Clinical Case Report

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Epithelial-myoepithelial carcinoma with high-grade transformation of parotid gland

A case report and literature review

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Abstract

Rationale: Epithelial-myoepithelial carcinoma (EMC) is regarded as a rare low-grade malignant tumor of the salivary gland, accounting for 0.4% to 1% of all salivary gland tumors. However, epithelial-myoepithelial carcinoma with high-grade transformation (EMC with HGT) is extremely rare, therefore it is easily to be inappropriately diagnosed and treated. Herein, we report an unusual case of EMC with HGT involving the parotid gland and discuss the clinical features and histological characteristic of EMC with HGT, in order to remind the doctors to take appropriate diagnosis and treatment.

Patient concerns: A 77-year-old female sought for treatment in our hospital due to pain mass in the left parotid gland for 6 months with rapid growth recently.

Diagnoses: EMC with HGT was confirmed by final pathology, and then the result showed there were 2 distinctly different areas in the tumor, including the typical EMC component and intensive spindle cells component.

Interventions: The extensive resection surgery was performed.

Outcomes: The patient was uneventful after surgery and no recurrence or metastasis has been observed after follow-up of 4 years.

Lessons: A review of literature suggested that EMC with HGT patients trend to be more aged, more aggressive and poorer prognosis than typical EMC patients. In order to avoid misdiagnosis and inappropriate treatment, it is necessary to accurately recognize the differences between the EMC with HGT and typical EMC.

Abbreviations: CK = cytokeratin, EMC = epithelial-myoepithelial carcinoma, EMC with HGT = epithelial-myoepithelial carcinoma with high-grade transformation, MRI = magnetic resonance imaging.

Keywords: clinicopathological characteristics, epithelial-myoepithelial carcinoma, high-grade transformation, salivary gland

1. Introduction

Epithelial-myoepithelial carcinoma (EMC) is a rare malignant neoplasm of the salivary gland, accounting for 0.4% to 1% of all salivary gland tumors.[1] Typically, the EMC is described as a firm tumor, which is hard to invade to the adjacent tissues. Although it has a high rate of recurrence ranging from 35% to 40%, the mortality is low.[2] Therefore, it is considered as a low-grade tumor. Histologically, the EMC generally presents a typical biphasic pattern composing of 2 cell types with variable proportions. The morphology shows the clear myoepithelial cells surround the epithelium-lined ducts, which resemble intercalated ducts in the inner layer.[3] However, several new morphologic subtypes of EMC, which includes double clear EMC, oncocytic EMC, sebaceous EMC, apocrine EMC, EMC ex pleomorphic adenoma as well as EMC with high-grade transformation (HGT) have been recognized recently.[4] HGT is defined as a histological progression of low-grade tumor to high-grade morphology, where the original histological characteristics are lost.[5] The concept of HGT was also known as dedifferentiation previously[6] and was first proposed by Dahlin and Beabout in 1971. The HGT components commonly reported to be undifferentiated carcinoma, poorly differentiated adenocarcinoma or high-grade myoepithelial carcinoma,[5] so the conventional and high-grade transformation components are distinguishable. Recently, this phenomenon of EMC has been define as the concept of HGT, but EMC with HGT is extremely rare.[3] Due to few cases were reported, the clinicopathologic features and treatment of this neoplasm are not yet clear.

In this report, we present an interesting case of EMC with HGT located in the left parotid gland. To our knowledge, there are only 21 EMC with HGT cases reported in the literature to date. Patient provided written informed consent.

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2. Case report

A 77-year-old female sought for treatment in our hospital due to pain mass in the left parotid gland. The lesion was symptomatic and had been present about 6 months with a recent rapid increase in size. The patient reported no prior surgeries.

Upon examination, there was a $3.5 \times 3.0 \times 1.5$ cm medium texture, unclear boundary, immobile, and pain mass, but the facial nerve function was intact. There was no palpable lymphadenopathy. The remaining oral cavity and head and neck examinations were normality.

A large mass sized $35 \times 30 \times 15$ mm in the left parotid gland was identified on MRI (Fat suppressed T2-weighted images showed mild hyperintensity, T1-weighted images showed hyperintensity). The mass was heterogeneous and had an unclear margin, so MRI suggested the mass could be a malignant tumor.

