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Case Report

Intracranial Mesenchymal Tumor: A Misdiagnosed Entity, about a Moroccan Case Report

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Abstract

Intracranial mesenchymal tumor (IMT) is a rare tumor that has recently been identified in children and young adults as a provisional entity with uncertain differentiation. It was previously referred to as the intracranial myxoid variant of angiomatoid fibrous histiocytoma; however, this term is not recommended in the latest World Health Organization (WHO) classification (5th edition, 2021).

IMT exhibits diverse histological features, including stellate and spindle cell morphology, mucin-rich stroma, hemangioma-like vasculature, and an epithelioid cell pattern with mucin-poor collagenous stroma. The tumor often presents polyphenotypic immunoprofiles, frequently showing positivity for desmin, EMA, and CD99, which can complicate diagnosis.

Due to its rarity, the biological behavior, outcomes, and management remain undefined in the literature.

Herein, we present a new case initially suspected to be a cavernoma based on preoperative imaging. It was misdiagnosed as a meningioma during intraoperative frozen section consultation. This case illustrates the diagnostic challenges encountered in pathological analysis.

Keywords: *Intracranial; Mesenchymal Tumor; Morphology; Pitfalls; Case Report*

Introduction

Intracranial myxoid tumors (IMTs) are rare brain neoplasms characterized by gene fusion between the FET family of RNA-binding proteins (EWSR1 or FUS) and one of the cyclic AMP response element-binding (CREB) family transcription factors (CREB1, ATF1, or CREM) genes [1].

This fusion is involved in various tumoral entities, and their correlations with tumor phenotypes have not been fully clarified. Among them are angiomatoid fibrous histiocytomas (AFH), clear cell sarcomas (CCS), clear cell sarcoma-like tumors of the gastrointestinal tract, and primary pulmonary myxoid sarcomas (PPMS) [2]. The wide morphological and molecular overlap of IMTs with soft tissue AFH raises the question of whether these tumors represent a spectrum of the same disorder or not [2]. Recent studies [2,3] based on DNA methylation profiling have uncovered heterogeneity within what has previously been considered a single tumoral entity and clearly distinguished intracranial tumors from their soft tissue counterparts [2].

This tumor has been reported to show low proliferation indices [4], but the clinical features, patient outcome, and optimal treatment strategies remain largely undefined [3]. Gross total resection could be the key prognostic factor for better disease control [1].

Case Presentation

Clinical presentation

This is a 30-year-old man who did not have any prior medical history. He had drug-resistant seizures. He was admitted for neurological consultation for the appearance of right hemiplegia, without disturbance of consciousness.

Diagnostic assessment

The MRI showed a well-defined, extra-axial tumor in the left parietal lobe. Contrast-enhanced images revealed that the lesion was attached to the dura mater and was diagnosed as a cavernoma (Figure 1).

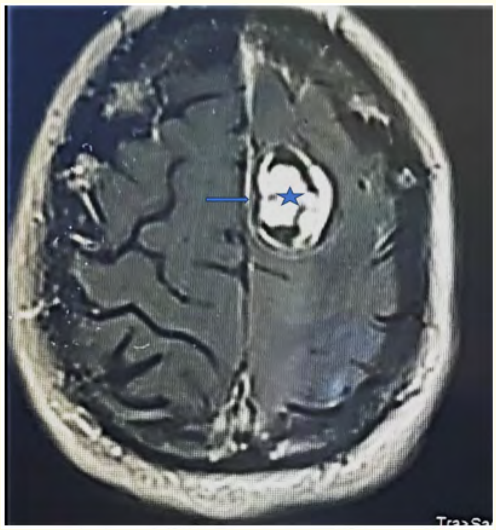

Figure 1: *Cerebral magnetic resonance imaging: showing a well-defined parasagittal tumor in his left parietal lobe (star) with attachment to the dura mater (arrow).*

Management

A surgical exploration was indicated. Intraoperative frozen section analysis of the tumor biopsy led to the diagnosis of meningioma. Thus, a total surgical resection of the mass was performed.

Histologically, the tumor appeared richly vascularized with a haemangioma-like pattern, forming a multilobulated structure within a rich myxoid stroma. The proliferation contained uniform ovoid to spindled cells arranged in reticular, cord-like, and epithelioid-like patterns. Rhabdoid cells were also observed. At the tumor periphery, we noted a dense lymphoplasmocytic infiltrate. There was no mitosis, necrosis, or microvascular proliferation (Figure 2).

