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Case Report
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A Rare Case of Late Recurrence of Inflammatory Myofibroblastic Tumor Involving the Meninges and Skull

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Abstract

Inflammatory Myofibroblastic Tumors (IMT) is a heterogenous group of neoplasms characterized by the proliferation of myofibroblastic spindle cells with inflammatory infiltrates. They exhibit a wide spectrum of histologic and clinical features. Accurate incidence is unclear as they have been described under different terms, including "inflammatory pseudotumor," "inflammatory myofibroblastic tumor. IMTs can recur and rarely show invasive features. Given high rate of recurrence, especially with CNS involvement, a close monitoring is needed. As our case illustrates, very late recurrences are possible, even after resection of localized disease, thus suggesting a need for long term follow up and surveillance imaging.

Keywords: Brain neoplasms; Central nervous system; Inflammatory myofibroblastic tumor; Recurrence

Introduction

Inflammatory Myofibroblastic Tumors (IMT) is a heterogenous group of neoplasms characterized by the proliferation of myofibroblastic spindle cells with inflammatory infiltrates. They exhibit a wide spectrum of histologic and clinical features. Accurate incidence is unclear as they have been described under different terms, including "inflammatory pseudotumor," "inflammatory myofibroblastic tumor" [1,2]. IMTs are of mesenchymal origin and most commonly present in the lung and abdominopelvic region but can affect any part of the body. They have a predilection for children and young adults, though they can occur over a wide age range. IMTs usually follow a benign clinical course but malignant transformations have been reported. About 50% cases have been found to express chromosomal translocations involving the ALK gene locus on 2p23, suggesting that these tumors are of neoplastic origin rather than a result of reactive or reparative process [1]. IMTs of the central nervous system are rare and tend to arise from meningeal structures. Here, we report a case of IMT in the CNS with recurrence 15 years after a gross total resection.

Case Presentation

A 71-year-old right-handed man presented as a transfer from his local hospital with a sudden onset of confusion, mixed expressive and receptive aphasia, and right arm weakness. He had a past history of a left frontal skull lesion (Figure 1A) that was surgically resected 15 year prior to this admission, with pathology findings consistent with Inflammatory Myofibroblastic Tumor (IMT). After the resection, he was started on phenytoin for seizure prevention and followed for at least six years with no recurrence of the tumor.

His presentation raised a concern for a seizure and as he did not respond to benzodiazepines, he was given tissue Plasminogen Activator (tPA) for concern for stroke at his local hospital. Upon arrival to our hospital, his right sided weakness had improved. CT head raised concern for a possible subdural hemorrhage and he was given amino caproic acid for tPA reversal. CT head venogram demonstrated superior saggittal venous sinus thrombosis and on further evaluation with MRI venogram, the sinus thrombosis appeared to be chronic in nature. The possible SDH was more consistent with a plaque meningioma. MRI head with and without contrast revealed diffusely gadolinium enhancing lesion involving the dura along the left convexity, the falx and the right frontal region (Figure 1B), concerning for a plaque meningioma *vs.* recurrence of his tumor. CT chest, abdomen and pelvis showed no evidence of metastasis. He underwent an open left sided dural biopsy. Histopathology revealed dense inflammatory infiltrate comprised of plasma cells, lymphocytes and scattered eosinophils, consistent with recurrent IMT (Figure 2). Given the extension of the lesion, surgical removal was not optional. Testing for ALK mutation was negative.

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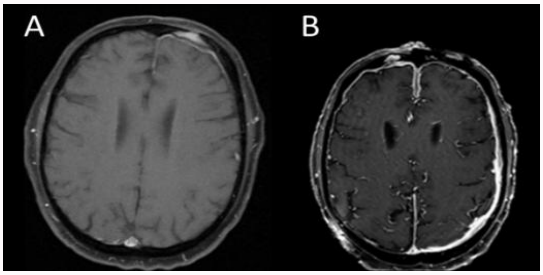

Figure 1: A) Axial T1 post-contrast MRI image from 2004 demonstrating an enhancing mass-like skull- based lesion in the left frontal convexity with underlying dural enhancement along the left frontal lobe. B) Axial T1 post-contrast MRI image from 2019 demonstrating diffuse extra-axial enhancement along the entire left frontal convexity, falx, and right frontal convexity.

