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Malignant progression of cerebellopontine angle solitary fibrous tumors following radiation: illustrative case

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BACKGROUND Intracranial solitary fibrous tumors (ISFTs) are rare mesenchymal tumors originating in the meninges and constitute a heterogeneous group of clinical and biological behavior. Benign histotypes, such as hemangiopericytomas are now considered as a cellular phenotypic variant of this heterogenous group of rare spindle-cell tumors. IFSTs are poorly recognized and remain a diagnostic challenge due to rarity and resemblance to other brain tumors. Previously, IFSTs were thought to pursue a slow, indolent, and nonaggressive course, however, a growing body of literature based on longer follow-up demonstrates an unpredictable clinical course and an uncertain diagnosis.

OBSERVATIONS A rare case report of malignant transformation of IFST following radiation therapy is reported. In this case a 60-year-old female who underwent gross total resection of the cerebellopontine angle tumor with histopathology consistent with solitary fibrous tumor followed by salvage stereotactic radiosurgery, presented with another recurrence after 2 years of surgery. The authors performed complete removal of the tumor with pathology now consistent with malignant solitary fibrous tumor. A recent follow-up magnetic resonance imaging did not show any recurrence or residual tumor, and the patient reports a generalized well-being.

LESSONS This report will help to understand the natural history and unusual clinical behavior of these intracranial tumors.

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KEYWORDS intracranial; solitary fibrous tumor; malignant; radiation; hemangiopericytoma

Solitary fibrous tumors (SFTs) are spindle cell neoplasms that mainly affect the visceral pleura,[1,2] but they are also found in the head and neck, including the orbit, nasal cavities, paranasal sinuses, thyroid, parotid glans, and buccal and parapharyngeal spaces. According to the World Health Organization (WHO) reclassification in 2016, SFTs and hemangiopericytomas (HPCs) are considered different manifestations of the same entity as supported by the finding of identical NAB2-STAT6 fusions and nuclear STAT6 expression in both tumors.[3] Primary SFT involving the central nervous system (CNS) was first reported in 1996 by Carneiro et al.[4] Involvement of CNS is rare due to paucity of true connective tissue elements. The clinical behavior of intracranial solitary fibrous tumors (ISFTs) has traditionally been a problematic area, and literature is lacking examples of malignant progression of ISFT from WHO grade I or II to WHO grade III in the literature. Here we report a rare case of recurrent ISFT immunohistochemically shown to have malignant progression closely following radiotherapy. This study is novel and significant because it may contribute to understanding a new or at least more cautioned approach to treating these patients.

Illustrative Case

A 60-year-old female with a known history of smoking, hypertension, and hyperlipidemia presented for evaluation of brainstem/left cerebellopontine angle (CPA) tumor. A few years prior, she had noticed weakness, ataxia, headaches, progressive difficulty with gait, numbness, tingling, and dysphagia. Magnetic resonance imaging (MRI) revealed a large left CPA mass originating from the jugular foramen. The patient underwent a gross total resection (GTR) via extended retrosigmoid craniotomy (Fig. 1A and B). The immunohistochemistry of the tumor cells expressed vimentin, CD34, BCL2,

ABBREVIATIONS CNS = central nervous system; CPA = cerebellopontine angle; GTR = gross total resection; HPC = hemangiopericytoma; ISFT = intracranial solitary fibrous tumor; MSFT = meningeal solitary fibrous tumor; SFT = intracranial solitary fibrous tumor; SRS = stereotactic radiosurgery; WHO = World Health Organization.

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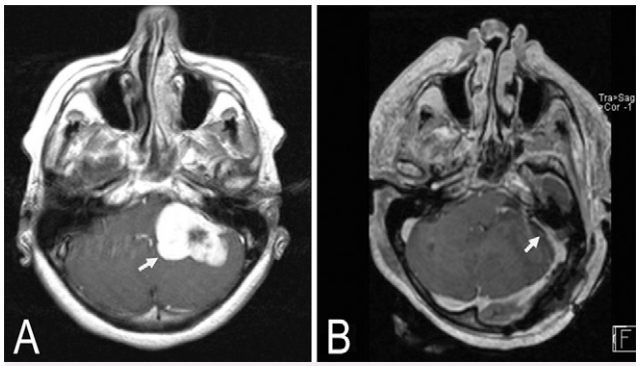

