CASE REPORT

Middle ear adenoma with uncommon presentation and literature review

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SUMMARY

Middle ear adenoma (MEA) is a rare benign tumour. Here we report a case of MEA in a 39-year-old man with hearing loss. Some significant histopathological features of MEA and neuroendocrine differentiation identified by immunohistochemistry are described. The tumour showed remarkable and rare degenerative histological characteristics. There were a few tumour cells which were covered by degenerated tissue. Consequently, following frozen biopsy, the tumour was misdiagnosed as chronic ear inflammation. No recurrence was seen in this patient after 45 months of follow-up; regular clinical and radiological follow-up is necessary since recurrence is possible. A literature review for MEA is presented and this type of tumour is discussed clinically, microscopically and immunohistochemically. The differential diagnosis and associated treatment are described.

BACKGROUND

Middle ear adenoma (MEA) is a rare benign tumour. About 100 cases¹ have been reported in the literature since it was first reported by Hyams and Michaels in 1976.² Preoperative clinical diagnosis of MEA is very difficult because it usually lacks specific findings or symptoms. Most cases are diagnosed through histopathology and immunohistochemical findings during or after surgery.³ Here, we report the case of a 39-year-old man who underwent surgery for MEA. Histologically, the tumour showed obvious degeneration, with no cell mitosis and a low MIB-1 index, results which differ from the findings in previously described cases. The degenerative tumour tissue can be easily overlooked or misdiagnosed as inflammation.

CASE PRESENTATION

A 39-year-old man presented with a 4-day history of hearing loss in his right ear, with dizziness and a skewed mouth. Pure tone audiometry showed severe hearing loss of 116 dB in the right ear and normal hearing in the left ear. The air-bone gap was about 50 dB. Audiometric assessment identified unilateral conductive hearing loss, prevalent in the conversational frequencies. The patient had no past medical or family history. Otoscopic examination showed a pink granulation-like tissue in the inner portion of the external auditory canal. The tympanic membrane was bulging, probably due to the neoplasm or hydrops in the tympanum.

INVESTIGATIONS

Imaging features

A CT scan of the temporal bones revealed a soft tissue mass in the right middle ear cavity without invasion of the ossicles. An MRI scan of the temporal bones showed a mass (white arrows) with a slightly hyper-intense signal on the T2-weighted image (TR/TE 4000/110 ms) and an intermediate signal on the T1-weighted image (TR/TE 450/12 ms) with mild enhancement after intravenous gadolinium as shown in [figure 1](#).

Histopathology

The mass was completely resected and some tumour tissue adherent to the drum sinus and mastoid area was seen. The specimen was described grossly as irregular, soft, and with pinkish fragments. It measured 0.8×0.5×0.4 cm. The intra-operative frozen biopsy showed a few cells seemingly benign at the edge, and the diagnosis was chronic inflammation. The other tissues were routinely processed, and a 4 µm-thick paraffin-embedded section was stained with haematoxylin and eosin (H&E).

Microscopically, some clustered cells were seen diffused into the fibrous tissue. The growth patterns of the tumour were solid, glandular or trabecular as shown in [figure 2](#). The tumour cells were uniform and cuboidal or cylindrical with moderately abundant acidophilic cytoplasm, as well as small and hyperchromatic nuclei. Some tumour cells were degenerative with vague shapes of cytoplasm and nucleus. No mitosis or necrosis was seen.

Immunohistochemistry

We performed immunohistochemical staining on the tumour sections with primary antibodies against epithelial membrane antigen (EMA), vimentin, cytokeratin (CK), CD56, chromogranin A, synaptophysin, P63, glial fibrillar acidic protein (GFAP), S-100 protein and Ki67. A Dako Envision Plus detection kit (Dako, Carpinteria, CA, USA) was used for visualisation. As shown in [figure 3](#), tumour cells were immunoreactively positive for CK, CAM5.2, EMA, CD56, chromogranin A and synaptophysin, and negative for P63 and S-100. Ki67 positivity was about 1% in the tumour cells.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis including salivary gland tumour, ganglion cell or nerve sheath tumours and adenocarcinomas has been reported previously.

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Figure 1 Imaging features of the middle ear adenoma. (A) CT scans show a soft tissue mass (white arrow) in the right middle ear cavity without invasion of the ossicles. Right mastoiditis (grey arrow) was found. (B) MR scans of the temporal bone show a mass (white arrow) with a slightly hyper-intense signal on the T2-weighted image (TR/TE 4000/110 ms) and an intermediate signal on the T1-weighted image (TR/TE 450/12 ms) with mild enhancement after intravenous gadolinium.

Lott Limbach *et al*⁴ suggested that MEA had at least two cell populations, including luminal and basal cells. However, unlike ceruminous adenomas, MEAs lack myoepithelial differentiation given the absence of S-100 protein and SMA staining. As a result, MEA can be easily distinguished from salivary gland tumours by negative staining to myoepithelial markers such as S-100, P63 and SMA protein immunohistochemically. In our case, the tumour cells were also immunoreactive with epithelium marker CK, but negative for P63 protein.

The differential diagnosis of benign tumours includes paraganglioma and nerve sheath tumours.⁵ Paraganglioma cells are surrounded by spindle supporting cells, positive for synaptophysin and chromogranin, and negative for CK. Supporting cells are positive for S-100 protein. Schwannoma contains Antoni type A and B areas and Verocay corpuscles can always be seen. The tumour cells are diffusely positive for S-100 protein.

