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Case Report

Malignant triton tumor diagnosed twelve years after radiosurgically treated vestibular schwannoma

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ABSTRACT

Stereotactic radiosurgery (SRS) has been used as the primary treatment for vestibular schwannoma (VS) over the last two decades. While literature is available on tumor response following SRS, very long-term follow-ups are not yet available. Malignant transformation of benign VS is very rare. There are only a few cases described in the literature, most of which report malignant transformation occurring between 5–10 years after radiosurgery. Here we report a case of a 65-year-old female, with no family history of neurofibromatosis, who presented with worsening mental status, gait instability and facial weakness. Twelve years prior to her presentation, she was diagnosed with a VS that was treated with stereotactic radiosurgery. The tumor had subsequently been stable on serial interval magnetic resonance imaging. She eventually presented with symptoms related to hydrocephalus and brain stem compression. Histopathologic analysis revealed a malignant peripheral nerve sheath tumor with rhabdomyoblastic differentiation. She succumbed to her disease and passed away 10 months after her resection surgery. This case highlights the necessity for lifelong follow-up following SRS and the need to be vigilant when performing SRS in large VS.

1. Introduction

Stereotactic radiosurgery (SRS) has become one of the standard treatment options for vestibular schwannomas (VS). The reported success observed with SRS has decreased tolerance for morbidity risks that are associated with microsurgery [1]. However, long term sequelae of SRS are still not completely understood, particularly the risk of malignant transformation of these tumors. Several reports suggested a possible association between SRS and malignant transformation of VS into malignant peripheral nerve sheet tumor (MPNST) [2]. Malignant triton tumor (MTT) is a MPNST with rhabdomyoblastic differentiation. It represents a rare and more aggressive phenotype of MPNST [3]. The low incidence of conversion coupled with the lack of prospective data limits our ability to infer the true associated risk of short and long-term malignant conversion following SRS.

Here we report an example of a patient that presented to our institution with a malignant conversion of her previously stable VS into MTT 12 years after SRS.

2. Case report

A 65-year-old female with no familial history of neurofibromatosis presented to our institution with worsening mental status, gait instability and facial weakness. Magnetic resonance imaging (MRI) showed a 5.0*4.0 cm right cerebellopontine angle (CPA) tumor causing brain stem compression and hydrocephalus (Fig. 1). She had originally presented in 2004, 12 years prior to the current presentation, to an outside institution for evaluation of hearing loss. She was found at that time to have a CPA tumor that was 3.8*2.4 cm along the long axis with intracanalicular involvement. Based on her radiographic and clinical findings she was diagnosed with VS. SRS was done and the patient was subsequently followed with serial MRI imaging. Both were performed in an outside institute, unfortunately, the MRI imaging from before radiosurgery is unavailable. The SRS prescription dose was 12.00 Gy to prescription Isodose: 50.00%. The treatment plan included a total of 33 isocenters with both the 4 and 8 mm collimator helmets. The patient underwent treatment of each of the 33 isocenters in turn, including both the APS and trunnion modes. Follow-up imaging demonstrated stable tumor size up to 8 years after SRS. Three years after the last stable MRI, the patient presented to her local emergency department with a two-day history of confusion, gait instability, and facial droop. Imaging obtained at that time demonstrated ventriculomegaly and a 300% increase in tumor volume with significant local mass effect. She was transferred to our institution for further management.

