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CASE REPORT

Epithelioid hemangioendothelioma of the parotid gland: a case report

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Abstract
We present the case of a patient with epithelioid hemangioendothelioma of the parotid gland. A 70-year-old female developed swelling and pain in the lower part of the left ear 18 months previously and had visited a local hospital. Fine-needle aspiration cytology revealed no definitive diagnosis, but incisional biopsy under local anesthesia suggested epithelioid hemangioendothelioma. She was then transferred to our hospital, where she underwent total extirpation of the left parotid gland, left cervical lymph node dissection, and postoperative radiation therapy. However, she died from distant metastases 13 months after surgery. No previous study has reported any case of distant metastasis or death due to epithelioid hemangioendothelioma of the parotid gland. To the best of our knowledge, this is the first case report on distant metastasis and death due to the development of parotid gland cancer.

Keywords Epithelioid hemangioendothelioma · Parotid gland · Surgical treatment · Radiation therapy

Introduction

Epithelioid hemangioendothelioma is rare and occurs mainly in the liver, lung, or bone, and only a very limited number of reports have described epithelioid hemangioendothelioma of the parotid gland. We performed surgery and postoperative radiation therapy in a patient with epithelioid hemangioendothelioma of the parotid gland. However, the patient developed distant metastases and died 13 months after surgery. Here, we report the course of epithelioid hemangioendothelioma of the parotid gland, with reference to other relevant reports.

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Case report

The patient was a 70-year-old female, with no suggestive medical history, who developed swelling and pain in the lower part of the left ear 18 months previously. She had visited a local hospital, where cytopathological investigation suggested a class III tumor, and the results of incisional biopsy under local anesthesia suggested epithelioid hemangioendothelioma. The patient was then transferred to our hospital for surgery.

On initial examination, she demonstrated induration and skin redness in the lower part of the left ear and left hypoglossal nerve paralysis with no facial nerve paralysis. Computed tomography (CT) and magnetic resonance imaging (MRI) depicted a marginally stained tumor measuring 42 mm in diameter between the deep lobe of the left parotid gland and left parapharyngeal space. Left internal jugular vein occlusion and deep neck muscle invasion were suspected. Although fluorine-18-2-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography (FDG/PET-CT) indicated that SUVmax for the tumor was 4.4, neither cervical lymph node metastases nor distant metastases were observed (Fig. 1).

Total extirpation of the left parotid gland and left cervical lymph node dissection was performed. The former included resection of the skin, hypoglossal nerve, main branch of the

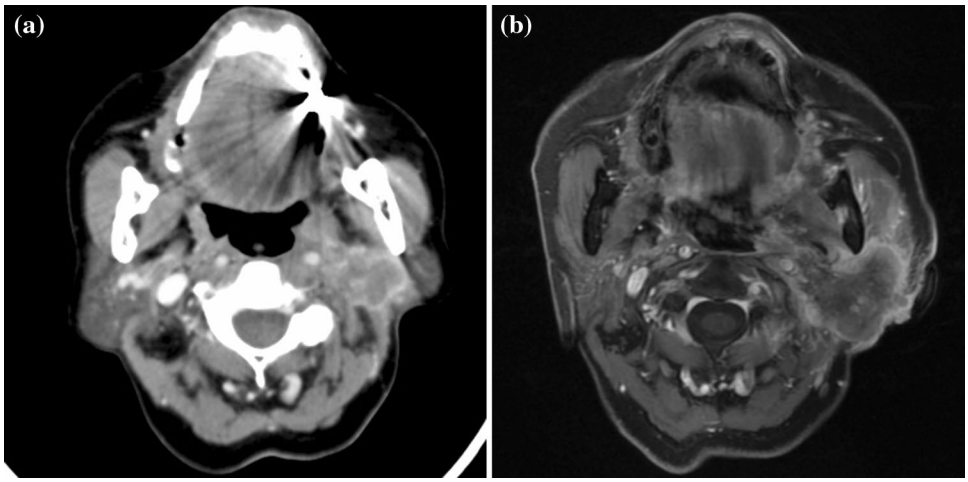

Fig. 1 Characteristics of the tumor. Contrast enhanced CT scan showing the parotid gland nodule with ring enhancement (**a**). MRI suggests deep muscle invasion (**b**)