At surgery, we remove the tumor to the biopsy, and then the lesion was considered as a malignant neoplasm. The tumor was not invaded to adjacent tissues, so the patient subsequently underwent extensive resection of the tumor with a safety margin of 1 cm under general anesthesia. Then the tumor was sent for histopathological and immunohistochemistry analysis to confirm the histogenetic origin of the lesion. There were 2 different components including typical EMC and high-grade carcinoma in the lesion. The EMC component includes the inner layer of duct consisted of cuboidal epithelial cells and the outer layer consisted of clear myoepithelial cells. They present various tumor cells, which arrange in trabecular, tubular, or islands. The high-grade transformation component was composing of intensive spindle cells with increased nuclear pleomorphism, mitotic activity, prominent nucleolus and acidophilic cytoplasm. The large amount of spindle cells arranged in fascicular clusters (Fig. 1). Immunohistochemical examination indicated that the EMC component was diffusely positive to CK. The tumor cells of the EMC were only positive for CD117 in the duct, and the outer myoepithelial cells were positive for P63, Calponin and S-100 (Fig. 2). However, the high-grade transformation component was all negative for these biomarkers of the typical EMC. The final pathologic diagnosis was the EMC with HGT.

Adjuvant radiotherapy was suggested, but the patient refused the proposition because of her age. Fortunately, no complications were observed during recovery. The patient was uneventful after surgery and no recurrence or metastasis has been observed after follow-up of 4 years.

3. Discussion

The EMC with HGT is exceedingly rare. HGT may be considered as a slow process with increasing genomic heterogeneity or as a result of an abrupt transition event. So far, 2 forms of the EMC with HGT have been found. The one form was described as EMC with myoepithelial anaplasia or myoepithelial carcinoma arising in EMC, which was defined as severe nuclear atypia and pleomorphism that occurs gradually in the myoepithelial component.[7–9] The nuclear atypia usually is great than 20% in myoepithelial cells.[10] It means a gradual transition of the myoepithelial component of EMC into a more aggressive carcinoma. In the other form, the ductal component can transform into a high-grade carcinoma but the transition is abrupt and rarely. In addition, there is a large amount of nuclear fission and necrosis in the conversion component. In the present case, there were large areas of typical biphasic EMC but the

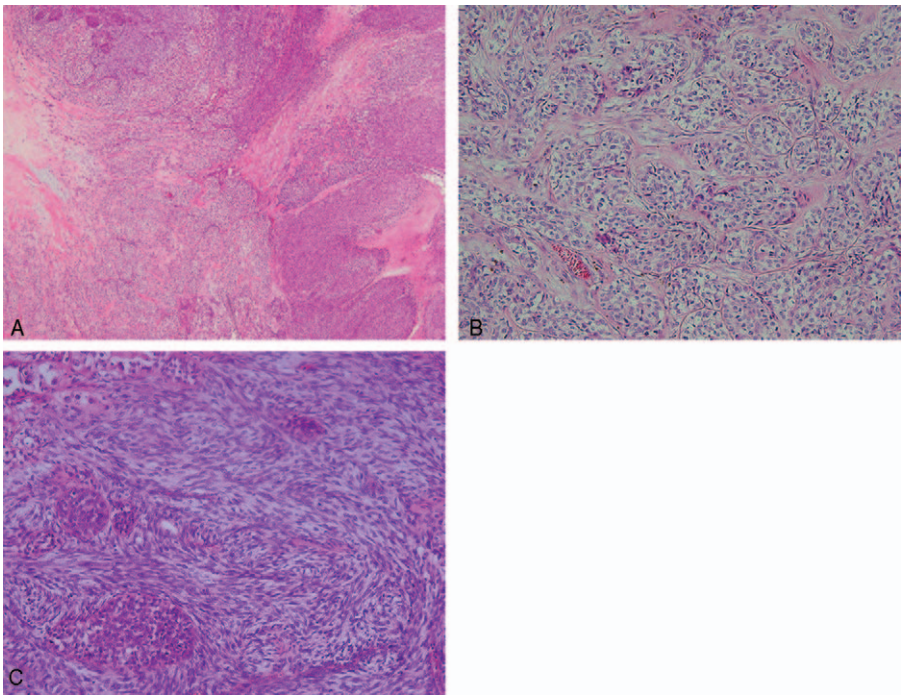

Figure 1. (A) The tumor presents a transition from typical EMC (right) to a high-grade component (left) (HE, 40 ×). (B) The component of typical EMC with inner layer of epithelial cells and an outer clear myoepithelial cell layer (HE, 200×). (C) The HGT component showed intensive spindle cells with increased nuclear pleomorphism, mitotic activity, prominent nucleolus and acidophilic cytoplasm (HE, 200×). EMC = epithelial-myoepithelial carcinoma, HE staining = hematoxylin-eosin staining, HGT = high-grade transformation.