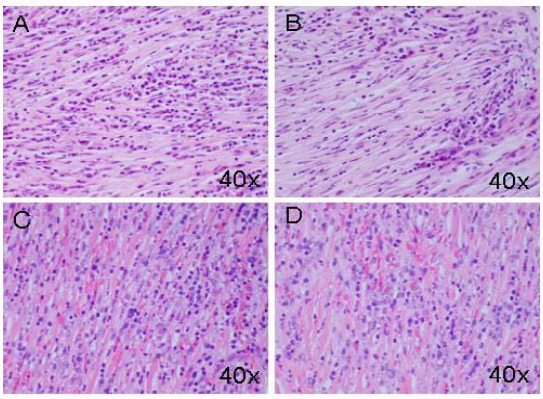

Figure 2: H&E images of the patient's primary tumor (A&B) and recurrence (C&D) show a spindled cell lesion with an associated dense inflammatory infiltrate consisting of lymphocytes, prominent plasma cells, and scattered eosinophils consistent with inflammatory myofibroblastic tumor. Although the spindled cell component is more prominent in the primary tumor, both specimens show the same mixed inflammatory infiltrate. Molecular testing in the patient's recurrence was negative for the presence of an ALK translocation.

The patient was treated with involved-field radiation therapy, which he tolerated well. He remains on anti-epileptic therapy with surveillance MR imaging.

Discussion

We present a rare case of adult onset IMT with diffuse meningeal recurrence fifteen years after local dural and skull based resection. IMTs are classified as tumors of intermediate biological potential by the World Health Organization classification. They were initially considered benign and non-neoplastic lesions, but were later found to have a potential for recurrence and a small risk of distant metastasis [2]. The recurrence rate varies between 2 and 25% and is higher in IMTs involving the CNS, with rates reported as high as 40% within two years [1-3].

IMTs rarely involve the central nervous system and thus far only 100 cases have been reported. Symptoms are usually non-specific and vary according to the location and the extend of involvement. More than 60% of intracranial IMTs arise from dural and meningeal structures, which might be related to the rich vascular fibrous membrane of the dura mater. On neuroimaging, IMTs show a low signal enhancement after contrast administration on both T2 and T1 weighted images. These features can overlap several other conditions, including a plaque meningioma, sarcoidosis, lymphoma and pachymeningitis. Adjacent leptomeningeal involvement and dural venous sinus thrombosis is frequently seen, as our case presents [4]. Given the non-specific radiological findings, the diagnosis is predominantly based on histopathological features, characterized by myofibroblastic spindle cell proliferation with inflammatory infiltration of lymphocytes, plasma cells and eosinophils along with fibrosis.

Overexpression of Anaplastic Lymphoma Kinase (ALK), caused by structural rearrangements of the ALK locus on chromosome 2p23, has been reported in approximately 50% of case and is associated with higher rates of local recurrence of IMT-CNS (33% *vs.* 9% respectively). Most recurrences in ALK-positive patients occur within two years after surgery. ALK expression has not been associated with distant metastasis or shown to affect prognosis [2,3].

Currently there is no unified treatment protocol for IMTs. Complete surgical resection is considered to be the treatment of choice and is the only known curative treatment [1]. The use of radiotherapy, immunosuppressive therapy and chemotherapy has been described in the literature for recurrent or unrespectable tumors. ALK inhibitors have been used successfully in several clinical trials for ALK-mutant tumors. Crizotinib was the first ALK tyrosine kinase inhibitor to become clinically available. In a case series with 14 patients with IMT, ALK-inhibition was a highly effective therapy, supporting consideration of frontline therapy with crizotinib [5]. Crizotinib has limited penetration across the blood brain barrier and thus limited efficacy of CNS tumors. Concurrent radiotherapy may improve its efficacy by increasing the permeability of the blood brain barrier, resulting in partial response. The exact impact of crizotinib on outcome is unclear and the exact follow-up period after discontinuation of crizotinib has not been included in prior reports, limiting the ultimate assessment of the efficacy of the treatment. Unfortunately, the patient in our case did not express ALK mutation and thus treatment with ALK inhibitors was not optional.

Conclusion

IMTs can recur and rarely show invasive features. Given high rate of recurrence, especially with CNS involvement, a close monitoring is needed. As our case illustrates, very late recurrences are possible, even after resection of localized disease, thus suggesting a need for long term follow up and surveillance imaging. To our knowledge, there have no cases been reported with recurrent tumor after such a long time. Although the literature suggests that tumors expressing ALK are more prone to recur, the confirmed IMT in our case was negative for ALK expression. Given the long disease-free interval, there was some delay in obtaining the correct diagnosis which can render patient susceptible for unnecessary studies. Other important differential diagnosis to keep in mind when patients present with skull-like lesion involving the meninges include plaque meningioma, lymphoma, sarcoid and dural based metastases.

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