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Primary Extracranial Meningioma of Mastoid in a Patient With History of Skin Squamous Cell Carcinoma, Lung Adenocarcinoma and Prostatic Carcinoma

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Abstract. *Background: Meningiomas are the most common benign intracranial tumors and frequently develop in the parasagittal region, but can also present extracranially. Rarely, meningiomas may involve the middle ear and mastoid, resulting from contiguous spread of adjacent intracranial tumor, or extremely rarely, as an isolated primary tumor, which is frequently misdiagnosed and unrecognized, resulting in inappropriate clinical management. Case Report: Herein we report such a case of an 80-year-old man with history of multiple cancer who presented with ear pain, vertigo and hearing loss. Audiometry demonstrated bilateral sensorineural hearing loss. Contrast-enhanced temporal bone computed tomography revealed a soft-tissue mass in the right epitympanum without bone erosion or any intracranial involvement. Radiological and operative findings were suspicious for cholesteatoma. Histological examination showed an epithelial neoplasm arranged in nests and whorls with intranuclear inclusions. No psammoma bodies, mitotic figures, or tumor necrosis were identified. The tumor cells were positive for epithelial membrane antigen, vimentin, progesterone receptor and CD56; and negative for synaptophysin, chromogranin, pancytokeratin (AE1/AE3), cytokeratin 7, prostate-specific antigen, inhibin, S100, P63, and P40. Ki67 highlighted about 2% of the tumor cells. Based on the morphological features and immunohistochemical profile, the tumor was diagnosed as primary extracranial meningioma of the mastoid, meningothelial subtype, World Health Organization grade 1. Conclusion: To the best of our knowledge, primary mastoid meningioma clinically mimicking a cholesteatoma presenting in a patient with a history of multiple primary carcinomas has not been previously reported. The pathogenesis, diagnosis and treatment of this entity are discussed.*

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Meningioma arises from meningothelial arachnoid cells, which are derived from the neuroectoderm (1). They account for 30% of all adult central nervous system (CNS) tumors and can be classified into three categories: Benign (grade I), atypical (grade II) and malignant (grade III), based predominantly on histological variant, mitotic activity, and brain invasion. About 80% of meningiomas are benign (1). Meningiomas are well known in terms of intracranial pathology, however, they can also present extracranially. Extracranial meningiomas of the temporal bone are rare, with middle ear and mastoid involvement being exceedingly rare. Middle ear and mastoid meningiomas are classified into primary and secondary types based on their origins (1). Secondary extracranial meningiomas, which extend from an intracranial mass, can take three different routes to reach the middle ear and mastoid: the internal auditory canal, the *tegmen tympani* and the jugular *foramen*. Primary meningioma of the middle ear or mastoid is thought to arise from ectopic arachnoid cells. In this study, we report an exceedingly rare case of an isolated primary meningioma of the mastoid in a patient with history of multiple cancers and discuss the pathogenesis, diagnosis, treatment and prognosis of this entity.

Case Report

An 80-year-old male was referred to our Ear, Nose and Throat Department for evaluation of ear pain, hearing loss, and vertigo of 2 months' duration. Episodes occurred a few times per week, lasting several minutes each time, and triggered by positional change and lying down. Computed tomographic (CT) and magnetic resonance (MRI) imaging findings revealed a mass measuring 1.0 cm in its greatest dimension in his right mastoid. He had a history of noise exposure from competitive shooting without hearing protection and had worn bilateral hearing aids for about 2 years. He had a past medical history of cutaneous squamous cell carcinoma, lung adenocarcinoma, and prostatic adenocarcinoma. He aIso had history of nasal septum surgery in 1970, uvulectomy in 1985, lung lobectomy in 2004, and prostatectomy in 2011. He had a family history of prostatic and lung carcinomas, specifically his father had prostatic carcinoma in his 60s and died of lung carcinoma at age 86 years, and his uncle had died of prostate cancer at age 86 years.

Otoscopy showed a normal external auditory canal without lesions or inflammation and an intact, translucent and mobile tympanic membrane of each ear. Balance testing showed compensated head thrust and a negative Dix-Hallpike test. Facial nerve examination showed intact and symmetric facial nerve function bilaterally. Audiometry demonstrated bilateral sensorineural hearing loss. The speech reception threshold was 40 dB on the right and 40 dB on the left. Speech discrimination score was 44% on the right and 60% on the left at 80 dB. Contrast-enhanced temporal bone CT revealed a soft-tissue mass measuring 1.0 cm in its greatest dimension in the right epitympanum and mastoid, without obvious bone erosion or tegmen dehiscence (Figure 1A and B).

