Case Report

DNA methylation subtype and H3K27Me3 status of a case of clear-cell meningioma of the lateral sphenoid wing

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Abstract

We report a case of lateral sphenoid wing clear-cell meningioma in a 68-year-old male. Clear-cell meningiomas account for 0.2%–0.8% of meningiomas and are notorious for their aggressive clinical behavior. To our surprise, DNA methylation profiling and H3K27Me3 testing suggested an indolent meningioma subtype in our patient's case. This case illustrates discrepancies between histopathological and molecular-based classification systems and highlights the importance of considering the molecular profile of tumors during prognostication.

Keywords: Clear-cell meningioma, DNA methylation, H3K27me3

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INTRODUCTION

Clear-cell meningiomas are rare tumors accounting for only 0.2%–0.8% of all meningioma cases.[1] Classically, these tumors are adorned with glycogen-rich cells, which give rise to their distinctive "clear-cell" appearance.[2] Atop having a propensity for young adults and a predilection to grow in the cerebellopontine angle and lumbosacral regions, clear-cell meningiomas are also characterized by their aggressive clinical behavior.[2] Due to the rareness of these lesions, data on their genetic footprint remain scarce despite recent advances in molecular oncology.

Recent interest in meningioma genetics has prompted attempts to reclassify this group of tumors based on their molecular features.[3,4] To add to this body of knowledge, we present a case of clear-cell meningioma of the lateral sphenoid wing with its histo-molecular profile.

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CLINICAL PRESENTATION

Our patient is a 68-year-old male who presented with new-onset seizures. His comorbidities included atrial fibrillation and ischemic heart disease. Magnetic resonance imaging of the brain revealed a contrast-enhancing dural-based mass arising from the left lateral sphenoid wing with perilesional edema extending into the left temporal lobe [Figure 1a]. He underwent surgical excision through a left pterional craniotomy. The tumor was moderately vascular, and there was a clear plane of dissection which defined the brain–tumor interface. A Simpson II excision was achieved with the dura base coagulated. He recovered well with no immediate complications [Figure 1b]. The tumor was identified to be a clear-cell meningioma on histopathological examination. The patient received radiotherapy to the tumor bed 3 months postresection and remains well 6 months postresection.

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HISTOPATHOLOGY

Microscopic examination of sections from the formalin-fixed, paraffin-embedded tissue sample revealed a tumor with sheet-like and nested patterns. Occasional areas of hyalinized stroma and foci of perivascular hyalinization are also identified within the tumor. The polygonal tumor cells exhibited round-to-ovoid nuclei with mild nuclear pleomorphism [Figure 2a] and moderate amounts of clear cytoplasm containing abundant glycogen [Figure 2b and c]. Scattered mitotic figures are seen (1–2 mitoses/10 high-power fields). There were no areas of geographic necrosis, significantly increased cellularity, small cell change, or prominent nucleoli. There was also no brain invasion or tumor involvement of the underlying dura.

Immunohistochemical studies showed the tumor cells to be diffusely positive for vimentin and patchily positive for epithelial membrane antigen. The tumor cells were negative for Cam 5.2, alpha-inhibin, S100, and PAX8. H3K27me3 showed retained nuclear expression in the tumor cells [Figure 2d].

MOLECULAR SUBTYPING

Methylation profiling was conducted using Illumina Human Methylation 850k Array (Illumina, San Diego, CA, USA). Loss of chromosomes 1p, 3p, 12, and 22q was identified, and the MGMT promoter region was found to be unmethylated. The methylation profile was also aligned with the methylation classes previously established for meningioma.[3] These methylation classes have been shown to correlate with histology, mutations, cytogenetic alterations, and outcome. This patient's tumor specimen was classified under meningioma subclass ben-3, in which the risk of recurrence following complete resection is low.[3] This methylation class has already been shown to harbor frequently cases of microcystic, metaplastic, or clear-cell histology.[3]

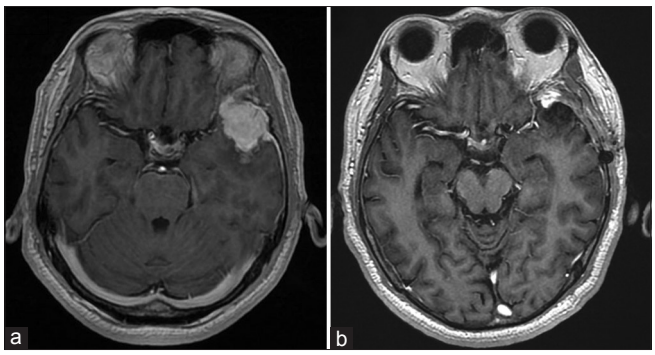

Figure 1: (a) Preoperative magnetic resonance imaging of the brain showing a left lateral sphenoid wing meningioma. (b) Postoperative magnetic resonance imaging image showing a Simpson II resection

DISCUSSION

Clear-cell meningiomas are classically associated with a higher risk of recurrence (29%–61%),[1,5,6] and there is a tendency to administer postoperative radiation in these cases. Although adjuvant radiotherapy improves recurrence-free survival in the World Health Organization Grade II atypical meningiomas,[7] this benefit has to be weighed carefully against the drawbacks of radiation-induced sequelae, especially in cases with good extent of resection (Simpson I–III). Despite their notoriety, it appears that not all clear-cell meningiomas display aggressive traits as there have been documented incidences in which long-term recurrence-free survival postresection was achieved without adjuvant radiotherapy. In the case of our specimen – a favorable DNA methylation profile, preserved H3K27Me3 expression and few mitotic figures per high-power field suggest a nonaggressive clinical phenotype, contrary to what is "classically" perceived of clear-cell meningiomas. The discrepancies between the histopathological and molecular classification systems for meningiomas such as that portrayed by this case suggest the need for molecular profiling to be taken into consideration during overall tumor prognostication.

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

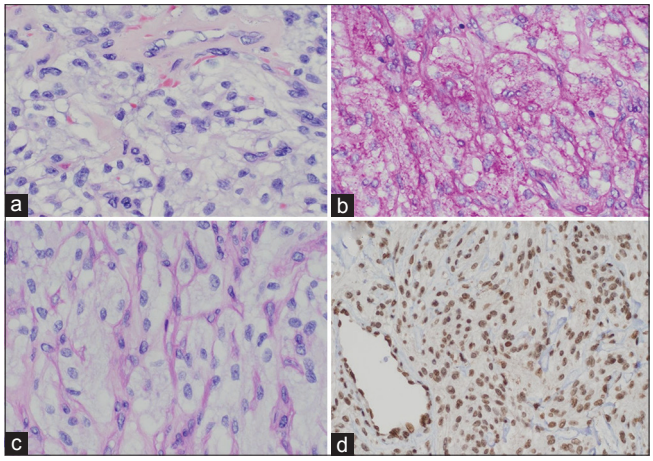

Figure 2: (a) In most parts, the tumor cells showed mild nuclear pleomorphism with round-to-ovoid nuclei and moderate amount of clear cytoplasm (H and E, ×400). Together (b and c) show increased cytoplasmic glycogen; ([b] periodic acid–Schiff stain without diastase pretreatment [×400]; [c] periodic acid–Schiff stain following diastase pretreatment [×400]). (d) H3K27me3 immunohistochemistry showed retained nuclear expression in the tumor cells, as well as in endothelial cells (H3K27me3 antibody, ×200)

be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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