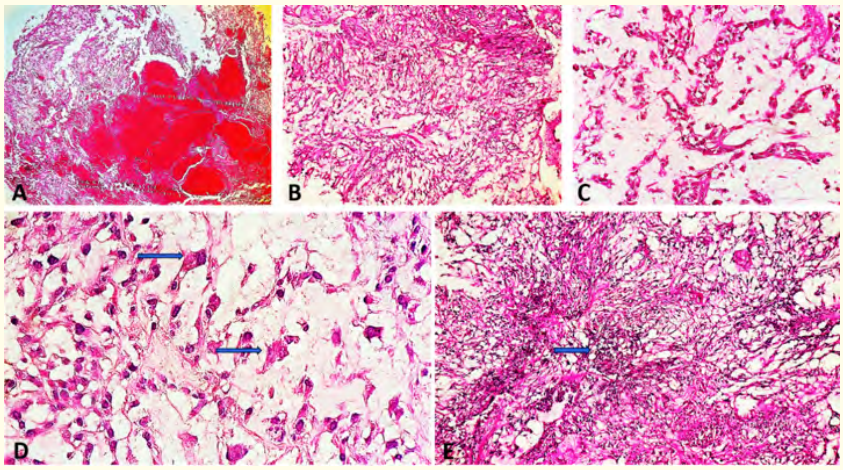

Figure 2: *Histological microphotography: showing a richly vascularized tumor with a haemangioma-like pattern (A) (Hematoxylin-Eosin x10). The proliferation contained uniform ovoid to spindled cells arranged in reticular and epithelioid-like patterns within a rich myxoid stroma (B, C) (Hematoxylin-Eosin x20). Rhabdoid cells (D, arrow) (Hematoxylin-Eosin x40) and dense lymphoplasmocytic infiltrate were also observed (E, arrow) (Hematoxylin-Eosin x20).*

Immunohistochemically, the tumor cells were diffusely positive for Desmin (skeletal muscle marker) and partially positive for EMA (epithelial membrane marker). INI1 (Rhabdoid tumor marker) expression was intact, and the Ki-67 proliferation index was low, estimated at 3% (Figure 3). Moreover, they were negative for vascular markers such as CD31, ERG, and CD34. STAT6 (Solitary fibrous tumor marker), PS100 (neuroid marker), Alpha Inhibin (Hemangioblastoma marker), Brachyuries (Chordoma marker), CKAE1/AE3 (epithelial marker), glial marker (GFAP, Olig2), RP (meningioma marker), and MUC4 (Low grade fibromyxoid sarcoma marker).

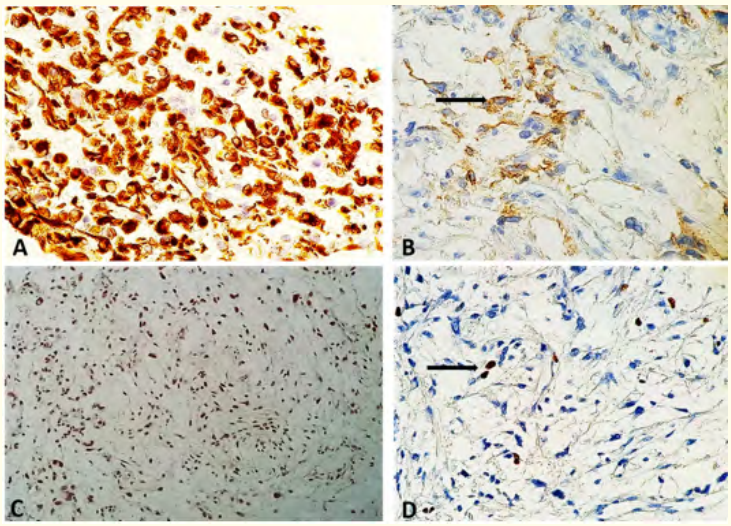

Figure 3: *At immunohistochemistry, the tumor cells express diffusely the Desmin (A) and partially the EMA (B, arrow). INI1 expression was intact (C), and the Ki-67 proliferation index was estimated at 3% (D, arrow).*

Based on the histological and immunohistochemical features, a diagnosis of intracranial mesenchymal tumor (IMT) was established. Unfortunately, the FET-CREB fusion could not be investigated due to the lack of a molecular platform at our institute.

Follow-up

The patient had a favorable postoperative follow-up and showed no signs of recurrence for the past 36 months.

Discussion

Intracranial Mesenchymal tumors (IMTs), first reported in 2008 by Dunham., *et al*. [5] as "intracerebral angiomatoid fibrous histiocytoma" (AFH), are rare brain neoplasms and genetically defined by gene fusions of the FET family of RNA-binding proteins to the CREB family of transcription factors [1]. Identical FET-CREB fusions are recurrently found in extracranial AFH, clear cell sarcoma of soft tissue, clear cell sarcoma of the gastrointestinal tract, primary pulmonary myxoid sarcoma, hyalinizing clear cell carcinoma of the salivary gland, and a subset of malignant mesotheliomas lacking BAP1 and NF2 alterations [3,6]. The controversy at the time revolved around whether this was a new entity or an intracranial variant of myxoid angiomatoid fibrous histiocytoma (AFH) or other FET-CREB fusion-driven neoplasms [3]. Notably, AFH had not been previously described in the central nervous system [7,8], additionally, ultrastructural analyses revealed the presence of junction-type desmosomes, zonula occludens, and zonula adherens, suggesting that the tumor cells of IMTs may have arachnoidal origin for IMT tumor cells [9]. Findings from DNA-methylation profiling analyses have further demonstrated that FET-CREB fusion-positive IMTs are distinct from AFH of soft tissues [9]. Consequently, the term intracranial myxoid variant of Angiomatoid Fibrous Histiocytoma is not recommended in the latest edition of the World Health Organisation (WHO) classification (5th edition 2021).

