Otopathology in Angiosarcoma of the Temporal Bone

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INTRODUCTION

Angiosarcoma is a rare malignant cancer of the endothelial cells that line blood or lymphatic vessels and represents 1% to 2% of all sarcomas.1 Half of all angiosarcomas are found in the skin of the head and neck. However, angiosarcoma of the temporal bone is exceedingly rare, with only three previously published cases.2–4 Risk factors for angiosarcoma include radiation therapy, arsenic exposure, and chronic lymphedema.5 Although surgery is the primary treatment for angiosarcoma,6 resection in the version of this article.

RESULTS

Clinical Presentation

A 50-year-old man with a 15-year history of right chronic otitis media with intermittent otorrhea presented with 6 months of progressive right hearing loss and 2 months of otalgia and disequilibrium. Otomicroscopy revealed a non-tender, polypoid mass filling the right external auditory canal (EAC). Tuning fork tests indicated a conductive hearing loss in the affected ear. Temporal bone computed tomography showed soft tissue filling the right EAC and middle ear. The tegmen appeared intact. An office biopsy of the EAC showed granulation tissue with inflammatory changes.

One week later, the patient developed rapid-onset facial weakness. Presumed to have cholesteatoma, he underwent a canal wall down tympanomastoidectomy. Intraoperatively, the polyp in the right EAC was excised. The mastoid bone was soft, the incus was partially eroded, and the stapes was encased in thickened mucosa. The

angiosarcoma of the middle ear and mastoid with extension into the temporal lobe. The temporal bones were removed after death, histologically processed, and examined by light microscopy. The otopathology findings are presented.

OBJECTIVES/HYPOTHESIS: Investigate the otopathology of angiosarcoma of the temporal bone, which has not been previously described in the literature.

STUDY DESIGN: Postmortem evaluation and literature review.

METHODS: Postmortem histological evaluation of the temporal bones and review of the literature for the treatment and prognosis of this rare disease were performed.

RESULTS: A 50-year-old male with right chronic otitis media presented with progressive hearing loss, disequilibrium, otalgia, and acute facial paresis. Biopsy of the external auditory canal was unrevealing, but specimens from a canal wall down tympanomastoidectomy later showed high-grade angiosarcoma. Magnetic resonance imaging demonstrated an unresectable middle ear and mastoid mass extending superiorly into the temporal lobe. The patient received induction chemotherapy followed by proton beam radiation therapy and concurrent paclitaxel and bevacizumab. His course was complicated by a cerebrospinal fluid leak and cauda equina syndrome from leptomeningeal sarcomatosis. The patient died after developing meningitis and a temporal lobe abscess. Postmortem otopathology revealed persistent angiosarcoma in the internal auditory canal, although none was found in the middle ear or mastoid. There was inflammatory infiltrate throughout the mastoid, with direct extension of neutrophils and bacteria into the cochlea and through the tegmen into the middle cranial fossa.

CONCLUSIONS: Angiosarcoma of the temporal bone can arise in the setting of chronic otitis media. In this case, postmortem temporal bone sections demonstrated viable cancer despite chemoradiation. Inflammatory infiltrates crossing from the middle ear/mastoid into the labyrinth and central nervous system illustrate pathways for the development of otogenic meningitis.

KEY WORDS: Otopathology, chronic otitis media, intracranial abscess, meningitis.

Level of Evidence: 4

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facial nerve was identified by tracing the chorda tympani and did not stimulate, so it was decompressed in the lower mastoid segment where the bone appeared most affected. Surgical pathology showed atypical, pleomorphic endothelial cells with hyperchromatic nuclei and forming irregular vascular spaces, consistent with high-grade (grade 3 of 3) angiosarcoma with epithelioid and spindle cell features (Fig. 1).

Magnetic resonance imaging (MRI) with contrast showed an enhancing, heterogeneous, multilobulated mass extending through the tegmen into the temporal lobe (Fig. 2). The tumor was deemed surgically unresectable and the patient was treated with induction chemotherapy (cisplatin and paclitaxel) before completing 7 weeks of paclitaxel and bevacizumab with concurrent proton beam radiation therapy (70 Gy, 35 fractions). Post-treatment audiogram showed right severe to profound mixed hearing loss, with a word recognition score of 60% and left moderate high-frequency sensorineural hearing loss (see Supporting Figure 1A) in the online version of this article.