The patient underwent complete mastoidectomy with suspicion for cholesteatoma, and the specimen was sent for further pathological evaluation. Gross examination revealed a 0.8×0.5×0.4 cm aggregate of pink-tan soft tissue. Histological examination showed an epithelial neoplasm arranged in nests and whorls. Intranuclear pseudoinclusions were frequently seen (Figure 1C and D). No psammoma bodies, mitotic figures or spontaneous tumor necrosis were identified. The tumor cells were positive for epithelial membrane antigen (EMA) (Figure 2A), progesterone receptor (PR) (Figure 2B), vimentin (Figure 2C), and focally positive for CD56. They were negative for synaptophysin (Figure 2D), chromogranin, neuron-specific enolase, pancytokeratin (AE1/AE3), inhibin, cytokeratin (CK)5/6, CK7, prostate-specific antigen (PSA), S100, P63, and P40. Ki67 highlighted about 2% of tumor cell nuclei. Reticulin and collagen IV highlighted the nested arrangement. The intranuclear pseudoinclusions were negative on periodic acid–Schiff–diastase (PASD) staining. The pathological diagnosis was meningioma, meningothelial type, WHO grade 1.

Post-surgery, the patient recovered well. At the 6-month follow-up, the patient was doing well and no tumor recurrence was identified.

Discussion

Meningiomas most commonly develop from the arachnoid cells of the meninges overlying the convexities of the cerebral hemispheres or the skull base, leading to the characteristic dural-based tumor on imaging (1). Meningiomas can also be intraventricular or intraosseous. Although much less common, meningiomas also occur in extracranial locations, specifically the head and neck region and lungs. The most frequent extracranial sites reported are the nasal cavity and paranasal sinuses (2), cranial bones (3), scalp, and the middle ear and mastoid (1). Middle ear and mastoid meningiomas are classified into primary and secondary types based on their origin (1). Secondary extracranial meningiomas of the middle ear and mastoid result from direct extensions of intracranial masses (1). Primary meningiomas of the middle ear and mastoid are believed to arise from ectopic arachnoid cells. The ectopic tissue is speculated to be an embryological rest of pinched-off arachnoid cells lying outside of the neuraxis, along the line of fusion of primitive nerve and bone sheaths (4). Here we report a rare case of an isolated primary mastoid meningioma arises from ectopic arachnoid cells.

Radiological investigations (CT and MRI) are important in diagnosing the extent of the disease, and in ruling out any intra-cranial extension of the mass, as this would help in diagnosing extra-cranial meningioma as primary or secondary. MRI has a higher sensitivity than CT and may show a homogeneously enhancing dural-based soft-tissue mass with a characteristic dural tail (5). Our case is unique in that the imaging and operative findings were suspicious for cholesteatoma.

Based on location and histology, the differential diagnosis includes a variety of benign and malignant neoplasms, including middle-ear adenoma, paraganglioma, neuroendocrine tumor, schwannoma, and meningioma. Reportedly, paraganglioma and schwannoma are the most frequent misdiagnoses for ear and temporal bone tumors (6, 7). Given the complex history of multiple primary carcinomas in our patient, a metastatic tumor had to be excluded. These entities were excluded by our immunohistochemical panel showing negative CK7, synaptophysin, chromogranin, S100, P40, P63, CK5/6, and PSA excluded the diagnosis of middle ear adenoma, paraganglioma, and metastatic carcinoma. The presence of cytologically bland epithelial cells arranged in a vague lobulated pattern with whorls and intranuclear pseudoinclusions were suggestive of a meningioma and the diagnosis was confirmed with an immunoprofile positive for EMA, and PR. Extracranial meningiomas are graded using the same criteria as their intracranial counterparts, therefore, with the meningothelial