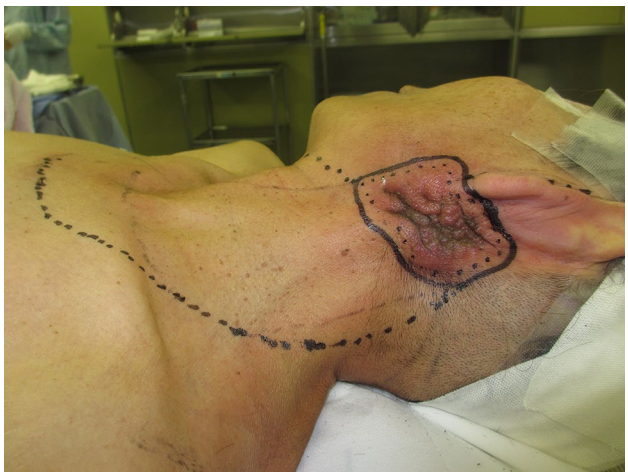

Fig. 2 Tumor invasion of the skin. Rotation flap was used for coverage of skin defect

facial nerve, accessory nerve, posterior belly of the digastric muscle, and sternocleidomastoid muscle, while the latter included removal of the regions between level I and level V. The skin defect area measured 55 mm × 50 mm and the operative wound was closed using rotation flaps (Fig. 2).

Epithelioid tumor cells with nuclear irregularity demonstrated alveolar or cord-like structures with myxoid or hyaline matrixes. Furthermore, tumor cells with cytoplasmic vacuoles were observed. Immunostaining revealed that the tumor cells were positive for CD31, CD34, and D2-40 and locally positive for CK-OSCAR (Fig. 3). Genetic analysis of formalin-fixed paraffin-embedded tissue demonstrated that the tumor was positive for *WWTR1–CAMTA1* fusion (Fig. 4). Based on these findings, epithelioid hemangioendothelioma was diagnosed.

Although the denuded area of the deep cervical muscle at the resection stump was positive for tumor cells, no cervical lymph node metastases were observed. For postoperative adjuvant treatment, radiation therapy was performed 30 times at 60 Gy. However, because FDG-PET/CT depicted distant metastases in the right lung, lumbar spine, and liver 4 months and 22 days after surgery (Fig. 5), the patient was asked to select between anticancer drug treatment or supportive treatment. She selected supportive treatment and died 13 months and 15 days after surgery.

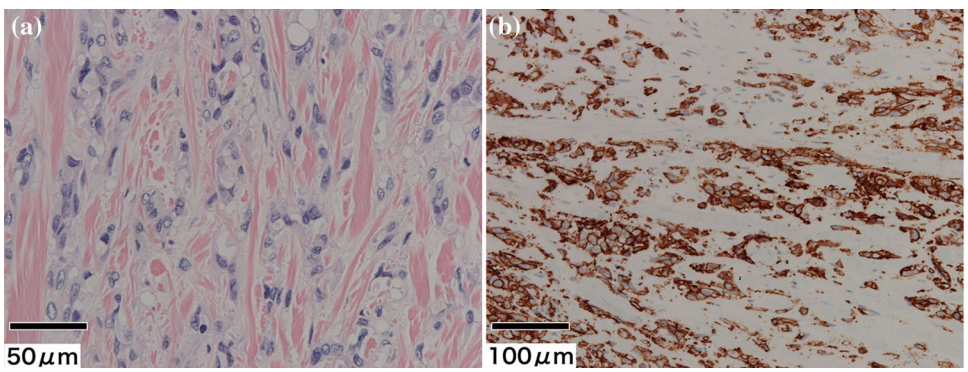

Fig. 3 Histopathological images. H and E staining showing epithelioid morphology with intracytoplasmic lumina (**a**). Immunohistochemical staining showing CD34 positive cells (**b**)

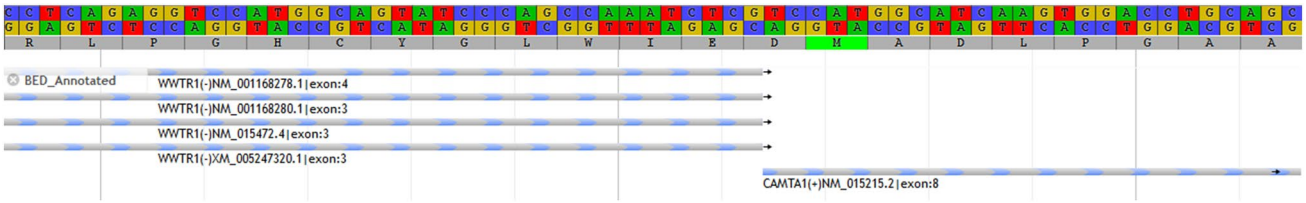

Fig. 4 Molecular analysis by next-generation sequencing. The tumor harbored a fusion of *WWTR1–CAMTA1*