The patient had several complications including Haemophilus influenzae meningitis and cerebrospinal fluid (CSF) leak, for which he underwent right mastoid obliteration with abdominal fat graft and temporoparietal fascia flap. Intraoperatively, there were large areas of middle and posterior fossa dehiscence. CSF rapidly filled the mastoid cavity, originating from the fallopian canal. The fallopian canal and eustachian tube were both plugged with temporalis muscle and Surgicel. The patient then developed cauda equina syndrome and was found to have leptomeningeal sarcomatosis, which was treated with spine radiation. Several weeks later, he developed a mastoid cutaneous fistula and acute mastoiditis with right temporal lobe abscess. The patient underwent craniotomy for abscess drainage, debridement of the mastoid cavity, and excision of the mastoid cutaneous fistula. He passed away 2 weeks later, 9 months after diagnosis.

On autopsy, the right middle fossa and the overlying temporal lobe had a large cavitary lesion corresponding to the known abscess (Fig. 3A,B). Nerve rootlets of the cauda equina were several times thicker than normal, suggestive of metastatic disease (Fig. 3C).

Histopathologic Evaluation of the Temporal Bones

Bilateral temporal bones were removed 17 hours after death, fixed in formalin, decalcified with ethylenediaminetetraacetic acid, and embedded in celloidin. The specimens were horizontally sectioned at 20-μm intervals, and every 10th section was stained with hematoxylin and eosin. Sections were examined by light microscopy.

In the left ear, the middle ear and mastoid were normal and there was no inflammatory infiltrate. The cochlea and vestibular organs were essentially normal with grossly preserved hair cell populations and no hydrops.
Fig. 3. (A) Ventral view of the fresh brain showing the cavitation corresponding to the right temporal lobe abscess. (B) Coronal section of the brain demonstrating the abscess in the temporal lobe adjacent to the temporal skull base. (C) The spinal cord specimen shows markedly thickened nerve roots consistent with leptomeningeal sarcomatosis.

Fig. 4. Low-magnification views of the right temporal bone (1.25×). (A) Midmodiolar section of the cochlea with a view of the vestibule (V) and lateral semicircular canal (LSC). Note the acute inflammatory infiltrate throughout the vestibule and the LSC, and the proteinaceous fluid within the cochlea. (B) Section through the internal auditory canal (IAC) filled with inflammatory infiltrate as well as areas concerning for persistent angiosarcoma (*).
Low magnification histopathological views of the right ear are shown in Figure 4. Large numbers of neutrophils filled the middle ear and mastoid. The bony labyrinth was severely eroded at the anterior margin of the basal turn of the cochlea and the inflammatory infiltrate transgressed into the scala tympani, scala media, and scala vestibuli of the cochlea (Fig. 5). There was an acute inflammatory infiltrate throughout the semicircular canals. Inflammatory

Fig. 5. Right cochlea. (A) Section through the bony labyrinth of the cochlea showing cochlear erosion (solid arrows) (4×). (B) Higher magnification section demonstrating cochlear erosion (solid arrows) from the dense neutrophilic infiltrate (40×). (C) Middle turn of the cochlea with a collection of neutrophils in the scala media (20×). (D) Neutrophilic infiltrate in the round window niche (RWN), extending across the round window (arrow heads) and forming a dense collection of neutrophils surrounded by necrotic neutrophils and macrophages (open arrow) in the scala tympani (4×). IAC = internal auditory canal.

Fig. 6. Destructive outcomes of infection and inflammation in the right temporal bone. (A) Neutrophilic infiltrate from the mastoid (M) transgressing the tegmen mastoideum (TM) into the middle cranial fossa (MCF) (20×). (B) Dehiscence of the fallopian canal (solid arrows) overlying the facial nerve (FN), surrounded by inflammatory cells (20×).
infiltrate also eroded through the tegmen mastoideum into the temporal lobe (Fig. 6A). The facial nerve contained sheets of neutrophils interspersed among nerve fibers, and there was a dehiscence of the facial nerve within the fallopian canal surrounded by inflammatory cells (Fig. 6B).