FIG. 1. Axial view MRI T1 with contrast. **A:** Preoperative image showing heterogeneously enhancing mass in the left perimesencephalic/CPA cistern. **B:** Postoperative image showing gross total resection of the tumor through extended retrosigmoid craniotomy.

and STAT6 consistent with an SFT (Fig. 2), and were negative for EMA, S100, and GFAP ruling out meningioma, schwannoma, and a low-grade glioma. A Ki-67 stain was positive in 5% of nuclei (Fig. 3). The patient was asymptomatic until recurrence of the tumor was noted on surveillance imaging 1.5 years later. She then underwent salvage stereotactic radiosurgery (SRS) consisting of three fractions of 18 Gy for local tumor control. Following this, she complained of mild self-resolving headaches that persisted for more than 6 months but then resolved. Recurrence was then again noted 1 year after completion of radiation (Fig. 4A–C). She underwent complete resection of the tumor following transotic approach. Histopathology from the tissue of left skull base, 10th to 12th cranial nerves, dura, and bone shows a pattern-less arrangement of crowded pleomorphic cells with areas of marked nuclear atypia, mitotic activity, and focal necrosis. Tumor cells expressed vimentin, CD34, BCL2, and CD99, and were negative for EMA, pankeratin, and GFAP. These findings are diagnostic of a malignant high-grade solitary fibrous tumor (Fig. 5). A recent follow-up MRI did not show any recurrence or residual tumor, and the patient reported a generalized well-being.

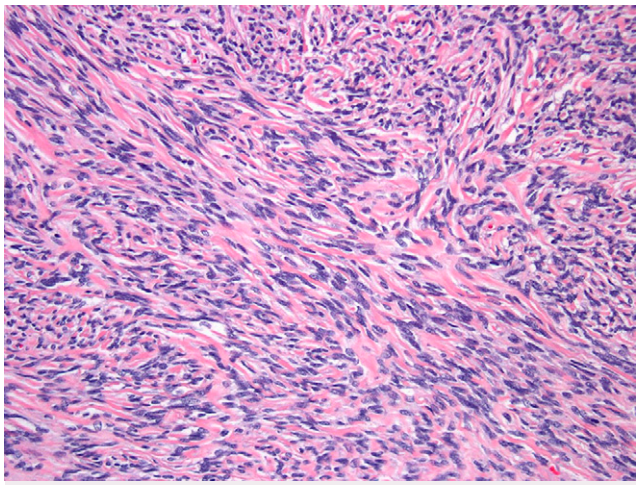

FIG. 2. Histopathology of the resection demonstrates histological features of an SFT.

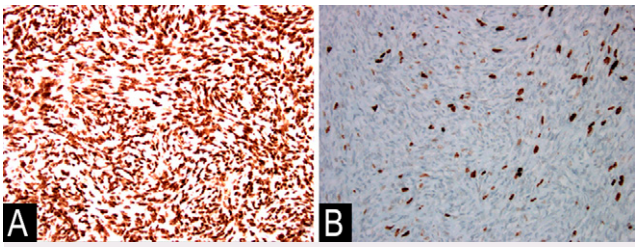

FIG. 3. Immunohistochemistry. **A:** Strong nuclear expression for STAT-6 (200×) confirming solitary fibrous tumor. **B:** Low Ki-67 of 10% positivity in hotspot (200×).

Discussion

Observations

Our report presents a unique case of rapid progression of SFT following radiation. Our study is novel and significant because it may contribute to understanding a new or at least more cautioned approach to treating these patients. Usually, treatment options for SFT include surgery and radiation. GTR has the greatest positive correlation with overall survival (OS) and progression-free survival (PFS).[5] However, there has not been indication for GTR as standard care because often the risks outweigh the benefits for GTR of a slow-growing benign tumor. Radiotherapy has also been shown to be positively correlated with OS and PFS.[6–8] Guthrie et al.[9] in a review of 44 meningeal SFTs reported 5- and 15-year survival rates of 67% and 23%, respectively. However, individual reports of malignant progression following radiotherapy such as that of Apra et al.[10] call into question the efficacy of this treatment for tumor control and PFS.[7,11,12]