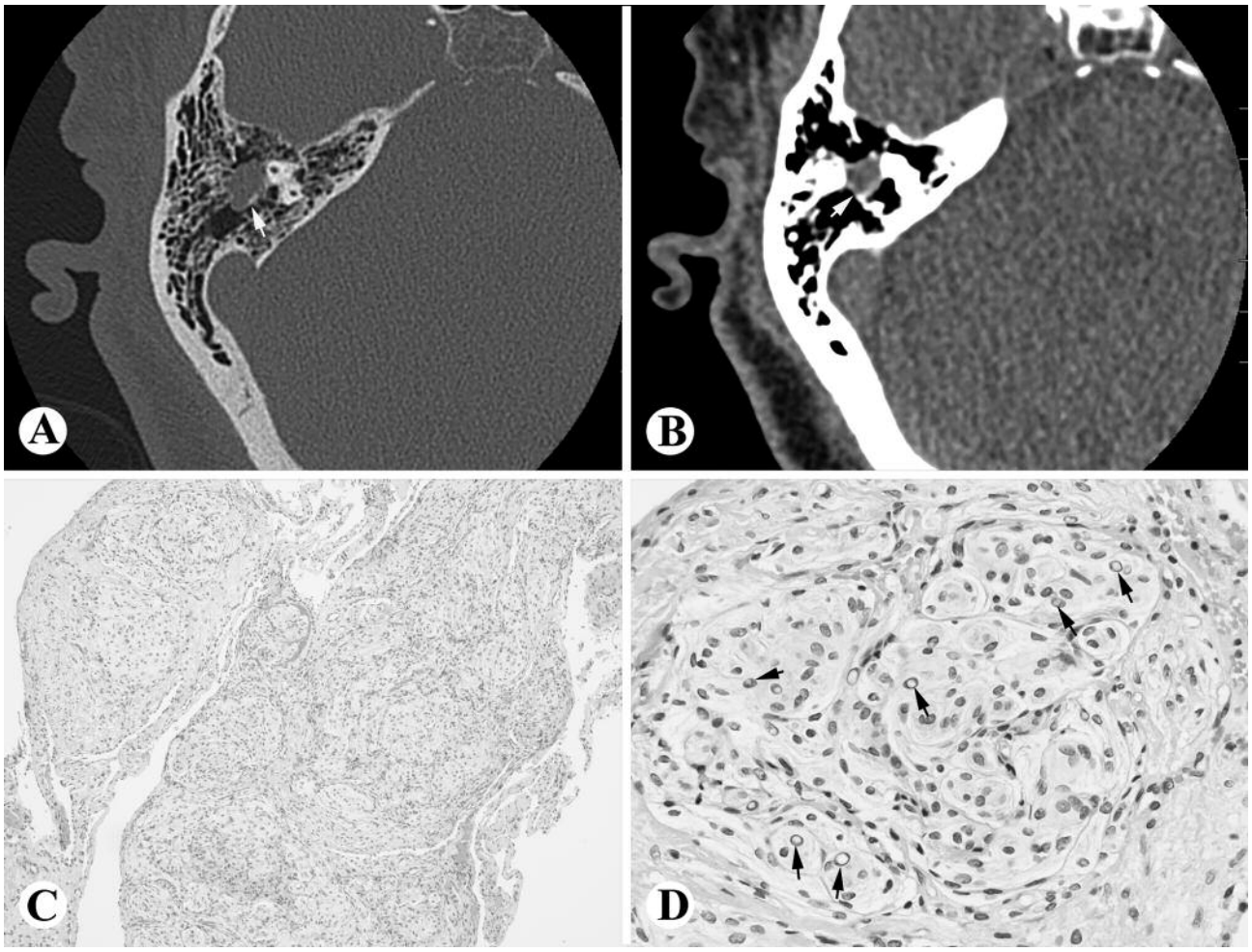

Figure 1. *Primary mastoid meningioma. A, B: Computed tomographic scans showing a 1.0 cm soft-tissue mass (arrow) present in the mastoid. C, D: Histologically, the tumor was composed of nests with whorl arrangement of the epithelial cells with intranuclear pseudoinclusions (arrows) (H&E stain; C: 100×, D: 400×).*

histological variant and the absence of mitotic activity, the tumor was classified as a benign WHO grade 1.

The pathogenesis of meningiomas is not entirely understood. The most common genetic abnormality is a loss of heterozygosity of chromosome 22. Pertinent to our case, a recent study of 50 male patients over 55 years with meningioma showed *BRCA1* to be methylated in their tumor cells in all cases. The silencing of *BRCA1* through hypermethylation may play an important role in meningioma formation in this population (8).

Due to the generally indolent growth rate and benign nature of meningiomas, many patients remain asymptomatic for long periods of time and thus can be managed conservatively with close observation. Gross total resection, when safely feasible, is often curative for symptomatic meningiomas. In some instances, subtotal resection for debulking should be considered in patients with extensive adherent middle-ear disease who possess normal preoperative sensorineural hearing and facial nerve function. Subsequently, radiation therapy is applied for most malignant cases of meningiomas, or when surgery is not feasible due to the meningioma location. Lastly, long-term follow-up with serial imaging is necessary for patients with meningiomas to exclude recurrence. Generally, the overall survival rate after surgical excision of meningiomas is 85%, 75%, and 70% at 5, 10, and 15 years, respectively [reviewed in (9)].