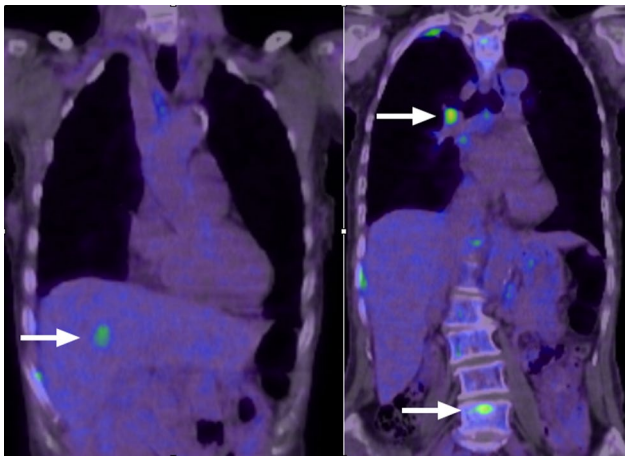

Fig. 5 Distant metastases in the right lung, lumbar spine, and liver

Discussion

Epithelioid hemangioendothelioma is rare vascular tumor. In 1982, Weiss et al. referred to endothelial-derived mesenchymal tumor in the soft tissue as epithelioid hemangioendothelioma [1]. Major primary sites are the liver, lung, and bone; however, cases have also been reported in the head and neck area, breast, lymph nodes, and other soft tissues [2]. In 2013, the World Health Organization (WHO) classified epithelioid hemangioendothelioma as a malignant tumor. Although epithelioid hemangioendothelioma progresses slowly, the reported incidence of metastases is 20–30% and mortality is 15% [3].

Epithelioid hemangioendothelioma is characterized by acidophilic epithelial cells with myxoid/hyaline matrixes and cytoplasmic vacuoles. Immunostaining indicates that the epithelioid hemangioendothelioma is positive for CD31, CD34, factor VIII-related antigens, FLI1, other endothelial markers, and the lymphatic endothelial marker podoplanin [3–7]. *WWTR1–CAMTA1* gene fusion has recently gained attention as the specific gene abnormality of this tumor [8]. The characteristics and course of epithelioid hemangioendothelioma of the parotid gland in the three patients previously reported to date as well as in our case are presented in Table 1 [9–11]. All four patients underwent surgery and one patient previously reported and our case underwent radiation therapy. Tumors were > 3 cm in diameter in two cases including our case; our patient had the largest tumor. Patients were followed up for 7–18 months. Unlike in the present case, recurrence was not observed in the previous three cases.

Deyrup et al. classified epithelioid hemangioendothelioma of the soft tissue as a high-risk tumor if it had > 3 mitotic figures per 50 HPF or size > 3 cm. Neither of these characteristics was considered as low risk. They reported that the 5-year disease-specific survival and metastatic rates in the high-risk group were 59% and 32%, respectively [12]. Our present patient was assigned to the high-risk group, since the tumor diameter was 42 mm and the average number of mitotic figures in 50 HPFs was 5.

We performed radiation therapy after surgery to control the residual disease. Radiation therapy can be used as a therapeutic option. Despite the poor prognosis, evidence is in favor of radiation therapy, which offers local pain control, and while chemotherapy is preferred in cases of distant metastasis, its beneficial effect remains unconfirmed [13].

Table 1 Reported cases of parotid gland epithelioid hemangioendothelioma

References	Gender	Age	Tumor size (mm)	Treatment	Outcome
Pigadas et al. [9]	F	48	15	Surgery	NED 18 months
Amin [10]	M	81	20	Surgery	NED 7 months
Falvo et al. [11]	M	28	38	Surgery, radiation	NED 18 months
Our case/2017	F	70	42	Surgery, radiation	DOD 13 months

NED no evidence of disease, *DOD* died of disease

No standard treatment for epithelioid hemangioendothelioma has yet been established.

Conclusion

We report the case of a patient with epithelioid hemangioendothelioma of the parotid gland.

Despite surgical treatment and postoperative radiation therapy for local progressive cancer, the patient died due to distant metastases. Further investigation is necessary to establish an effective treatment regimen.

Compliance with ethical standards

Conflict of interest The authors report no conflict of interest.

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