Leiomyosarcoma of the infratemporal fossa with perineurial spread along the right mandibular nerve: a case report

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Leiomyosarcomas are malignant tumors displaying strong smooth muscle differentiation. They can often develop within the GI tract and myometrium, but are particularly rare in the head and neck. Perineurial spread of head and neck cancer is observed in patients with neoplasms of the skin (squamous cell carcinoma, melanoma) or skin appendages (adenoid cystic carcinoma). We report the case of a woman who presented with diplopia and headaches. MRI showed an infratemporal mass lesion and faint enhancement tracking along the mandibular nerve into the wall of the right cavernous sinus. A nerve biopsy revealed leiomyosarcoma. We review the medical literature to provide further insight into the diagnosis and management of this tumor and its peculiar pattern of spread. A similar case was unidentifiable in the literature.

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Practice points

Background

- A woman presented with perineurial spread (PS) along the mandibular nerve in the setting of radiation-induced leiomyosarcoma of the infratemporal fossa.

Case report

- 47-year-old woman status postradiotherapy 30 years prior to presentation complained of diplopia, a burning sensation along the right V2/V3 dermatome, and headaches.
- A PET/CT scan raised concern for malignancy in the infratemporal fossa, but a biopsy was unremarkable.
- Her symptoms progressed. Imaging findings suggested PS along V3. Nerve biopsy confirmed PS by leiomyosarcoma.
- The tumor was deemed unresectable. Radiotherapy was initiated.

Discussion

- This case is unique based on its location, pathogenesis and pattern of spread.
- PS is defined and its reported incidence within the head and neck is showcased. Incidence of PS in the setting of other forms of cancer is discussed.

Conclusion

- Symptoms of PS spread mandate a thorough search for the origin of the underlying malignancy.
- Neuroimaging and histopathology play a pivotal role in its definitive diagnosis and management.
- When symptoms arise in a previously irradiated field, sarcoma ought to be included in the differential diagnosis.

Case report

A 47-year-old woman with a history of right parotid gland carcinoma status postradiotherapy (alternating photons and electrons to 64 gray in 32 fractions to the right parotid and neck region) 30 years prior to this presentation

Future
Medicine

Figure 1. MRI of brain and orbits (left) revealed enhancement along right V3 nerve, extending through the foramen ovale into right cavernous sinus. Asymmetric enhancement along the right lateral aspect of cavernous sinus. PET/CT (right) revealed 18-FDG uptake in the right mandibular condyle and mild hypermetabolism involving left-sided parotid gland, submandibular gland, tonsillar region and cervical lymph nodes.
FDG: Fludeoxyglucose.

complained of horizontal and vertical diplopia progressing over the course of 6 months. This was accompanied by a burning sensation along the right V2/V3 dermatome and right-sided mandibular pain. Her neurologic exam was remarkable for a right sixth nerve palsy. MRI of brain and orbits (Figure 1) revealed contrast enhancement along the right mandibular condyle, temporomandibular joint, right superior orbital fissure and adjacent cavernous sinus. Enhancement was also noted extending along the right temporalis muscle with thickening and abnormal enhancement of the right V3 nerve extending through the oval foramen. A PET/CT scan (Figure 1) raised concern for a malignant neoplasm in the region of the right mandibular condyle, but right parotid space and nasopharyngeal biopsies were unremarkable. 5 months following the initial consultation, her symptoms slowly progressed and a second biopsy, this time of the mandibular nerve, was performed. Histopathologic findings were diagnostic for a malignant spindle cell tumor consistent with leiomyosarcoma, grade II/III of the right infratemporal fossa with perineurial spread (PS) along the right mandibular nerve into the cavernous sinus (Figure 2) [7]. Immunohistochemistry demonstrated the presence of smooth muscle actin, calponin, muscle-specific actin and desmin within the tumor. A board-certified pathologist with expertise in sarcoma (Jose Costa) reviewed the pathology to confirm the diagnosis. A second PET/CT scan failed to reveal evidence for distant metastases. Sarcoma specialists recommended the patient to undergo radiation after surgery to achieve an optimal outcome. Response rates to conventional cytotoxic agents were considered limited. The radiation-induced tumor within the previously irradiated location was deemed unresectable, but radiation alone remained the best available treatment [8,9]. She was treated with fractionated external beam radiation therapy (66 Gy in 33 fractions [10]) to the entire mandibular nerve and right cavernous sinus, and her disease stabilized for 5 months.