SFTs are usually benign tumors with an indolent clinical course.[1] Whether radiation therapy could induce or accelerate the malignant progression could not be established in the literature. However, it should be noted that the malignant progression usually takes a long time after treatment, ranging from 10 to 12 years.[10,11] Radiation therapy might be just one of the several mechanisms of provoking the malignant progression. This is quite evident from our case report as well because the progression was reported within 1.5 years of first surgery or 6 months of salvage radiosurgery. In another large series, Mena et al.[13] noted a recurrence rate of 60.6% and a metastatic rate of 23.4%.[9] However, few reports suggested tumor progression and histological transformation of SFT progression closely following radiation.[14] One report notably did show a patient with multiple recurrences, and a sudden histological change of the tumor on fourth recurrence which occurred 16 months after irradiation to treat the third recurrence. In this case, radiation was considered to have played some role in the tumorigenesis, progression, and dedifferentiation of the SFT.[6,12]

Lessons

Given the disputes in the literature, the impact of radiation on recurrent SFT is still not entirely known. The association between radiation therapy and subsequent development of sarcoma has been appreciated since the original report by Cahan et al.[14] in 1948 of 11 sarcomas of bone following irradiation. Approximately 6% of all head and neck sarcomas occur in patients with a history of prior irradiation, with leiomyosarcoma and other subtypes of sarcoma more commonly seen with a history of prior irradiation.[14]

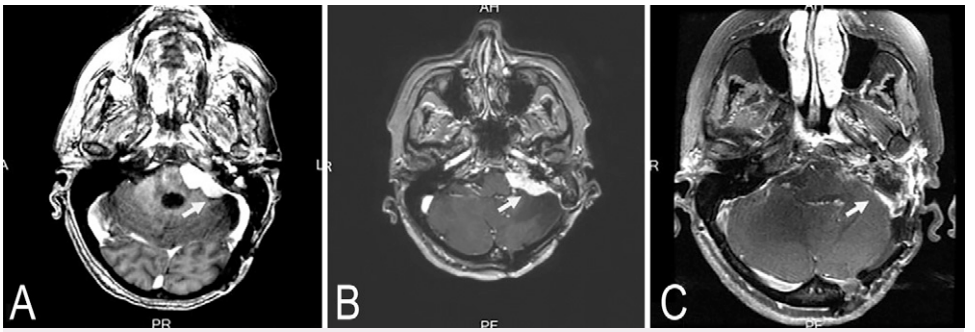

FIG. 4. Axial view MRI T1-contrast images showing s heterogeneously enhancing mass extending from the left perimesencephalic/CPA cistern through the left hypoglossal and jugular foramen to the cervical region. Recurrence of the tumor (**A**), preoperative (**B**), postoperative (**C**) scan showing gross total removal of the tumor through left transotic craniectomy and cranioplasty.

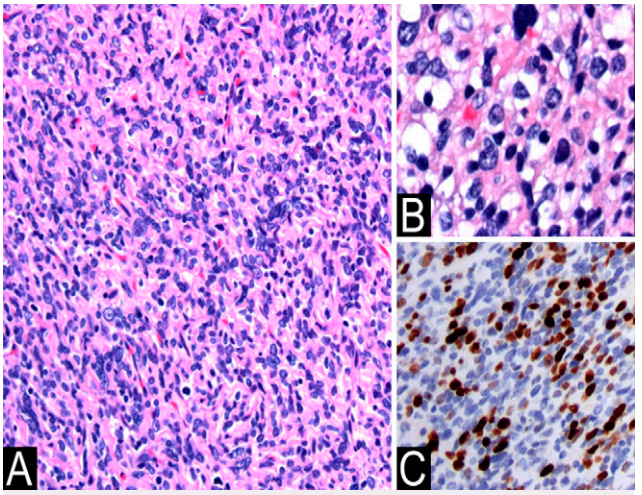

FIG. 5. Immunohistochemistry of the second resection demonstrates high-grade malignant histology with (*inset*) marked nuclear atypia (**A**), mitotic activity (**B**), and high Ki-67 proliferative activity (**C**).

However, this is the first study to determine the clinical impact of radiation on meningeal solitary fibrous tumors (MSFT)/HPC that might transform into malignant tumors after years of follow-up. A case report of SFT progression within one year of completion of radiation thus has clinical impact, considering the change of perspective and possible treatment recommendation after seeing that an initially benign MSFT/HPC may transform into malignant tumors after years of follow-up.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Lekovic, La Dine, Fatima. Acquisition of data: Lekovic, La Dine, Fatima, Slattery. Analysis and interpretation of data: Lekovic, Fatima. Drafting the article: Lekovic, La Dine, Fatima. Critically revising the article: Lekovic, La Dine, Fatima. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Lekovic. Administrative/technical/material support: Slattery. Study supervision: La Dine.

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