

## Case Report

# Epithelioid angiosarcoma of the middle ear: a rare case report

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**Abstract:** Epithelioid angiosarcoma (EAS) is a rare neoplasm characterized by an epithelioid morphologic appearance that mimics carcinoma. EAS usually occurs in extra skeletal sites and soft tissues, but rare in the middle ear. Here, we reported a male patient who presented at our hospital with hearing loss for 8 years, otalgia of the left ear and headache for over a month. Computed tomography (CT) scan revealed that a space-occupying lesion in the left mastoid area. The patient's otalgia and headache disappeared quickly after surgery. Finally, EAS was confirmed by histopathology and immunohistochemistry. Subsequently, the patient was discharged without postoperative radiation therapy or chemotherapy, and was followed-up regularly. EAS of the middle ear is very rare. Pathology and immunohistochemistry are needed for a definitive diagnosis while early detection and tumor removal can result in a better outcome.

**Keywords:** Epithelioid angiosarcoma, middle ear, histopathology, immunohistochemistry, surgery

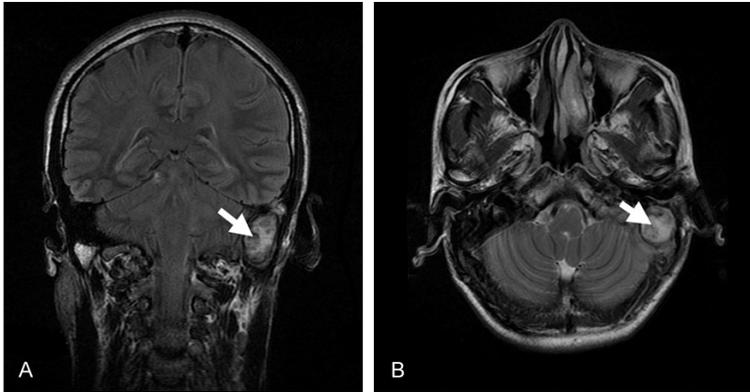
### Introduction

Epithelioid angiosarcoma (EAS) is a rare and high-grade aggressive malignancy originating from endothelial cells, most commonly arises in the deep soft tissues [1]. EAS is characterized by an epithelioid morphologic appearance that mimics carcinoma, making it difficult to diagnose [2]. Previous studies have reported that EAS can occur in a variety of primary sites [3]. However, it rarely occurs in the ear. The present study reported a case of EAS of the middle ear that was diagnosed based on clinical characteristics and pathological examination. It is important to consider the site of origin and histological images when distinguishing EAS from other tumors of the ear, as EAS does not commonly occur in this site.

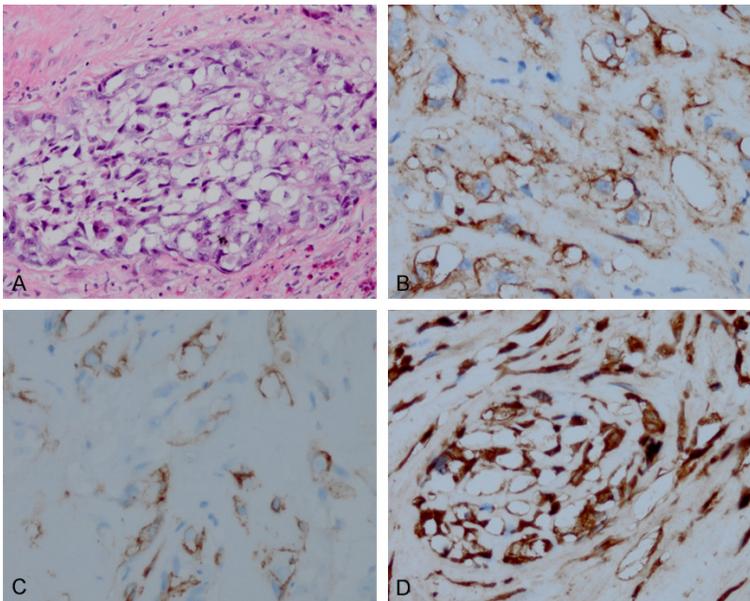
### Case report

A 36-year-old male patient had suffered from hearing loss for 8 years, otalgia of the left ear, and headache for over a month. He visited our hospital in August 2014 because of symptom aggravation. The patient's medical history re-