There was significant loss of inner and outer hair cells throughout the cochlea, worse at the basal end. The spiral ganglion neuron count was 57% of normal for the patient's age. In the vestibular system, there was complete loss of hair cells in superior and lateral semicircular canal cristae. The posterior semicircular canal cristae and maculae of the utricle and saccule were intact, with degeneration of vestibular hair cells. Residual nests and sheets of large hyperchromatic epithelioid cells forming atypical vascular spaces characteristic of high-grade angiosarcoma were found only in the internal auditory canal (Fig. 7).

**DISCUSSION**

Angiosarcoma of temporal bone is an extremely rare diagnosis, with only three prior cases reported in the English-language literature.2–4 Furthermore, the otopathology findings in a case of temporal bone angiosarcoma have not been previously reported. Herein, we present a striking case of angiosarcoma of the temporal bone in a patient with a long history of chronic otitis media. The diagnosis was made with tissue from a canal wall down tympanomastoidectomy. Surgical and postmortem otopathological specimens were reviewed, showing features consistent with angiosarcoma including disorganized clusters of atypical endothelial cells forming irregular vascular spaces. At the time of death, the locally aggressive nature of the tumor was evident. Otopathology demonstrated persistent tumor in the internal auditory canal despite chemoradiation therapy. In addition, mastoiditis, meningitis, and temporal lobe abscess were confirmed. There was diffuse inflammatory infiltrate throughout the temporal bone, including inside the perilymphatic and endolymphatic spaces of the auditory and vestibular organs, and neutrophils transgressing through the tegmen into the middle fossa. The severe loss of cochlear hair cells and vestibular hair cells in the right ear may have been due to the angiosarcoma, chemoradiation, or direct extension of infection into the inner ear.

Due to its rarity, there is limited information on the management and prognosis of temporal bone angiosarcoma. Management may be based on treatment paradigms for soft tissue sarcoma, which is a heterogeneous group of tumors.6,8,9 The pathogenesis of angiosarcoma in the unirradiated temporal bone is mysterious, but similarities to the development of squamous cell carcinoma in the setting of chronic otitis media can be drawn.10 The presence of a chronic inflammatory environment that promotes malignant transformation could be postulated.

The diagnosis of angiosarcoma can be difficult. Early imaging should be ordered for patients with severe or progressive symptoms, particularly if there is cranial nerve involvement. MRI with contrast can be useful to delineate the soft tissue involvement of tumors. Early biopsies and imaging can expedite diagnosis, which can steer patients toward appropriate therapies.

The histologic appearance of angiosarcoma can vary from well-differentiated to poorly differentiated spindle cells with a range of atypical cellular qualities. They can resemble carcinomas (especially epitheloid variants) as well as melanomas, and immunohistochemistry can be important for diagnosis. Positive staining for CD31, CD34, Fli-1, ERG, FVII, and D2-40 is characteristic of angiosarcomas.11 In this case, the histopathology was characteristic for angiosarcomas, with pleomorphic spindle and epithelioid cells organized into atypical vascular spaces.

The overall prognosis of angiosarcoma is poor, with 30% to 40% survival in 5 years across all patients.12 In the face and scalp, 5-year survival estimates are as low as 12%.13 In the calvarium, outcomes may be worse because of the inability to perform complete resections and the proximity of the brain/meninges. In general, surgery is the primary treatment recommended with adjuvant radiation.8 Adjuvant chemotherapy (taxanes, doxorubicin) is not standard therapy, but may be useful for high-risk tumors. Bevacizumab has also been studied, as there is increased expression of vascular endothelial growth factor (VEGF) and VEGF receptors in angiosarcomas. However, a recent phase II randomized study of paclitaxel versus paclitaxel and bevacizumab in advanced angiosarcoma showed no benefit to adding the biologic therapy.14 In this present case, the patient was treated with bevacizumab prior to the publication of this study.

**CONCLUSION**

Angiosarcoma of the temporal bone can arise in the setting of chronic otitis media, and tympanomastoidectomy may be necessary to obtain tissue for diagnosis. In this case, the tumor was locally aggressive, resulting in erosion through the skull base into the temporal lobe.
Otopathology of temporal bone sections demonstrated viable malignant epithelioid cells in the internal auditory canal despite chemoradiation treatment, as well as bacteria and inflammatory infiltrates crossing from the middle ear and mastoid into the central nervous system and the labyrinth, consistent with his clinical course.

BIBLIOGRAPHY