Discussion

The reported case is unique based on its location, pathogenesis and especially its pattern of spread. Leiomyosarcomas are uncommon malignant neoplasms, accounting for less than 7–10% of all soft tissue sarcomas and only 1% of head and neck sarcomas [3,11]. Specifically, radiation-induced leiomyosarcomas of the head and neck are exceedingly rare, accounting for just 19 of all 323 (5.6%) reported cases of radiation-induced head and neck sarcomas between 1995 and 2014 [11–13]. We found one report of a spontaneous infratemporal fossa leiomyosarcoma reported in the literature [5].

Figure 2. Hematoxylin and eosin staining of the tumor (left) demonstrates markedly atypical spindle cells with blunted nuclei arranged in a partly fascicular growth pattern. Mitotic figures are present. Immunohistochemical staining for S100 (right) selectively highlights entrapped nerve, whereas the surrounding tumor is negative for S100. Immunohistochemical staining also confirms that smooth muscle actin, calponin and muscle-specific actin are diffusely positive in tumor cells. Desmin was found to be focally positive in tumor cells. These findings were reviewed by a board-certified pathologist with expertise in sarcoma (Jose Costa).

PS denotes dissemination of cancer cells within the peri- and epineurium of peripheral or cranial nerves. It was first described in the mid-1800s [14]. Nerves are thought to provide pathways of least resistance for tumor progression; the intricate nerve fiber networks within the head and neck create a conducive environment for this pattern of spread. Essentially, tumors can spread along any nerve, but the facial nerve, as well maxillary and mandibular divisions of the trigeminal nerve, are most commonly infiltrated by neoplastic cells in this anatomical region [15]. PS causes nearly a threefold increase in local recurrence rate and decreases the 5-year survival rate by 30% [15]. The incidence of PS in the setting of all head and neck malignancies, however, is only about 2.5–5.0%. Reported relative incidence of perineurial involvement in the head and neck varies. Most of the literature agrees that adenoid cystic carcinoma has the greatest disease-specific incidence of perineurial spread [6,11,16,17]. In a retrospective series, the incidence of PS in the setting of adenoid cystic carcinoma was reported to be 31–96% [17]. Other cancers known to spread preferentially via the perineurial route are squamous cell cancer, melanoma and lymphoma [5,17–19]. PS is unusual in sarcomas. It is a challenging diagnosis and clinical suspicion is paramount for its early discovery. Tajudeen *et al.* found perineurial invasion in 6.5% of their 186 head and neck sarcoma sample [20]. Despite the lack of specific leiomyosarcoma data, their analysis concluded perineurial invasion to be an important predictor of survival and recurrence [11]. Paes *et al.* reported that 40% of patients are asymptomatic, yet even in those PS convey a poor prognosis [6]. Common symptoms include pain, paresthesias, sensory loss and weakness in muscles of mastication (V3) or facial muscles (VII). Neuroimaging studies, especially MRI, play a pivotal role in detecting evidence of PS. Definitive diagnosis requires a biopsy but its benefits have to be carefully weighed against its complications (loss of motor or sensory function in the distribution of the biopsied nerve). Detection methods of PS are not consistent within the literature. Reported incidence therefore varies according to histopathology and imaging techniques [17].

Conclusion

PS is an uncommon complication of head and neck cancer, especially in leiomyosarcoma [16]. When the condition is clinically suspected, comprehensive neuroimaging work-up using the most sensitive tools (high-resolution MRI with fat suppression; 18-FDG PET) ought to be used to identify the extent of dissemination. A tissue-based confirmation of diagnosis is desirable but empiric treatment may be justified when the cancer cannot be found or the morbidity of the surgical procedure is deemed unacceptable.

Future perspective

Modern diagnostic technology paired with knowledge of the neurologic syndrome will facilitate the diagnosis of perineurial spread. At this point, high-resolution MRI with fat suppression and 18-FDG PET imaging represent the most sensitive detectors of PS, but biopsies will remain the gold standard. Improved diagnostic sensitivity may increase observed incidence rates, but considering how rare PS is, this trend may not be seen for years.

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Informed consent disclosure

The authors state that they have obtained verbal and written informed consent from the patient/patients for the inclusion of their medical and treatment history within this case report.

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