The differential diagnosis of malignant tumour includes adenocarcinoma. In general, MEA is considered benign but may be mistaken for adenocarcinomas because of their histological heterogeneity.⁶ However, adenocarcinoma has much more polymorphism and tumour necrosis than MEA. Previous reports suggested that MEA was benign, lacking any capacity for metastasizing.⁷ Primary MEA generally develops slowly, and local invasion is usually non-destructive.⁸ In contrast, most adenocarcinoma is metastatic. MEA can easily be distinguished from adenocarcinoma due to its benign cell morphology, lack of destructive characteristics and imaging results.

Agaimy *et al*⁹ reported that a plasmacytoid cell appearance seemed to be infrequent but was observed in one of their six cases. Consequently, plasmacytoma should be considered.

Tomazic *et al*¹⁰ reported a case of MEA mimicking chronic otitis media with an episode of facial nerve palsy, so pathological and immunohistochemical investigation is necessary.

Figure 2 Histopathological features of middle ear adenoma. (A) The tumour cells have abundant eosinophilic cytoplasm, with a small nucleus. Some of the tumour tissue shows papillary (A, D) and glandular (B, C) architecture; (C, D) some of the tumour tissue is degenerative (H&E staining, A,C: $\times 200$; B,D: $\times 100$).

TREATMENT

Surgery is the only option to cure MEA. The size and range of the tumour determines the method of operation which includes radical mastoidectomy and tympanotomy. Our patient underwent a tympanomastoidectomy, retrieval of bone from the attic roof and medial wall of the attic and Eustachian tube, and removal of the tensor tympani muscle in the middle ear cleft. The mass was completely resected and the margin was negative.

The retrospective analysis of 46 patients conducted by Ramsey *et al*¹¹ showed that 48% of cases received radical mastoidectomy, 17% line tympanic cavity exploration, and 17% line tympanic cavity mastoidectomy, with the operation method also including rock cone resection and external auditory canal tumour resection. If the tumour tissue surrounds the ossicle, for complete surgical resection of the tumour, the ossicle should usually be removed, followed by auditory ossicle chain reconstructive surgery to improve hearing.⁵ The recommended treatment is total exploration. If the tumour has not been completely removed, there may be local recurrence.¹² The few cases of recurrence that do occur can be removed completely by repeat surgery.

OUTCOME AND FOLLOW-UP

Our patient recovered from facial nerve paralysis, while pure tone audiometry showed a conductive hearing loss of 75 dB in the

right ear at 18 months. No recurrence was found over 45 months of clinical and radiological follow-up. Regular clinical and radiological follow-up is necessary since recurrence is possible after a long period.

DISCUSSION

MEA accounts for approximately 4% of all ear tumours. It most likely arises from the mucosal epithelium of the middle ear and grows slowly. Surgery or a biopsy is usually needed for definitive histopathological diagnosis. Saliba and Evrard¹ examined 75 patients with a carcinoid tumour and 19 patients with MEA. The patients ranged in age from 16 to 77 years (median age: 44.6 years). A total of 41 women and 53 men were included in the study. There was no difference in MEA incidence between right and left ears.

The tumour is often unilateral. More than 90% of patients complain of hearing loss, with 20%–30% experiencing ear fullness, tinnitus, discharge and sometimes facial paralysis.¹³ Some patients were asymptomatic, with MEA only discovered during physical examination. The tumour usually has a complete tympanic membrane and appears to be a brown-red mass. It is relatively limited and has no obvious capsule. Auditory ossicles can be surrounded or destroyed by the tumour cells, but bone wall damage has not been seen.¹⁴

Figure 3 Immunohistochemical features of middle ear adenoma. The tumour exhibits a positive reaction to cytokeratin (A), CD56 (B), chromogranin A (C) and synaptophysin (D), but a negative reaction to P63 (E); the Ki67 (F) proliferative index is below 1% in the tumour (IHC, A,B: $\times 200$; C,D,E,F: $\times 400$).

Microscopically, the tumour is not encapsulated, but has moderate cellularity, is glandular and trabecular, and has solid patterns. The typical tumour cell has a round, regular nucleus which contains dense chromatin surrounded by eosinophilic cytoplasm as reported previously.^{8 13} These cells are laid out in a more or less abundant, fibrous, myofibrous stroma or

fine vascular tracts. There is usually no necrosis or mitotic activity.^{8 15}

Immunohistochemically, Torske and Thompson¹⁶ described the presence of markers such as vimentin, neuron specific enolase (NSE), CK and CAM5.2. Among the 48 cases of MEA they examined, 90% were CK positive, 50% were NSE positive, and 31%

were synaptophysin positive. These neuroendocrine positive cells are mainly distributed at the bottom of the glands. Therefore, MEA is characterised by a double glandular and neuroendocrine component. Identification of the immunohistochemical characteristics is important for MEA diagnosis.

Learning points

- ▶ This case describes a remarkable and rarely seen degenerative histological characteristic of middle ear adenoma (MEA) where there are few tumour cells and they are covered by degenerated tissue.
- ▶ Such tumour cells could be easily overlooked or misdiagnosed as chronic inflammation.
- ▶ Recognising this presentation of MEA is important for avoiding misdiagnosis.

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Competing interests None declared.

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