Due to the rarity of this tumor, clinical features, patient outcomes, and optimal treatment strategies remain largely undefined [3]. The study conducted by Sloan., *et al*. [3] demonstrated that IMTs occur with a female predominance, mostly in the second and third decades of life (median age of 17 years). These tumors mainly occur as extra-axial or intraventricular types and can develop anywhere along the neuroaxis, including the falx, tentorium, cerebral convexities, skull base, spinal cord, lateral ventricle, and third ventricle.

Radiologically, they are typically contrast-enhancing masses, well-circumscribed with solid and cystic growth patterns, often have pronounced peritumoral edema [3], and frequently connect with the dura mater [4].

The broad morphological spectrum of these tumors and the fact that their features overlap with other tumor entities make diagnosis challenging. Histologically, IMT demonstrates a wide morphological spectrum, usually including a mucin-rich stroma or mucin-poor collagenous stroma. Architecture ranges from syncytial or sheet-like growth to reticular cord-like structures, and a subset of tumors contains fibrous septa separating nodules of tumor cells. Not all examples contain myxoid stroma. Tumor cell morphology varies from epithelioid/rhabdoid cells to stellate/spindle cells to monotonous round cells. Mitotic activity is generally low. Haemangioma-like collections of dilated thin-walled vessels are a frequent finding. Dense lymphoplasmocytic cuffing at the tumor periphery or a long fibrous septa. Additional morphological features can include meningothelial-like whorls [10].

The immunohistochemical profile is also variable, with the most commonly reported immunoreactivities being for EMA, Desmin, and CD99. Histiocytic markers (CD68, CD163) and Vimentin, when assessed, are positive. Variable positivity has been reported for synaptophysin, PS100, and MUC4. INI1 is retained, and the Ki-67 labeling index is generally low [10].

The differential diagnosis typically includes meningioma, particularly the choroid, microcystic, or rhabdoid types [10]. Furthermore, the frequent expression of EMA in these tumors can further confound the diagnosis of meningioma. Fortunately, these tumors are negative for the specific meningioma marker SSTR2A and positive for desmin, which can be used to distinguish them immunohistochemically [3].

The extra-axial location and prominent collagenous stroma can also raise the diagnostic possibility of solitary fibrous tumor/hemangiopericytoma. However, IMTs lack nuclear STAT6 immunopositivity. They are characterized by the expression of Desmin, but lack expression of other skeletal muscle markers, including myogenin and MyoD1, that allow distinction from rhabdomyosarcoma. They uniformly have an intact expression of INI1, which distinguishes them from atypical teratoid/rhabdoid tumors [3].

IMT can also be confused with myxoid soft tissue tumors, such as myxoma, myxoid liposarcoma, myxoid chondrosarcoma, low-grade fibromyxoid sarcoma, and myxoid undifferentiated pleomorphic sarcoma (myxofibrosarcoma) [11].

In our case, in the absence of molecular analysis confirming the FET-CREB family fusion, the diagnosis of IMT was based on distinctive histological and immunohistochemical features. Using a broad immunohistochemical panel leads us, in practice, to eliminate the other differential diagnoses.

In terms of clinical outcomes, these tumors demonstrate a propensity for local recurrence and occasionally dissemination or metastasis, leading to mortality. While the optimal treatment strategy remains to be defined, adjuvant radiation may be a consideration, given the propensity for local recurrence, especially for incompletely resected tumors [3].

Conclusion

Intracranial mesenchymal tumor is a rare and recently described entity in the central nervous system. Characterized by significant histological and immunohistochemical diversity. They pose considerable challenges for pathological diagnosis. By augmenting the existing literature, we can illuminate the unique morphologic features and biological behaviors, ultimately enhancing our understanding and guiding future clinical management.

Disclosures

The authors did not receive any funding for the preparation of this case report. This article is an original work that is not being considered or reviewed by any other publication and has not been published elsewhere in the same or a similar form. All authors of the manuscript have read and agreed to its content and are accountable for all aspects of the accuracy and integrity of the manuscript.

Declaration of Patient Consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of Interest

There are no conflicts of interest.

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