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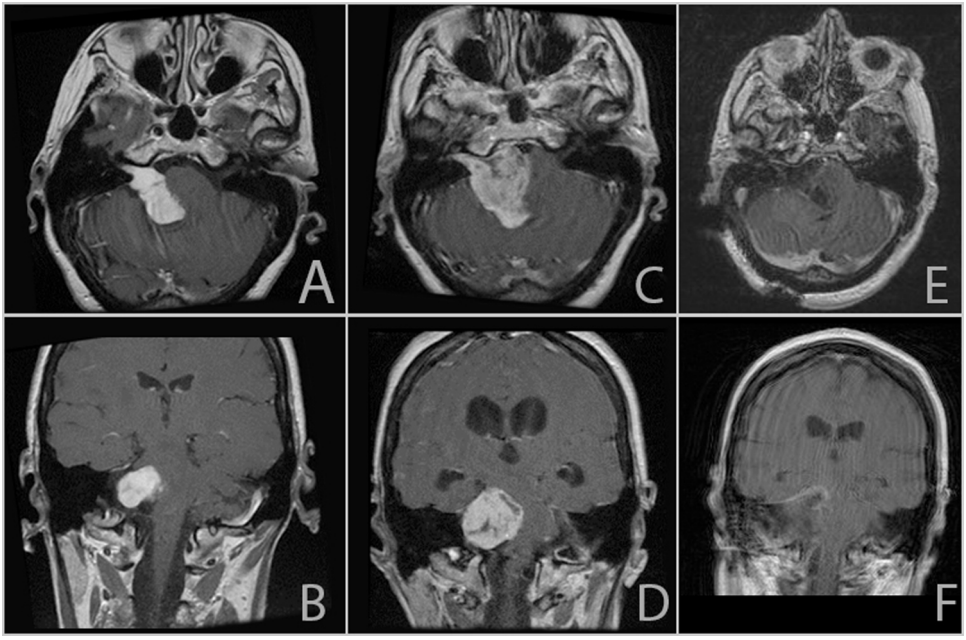

Fig. 1. T1-post contrast MRI scans. Axial and coronal studies from 3 years prior to presentation (A,B), preoperative (C,D), and postoperative after near total resection (E,F). Significant increased growth is noted from the last stable scan compared to the preoperative scan indicating a significant change in the tumor behavior.

The patient initially underwent endoscopic third ventriculostomy for obstructive hydrocephalus with the plan to undergo elective microsurgical resection. However, she returned 2 weeks after surgery with worsening mental status and a new right 6th nerve palsy. The patient was taken to surgery and underwent a retrosigmoid approach for near total resection of the CPA tumor (Fig. 1). Post-operatively, her confusion improved but preoperative cranial nerve deficits persisted. The histopathologic review confirmed a MPNST with rhabdomyoblastic differentiation (a.k.a. MTT) arising from a preexisting schwannoma. There were scattered cells with rhabdomyoblastic morphology, characterized by eccentric nuclei and eosinophilic cytoplasm. Tumor cells were positive for desmin and myogenin, and showed focal positivity for S100. Smooth muscle actin, EMA and GFAP were negative. Ki-67 proliferative index was 80% (Fig. 3). Foundation one testing was discussed with the family. However, they declined given the patient's very poor status. Thus, no further genomic testing is available. Post-operatively she underwent intensity modulated radiation therapy at 5940 cGy in 33 fractions.

She returned again approximately eight months later with worsening lower extremity weakness. Radiographic evaluation revealed decreased tumor size; however, there was leptomeningeal enhancement around the resection bed and nodular enhancement throughout the thoracolumbar meninges consistent with drop metastases and leptomeningeal disease (Fig. 2). She underwent palliative radiation therapy of her spinal disease and was discharged to a skilled nursing facility. She subsequently succumbed to her disease and passed away ten months after surgery.

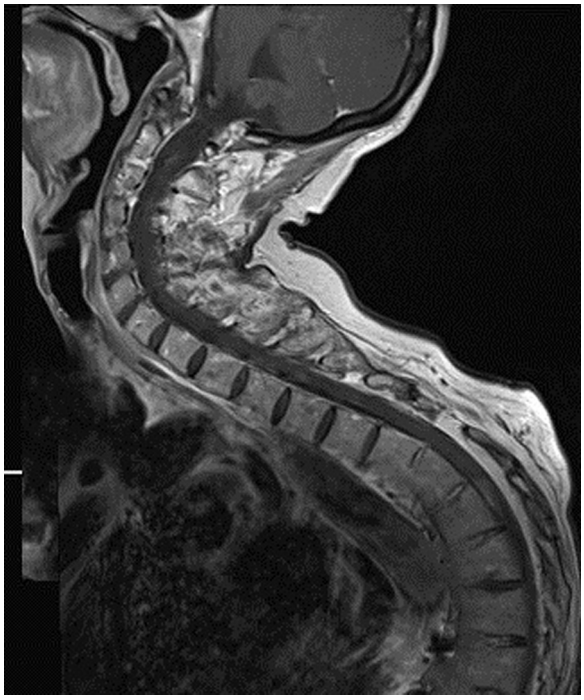

Fig. 2. Sagittal T1-post contrast MRI shows diffuse leptomeningeal enhancement throughout the cervical and thoracic spine.