In conclusion, we report a rare case of primary extracranial meningioma of the mastoid, which must be considered by otolaryngologists and pathologists in the differential diagnosis of middle-ear pathology. Due to the rarity of this primary tumor type and the nonspecific presenting symptoms, it lends itself to misdiagnosis,

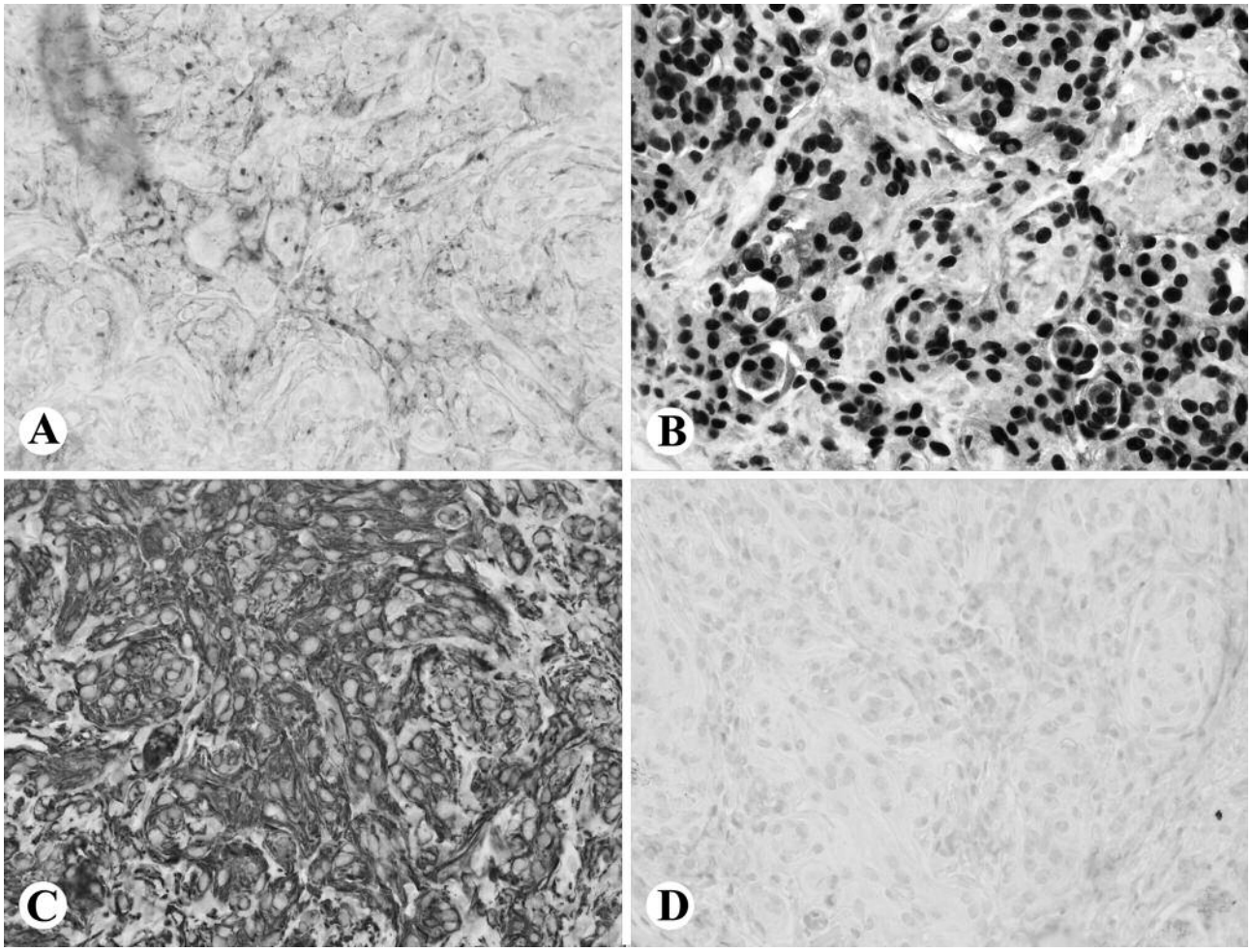

Figure 2. *Immunohistochemistry of the meningioma, showing the tumor cells to be positive for epithelial membrane antigen (A), progesterone receptor (B) and vimentin (C), and negative for synoptophysin (D) (400×).*

resulting in inappropriate clinical management, particularly in a patient with history of multiple cancers. Histology, augmented by immunohistochemistry when needed, is critical for accurate diagnosis, and MRI with gadolinium enhancement is necessary to rule out intracranial involvement. Patients with growing and symptomatic middle-ear meningioma should undergo surgical excision. Long-term periodic radiographic follow-up is necessary to monitor tumor recurrence.

Conflicts of Interest

The Authors have no conflicts of interest to declare.

Authors' Contributions

M.H. wrote the article. J.L. designed the study, reviewed the slides, made the diagnosis, collected and analyzed the data, and finalized the article. J.K. reviewed the slides and article. Y.T., G.L. and W.Z. reviewed the article.

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