion-weighted imaging and apparent diffusion coefficient mapping did not show significant diffusion restriction. Rosenthal fibres were absent. Given the specific imaging-pathology correlation, this report contributes imaging features associated with this novel diagnostic entity.

Introduction

High-grade astrocytoma with piloid features (HGAP) is a newly defined brain tumor that requires distinct DNA methylation profiling for diagnosis [1]. It often presents with high-grade piloid and/or glioblastoma-like histological features and was recently incorporated into the WHO 2021 CNS tumor classification [1]. It commonly affects patients with a median age of 41.5 years and with underlying neurofibromatosis type 1 [2,3]. It accounts for 1%-3% of all brain tumors and can occur anywhere in the CNS but most frequently originates in the posterior fossa (74%), typically affecting the cerebellum [2,3]. Diagnostic cues have recently been published, which largely correlate with our findings [4].

HGAP tumors are typically classified as IDH wild-type, ATRX-mutated, BRAF-V600 negative, and have alterations in the MAPK pathway [2,4]. Due to a paucity of reported cases,

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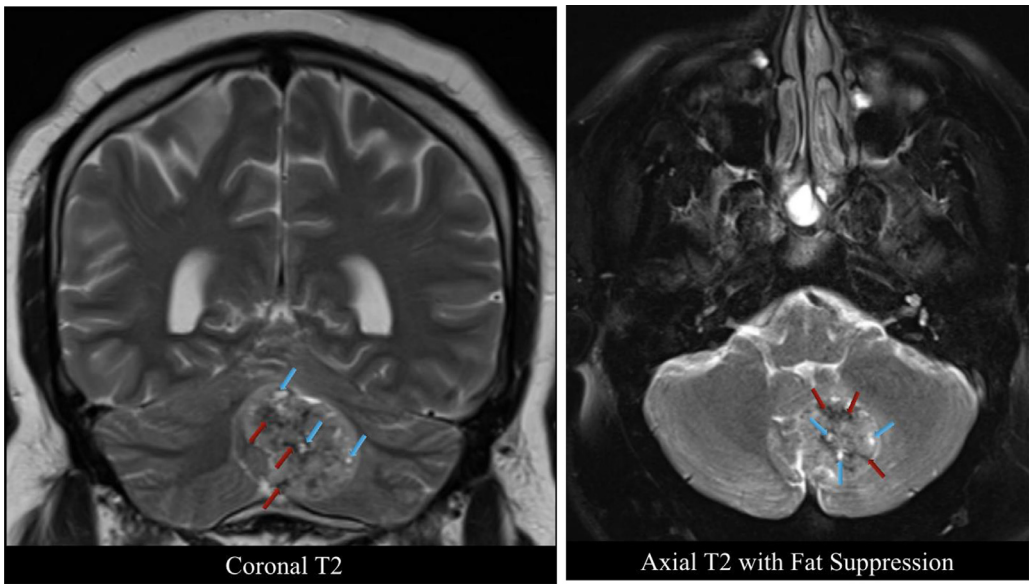

Fig. 1 – T2: well-circumscribed mass predominantly involving the left cerebellum with tiny hyperintense foci as well as some internal areas of T2 hypointensity.

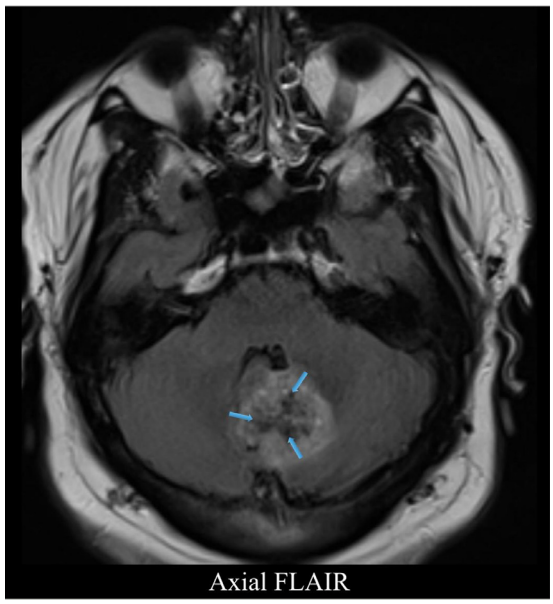

Fig. 2 – FLAIR: suppression of previously seen areas of T2-internal hyperintense foci.

the prognosis for these tumors varies between WHO Grade I to Grade IV [2]. Despite being a recognized diagnostic entity, imaging features specific to HGAP have yet to be adequately described in the radiological literature due to lacking imaging-pathology correlation. Current treatment options generally involve surgical resection with concurrent chemoradiotherapy [5]. This report aims to contribute toward establishing imaging features specific to HGAP by detailing the imaging-pathology correlation.

Case presentation

A 34-year-old man presented with a 4-week history of headaches and light-headedness that occurred with sudden standing. He experienced occipital pain, decreased appetite, occasional vomiting, and weight loss. His past medical history was unremarkable. The initial CT revealed a posterior fossa tumor with evidence of a local mass effect on the 4th ventricle. No frank herniation or obstructive hydrocephalus was identified. Preliminary differential diagnoses included primary brain tumors such as ependymoma, medulloblastoma, and pilocytic astrocytoma. An expedited referral was sent to neurosurgery.

In October of 2022, the tumor was surgically resected with satisfactory margins. The pathology report identified HGAP based on DNA methylation profiling. A multidisciplinary team of specialists started the patient on concurrent radiation with 59.4 Gy in 33 fractions and Temozolomide. After the first cycle of Temozolomide, the patient reported worsening nausea and further decreased appetite. This prompted dose adjustments, which resulted in symptomatic relief. His 11th and final dose of chemotherapy was received in November of 2023. With symptomatic relief, the patient is now looking to resume working again after neuropsychological testing. He is set to receive an MRI scan in 3 months and will continue following up with neuro-oncology.