vealed that he was a hepatitis B virus carrier with normal liver function. He did not use immune suppression agents or illegal drugs, and had no history of radiation therapy, no other infectious diseases and drug allergy history, and no similar disease in his family. On admission, physical examination showed that perforation of the tympanic membrane in the left ear, and a smooth mass was palpable in the mastoid area of the left ear, the mass was 2.5 cm in diameter and painful upon pressing. No laboratory abnormalities were detected. Computed tomography (CT) scan revealed that a space-occupying lesion in the left mastoid area, which had no clear boundary with the sigmoid sinus (**Figure 1**). Pure tone audiometry showed severe hearing loss in the left ear. The patient could not fall asleep without anodyne. During surgery, we found that the bone in the surface of the mastoid had been broken. White tumor tissue was detected in the mastoid area with membrane integrity and a size of approximately 3.5×2.0 cm; necrotic tissue could be seen inside. The base of the tumor adhered with the meninx, and the size of the meningeal exposure was about 1.5×1.0 cm, without smooth surface



**Figure 1.** CT scan of the ear. A. CT scan revealed a space-occupying lesion (white arrowhead) in the left mastoid area for coronal section; B. Space-occupying lesion (white arrowhead) for transverse section, and no clear boundary with the sigmoid sinus.



**Figure 2.** Pathological changes of tissue. (A) Heterogenic epithelial cells were present with clustered, abundant, and bright cytoplasm, distinct nucleoli, and parts of the cytoplasm were occupied by erythrocytes (hematoxylin-eosin staining  $\times 200$ ). Immunohistochemistry revealed that tumor cells were positive for CD34 (B  $\times 400$ ), CD31 (C  $\times 400$ ), and vimentin (D  $\times 400$ ).

and easy bleeding. The sigmoid sinus plate had an area of damage about  $1 \times 1$  cm in size. About 6 mm of the vertical segment of the facial nerve was exposed and the surface was not smooth. The invaded tissue was completely excised. Histopathology revealed heterogenic epithelial cells with clustered, abundant, and bright cytoplasm, distinct nucleoli, and part of the cytoplasm contained erythrocytes (**Figure 2A**). In addition, immunohistochemistry was performed and revealed that the tumor cells were posi-

tive for CD34 (**Figure 2B**), CD31 (**Figure 2C**), vimentin (**Figure 2D**), and Ki67 (approximately 20%) expression, while negative for SMA, Des, HMB45, and PCK (Figure not shown). Based on these findings, our diagnosis was epithelioid angiosarcoma of the middle ear. The patient's otalgia and headache disappeared quickly after surgery, and hearing of the left ear also partially improved, the patient was discharged without postoperative radiation therapy or chemotherapy and is followed-up as an outpatient every 3 months.

### Discussion

EAS is one of the malignant vascular tumors derived from mesenchymal cells. They can occur in many locations, including the bone [4], breast [4], heart [6], thyroid glands [7], skin [8], and soft tissues. However, it is extremely rare in the middle ear, although some cases of epithelioid hemangioendothelioma of the middle ear have been reported previously [9, 10]. Only 1 case of EAS in middle ear has been recorded in the published literature (**Table 1**) [11]. The etiology of EAS is not clear, including radiation, trauma, high estrogen levels and malignant transformation of a benign hemangioma [12]. The most common symptoms are pain and swelling, soft tissue swelling

is often discovered by physical examination. The tumor mostly occurs in middle-aged men and is the most malignant epithelioid vascular tumor, according to a previous study.