3. Discussion

MPNST is the most common tumor following malignant conversion of VS [1]. Our current understanding regarding the risk of malignant conversion and average time to conversion is limited to case reports and literature reviews. However, based on this data we can obtain some insight into this risk. In doing so, patients can be appropriately counseled when selecting the appropriate treatment for VS.

Patel et al. reported 13 cases of MPNST arising from radiosurgically treated VS. The latency period between SRS treatment and diagnosis of secondary neoplasm ranged between 0.7 and 19 years with most of the cases occurring within 8 years of treatment [1].

Seferis et al. identified 29 cases of MPNST following radiation therapy in the literature. Three of them were MTT. However, only 9 of these 29 patients had histological confirmation of benign tumor prior to radiation. They also reported 25 cases of spontaneous malignant transformation without prior irradiation. Based on their analysis, radiation treatment increases the risk of malignancy in VS over 20 years by 10 times in non-NF cases. The risk of 20 year malignancy transformation in non-NF cases was 1.09–1.74 and 15.6 per 100,000 for non-radiated versus radiated respectively [2].

Few case reports arose on malignant transformation following

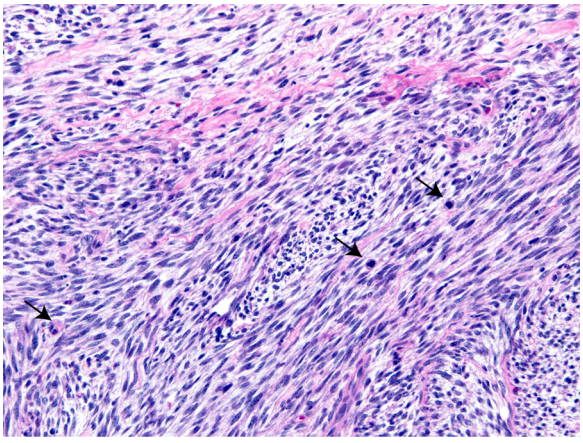

Fig. 3. Hematoxylin and eosin slide which reveals spindle cell neoplasm with dense cellularity and numerous mitotic figures (arrows).

microsurgery alone. The latency period between microsurgery and the diagnosis of a malignant tumor was significantly shorter and ranged from 2 to 12 months in most cases. This suggests the possibility to be secondary to preservation of potential malignant cells during the surgical process [2].

Although seeding of VS with unchanged histopathological features has been reported post-surgery, malignant transformation carries a different pathomechanism [4]. Frequently it is difficult to establish malignant transformation of a benign tumor treated primarily with SRS due to the usual lack of pre-malignancy tissue. Cahan's criteria, although established in 1948, are still utilized for characterizing malignant transformation following irradiation. This requires the following: 1) there must be a microscopic or radiologic evidence of the non-malignant nature before irradiation; 2) the malignant transformation must have arisen in the area included within the radiotherapeutic beam; 3) there must be a relatively long asymptomatic latent period between irradiation and clinical appearance of the malignant tumor, longer than the so-called five-year-cure period; and 4) the malignant tumor must be proved histologically [5]. VS displays typical radiographical and clinical features, therefore a biopsy is generally not considered prior to establishing a treatment plan. Thus, no histopathology could definitively confirm the diagnosis of VS.

The currently available data would suggest a slightly increased risk of malignant transformation to MPNST in non-NF patients when compared against patients that do not undergo irradiation; though these values are still quite low when compared against the overall risk. Although the overall risk of malignant transformation is very low and radiosurgery is considered safe, awareness of this potential mortal outcome is nonetheless important when considering treatment options. SRS is usually limited to VS smaller than 2.5 cm in diameter due to the concern of increased radiation dose to the adjacent brainstem and the larger tumor volume receiving radiation. The reported patient received SRS for a large VS (3.4 cm) which theoretically makes the VS rather susceptible to malignant transformation.

4. Conclusion

Malignant transformation of VS after SRS is rare. While the majority of documented cases occurred within 10 years after SRS, this patient presented 12 years following SRS. The number of cumulative cases of irradiated VS is growing over the last two decades and we are entering the third decade of observational data collection. This highlights the possibility of the occurrence of malignant transformation of VS beyond the existing long-term studies. It also indicates the importance of life-long follow up for patients who underwent SRS.

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Declarations of interest

None.

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