Discussion

HGAP was first described by Reinhardt and colleagues in 2018 [6]. Today, pathology-based identifiers are relatively well-studied, however, radiological features are largely indetermi-

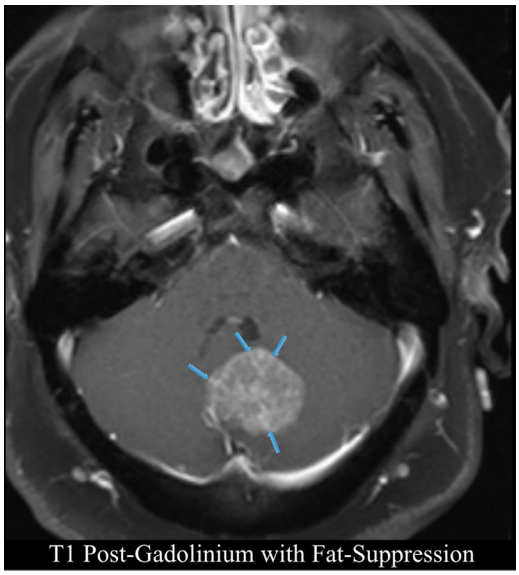

Fig. 3 – T1: heterogenous enhancement of cerebellar mass with tiny hyperintense foci and linear serpiginous areas.

nate due to HGAP being a relatively rare tumor. Further, only a limited number of cases have attempted to elucidate the imaging-pathology correlation necessary to further attribute imaging features to this diagnostic entity.

Histologically, several areas of high microvascular density were identified. A number of these vessels showed thickening and hyalinization, often seen in aggressive glioblastomas [7]. The glial tumor cells were smaller to more elongated and piloid in nature. There was evidence of previous microhemorrhages into the tumor, with residual focal hemosiderin deposits. Notably, Rosenthal fibres, typically seen in pilocytic tumors, were not evident. There was no tumor necrosis, no resetting, or other architectural patterns, and mitotic activity was sparse. Utilizing immunohistochemistry, IDH-1 was found to be immunonegative or wild-type; this is often seen in primary glioblastomas and confers resistance to treatment [8]. ATRX was immunonegative, indicating loss of normal nuclear wild-type immunopositivity, suggesting underlying ATRX mutation. BRAF V600 was negative, and MGMT promoter sequence methylation was not detected. These alterations in molecular characteristics are most associated with HGAP as described by previous literature, further supporting the imaging-pathology correlation [1,4].

The imaging features were correlated with the aforementioned and well-established histological features. T2-weighted imaging showed a well-circumscribed cerebellar mass which aligned with the glial tumor cells being thickened and hyalinized in nature (Fig. 1). There were also several internal areas of T2 hypointensity correlated with the presence of residual focal hemosiderin deposits seen in histology (Fig. 1). Additionally, there were several areas of internal T2 hyperintensity which are typically seen in cases of myelin and axonal loss [9] (Fig. 1). FLAIR showed suppression of internal hyperintense foci indicating a T2-FLAIR mismatch, a finding that is highly specific for IDH-mutant astrocytoma in adults, as opposed to other diffuse gliomas such as oligodendroglioma [10,11] (Fig. 2). T1-PG imaging showed heterogeneous enhancement of linear serpiginous areas which correlated with several areas of high microvascular density and vessels that showed thickening and hyalinization (Fig. 3). DWI and ADC mapping did not show significant diffusion restriction, typically associated with hypercellularity and indicative of aggressive glioblastomas [12] (Fig. 4).

The correlations made in this case reports were also described by Soni et al., who performed an image-centric review of HGAP to explore its association with neurofibromatosis type 1. Their study, which consisted of 8 patients, found that HGAP lesions were generally located in the posterior fossa, T1 hypointense, T2-hyperintense, and mostly without diffusion restriction. Additionally, they stated that all tumors were IDH1 wild-type, often with ATRX, CDKN2A/B, and often had NF1 gene alteration on histological examination [4]. Another study by Bender et al. described HGAP tumors as hypo- to isointense on native T1w and hyperintense on T2w MRI [1]. Both these studies corroborate our findings and indicate that characterization of this tumor may eventually be possible based on well-defined imaging features.

Conclusion

Given the apparent correlation between the radiological and histological reports, our case contributes to the sparse radiological literature on the imaging features associated with HGAP. While more studies are necessary to establish concrete radiological features, this report further strengthens

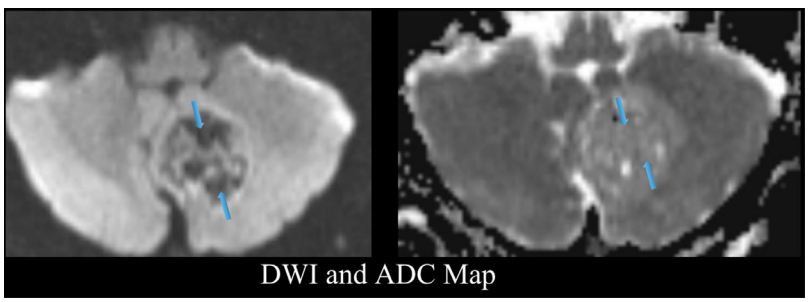

Fig. 4 – DWI and ADC: no significant diffusion restriction.

and corroborates recent studies that have correlated imaging-pathology features for this novel diagnostic entity. In the process, our report increases familiarity of this tumor among radiologists and may allow for the eventual diagnosis of HGAP primarily based on imaging features.

Patient consent

Written informed consent for publication was obtained from the patient.

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