The diagnosis of EAS mainly relies on surgical specimens analyzed using histopathology and immunohistochemistry. EAS is histopathologically characterized by infiltrative lesions composed of sheets of large oval or round cells with abundant eosinophilic nucleoli. Although cyto-

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**Table 1.** Information for present case and published case

Patient	Sex	Age (year)	Mass location	Immunohistochemistry	Treatment	Prognosis
Our case	Male	36	Left middle ear	CD34(+), CD31(+), Vimentin(+), ki-67 (20%), SMA(-), Des(-), HMB45(-), and PCK(-)	Surgery, no radiology and chemotherapy	2 years after surgery and still alive
Reported case by Cui et al [11]	Female	65	Right middle ear	CD34(+), Vimentin(+), CD31(+), FLI-1(+), ki-67(40%), CK5(-), CK7(-), GCDFP-15(-), CD68(-), CK(-), LCA(-), HMB45(-), S-100(-).	Surgery, no radiology and chemotherapy	Died 9 months after surgery

logical atypia is present, the tumor cells are relatively monomorphic. Mitosis, necrosis, and hemorrhage are common, and the tumor often invades adjacent tissues. Sometimes, a few cells show intracytoplasmic lumina containing occasional erythrocytes. The patient in our study visited doctor because of otalgia caused by the tumor pressing on the facial nerve. Using immunohistochemistry, the tumor cells were tested positive for endothelial cell markers CD31, CD34, factor VIII, Ulex europaeus agglutinin I (UEA-I) and vimentin. Endothelial cells markers are important for confirming a diagnosis of angiosarcoma. CD31 and CD34 are particularly important as they have the highest positive expression rate. Currently, CD31 is considered the most sensitive and specific endothelial cell marker for angiosarcoma. CD34 commonly expressed in many fibroblastic and myofibroblastic tumors, and is therefore less sensitive than CD31. In our case, CD34, CD31 and vimentin are positive, meeting the diagnosis criteria for angiosarcoma. The histopathology and immunohistochemistry of tumors will contribute to the differential diagnosis of other diseases, including metastatic carcinoma, epithelioid sarcoma, epithelioid hemangioendothelioma and malignant melanoma. For example, in metastatic carcinoma, the tissue usually expresses CK but not vimentin or CD34, according to the immunohistochemical results. Epithelioid sarcoma does not express CD34 or CD31, while in low-grade cancer, the tissues diffusely express CK, without expression of CD34 or CD31. All epithelioid mesenchymal tumors have some overlapping morphology and share variable immunophenotypic expression. Therefore, they represent a major diagnostic challenge for clinicians and pathologists [2]. EAS can mimic the angiomatous variant of epithelioid sarcoma, making a differential diagnosis challenging. Consequently, all markers of epithelioid mesenchymal tumors should be assessed.

Currently, there is no standard treatment for EAS, ESA treatment mainly relies on surgery moveout, followed by postoperative radiotherapy or chemotherapy. There is also no unified standard for chemotherapy and the effects are not ideal. Meanwhile, metastasis of EAS often occurs early, including to the lymph nodes and other organs. Without surgery, radiotherapy or chemotherapy, the prognosis of EAS is very poor. EAS has a high mortality rate with more than 50% of patients will die in 2-3 years [3, 4, 13]. Aging, tumor size, primary site and an increased proliferative index are associated with an adverse prognosis [14]. Therefore, clinicians should pay more attention to EAS and promote further understanding and research into the tumor.

In our case, the patient is a young man and the tumor in his ear was removed. His symptoms of otalgia and headache disappeared after surgery and the hearing in the left ear has partially recovered. The patient has had a favorable prognosis for 2 years but still needs further evaluation and long-term follow up.

In conclusion, EAS of the middle ear is very rare, and pathology and immunohistochemistry are needed for a definitive diagnosis. Early detection and removal of the tumor can result in a better outcome. This case report highlights the importance of recognizing that EAS can arise in locations other than the deep soft tissues. A more careful differential diagnosis is therefore required.

### Disclosure of conflict of interest

None.

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