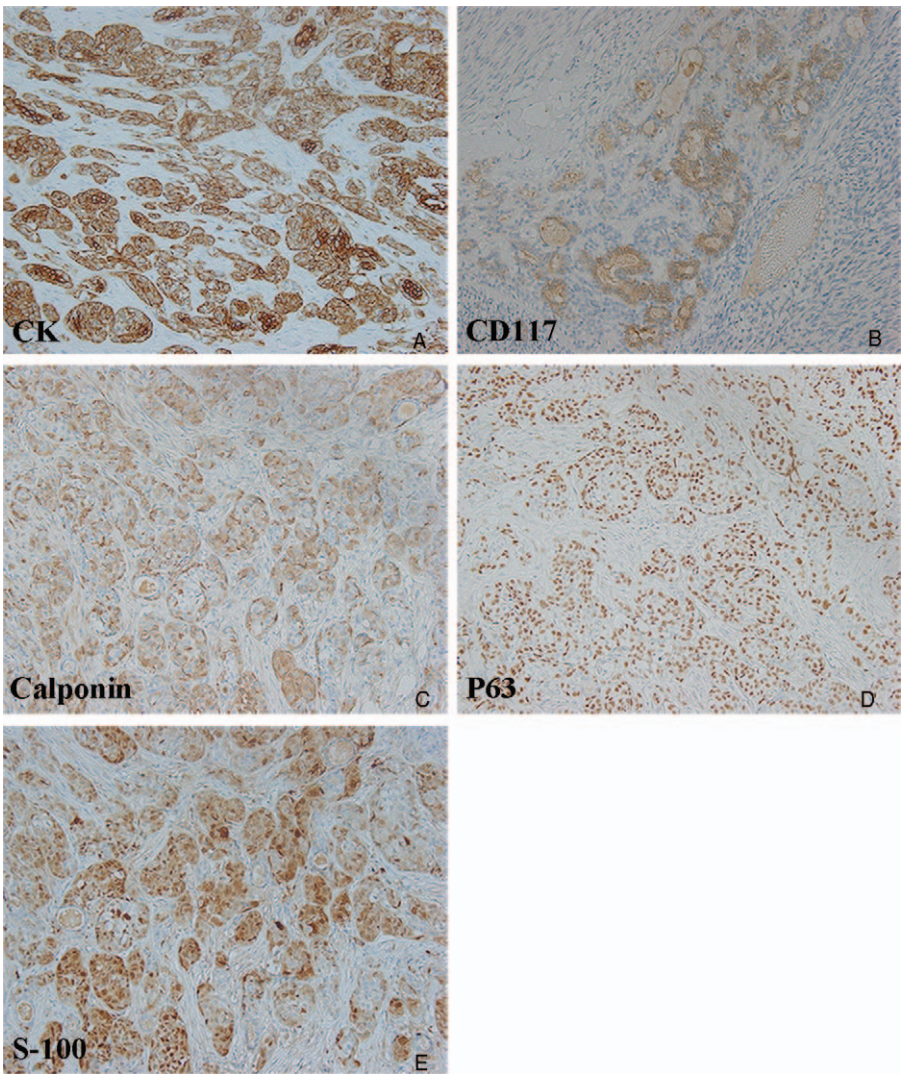

Figure 2. (A) CK was positive in the EMC epithelial component. (B) The CD117 only was positive in the duct of EMC component. (C) Calponin was positive in the EMC myoepithelial component. (D) P63 was positive in the EMC myoepithelial component. (E) S-100 was positive in the EMC myoepithelial component. (magnification, 200×). CK = cytokeratin, EMC = epithelial-myoepithelial carcinoma.

high-grade transformation component was made of intensive spindle cells with increased nuclear pleomorphism, mitotic activity and prominent nucleolus. Moreover, this high-grade component, being tightness adjacent to those low-grade areas, showed negativity for p63, S-100 and calponin. So the authors consider this case is more accord with the form that the EMC abruptly transform the pleomorphic sarcoma. In order to being fully understand the clinicopathological features, treatment modality and prognosis of EMC with HGT, so a literature search was performed. A summary of all 22 cases including our case are presented in Table 1. Overall, we found only 21 cases of the EMC with HGT has been reported. The age of patients' ranged from 46 to 103 years and the median age of diagnosis was 72 years. The male to female ratio is 7:11. As we known, the typical EMC has a slight female predominance and has occurred in patients between 8 and 103 years with a mean age of about 60 years,[4] so I speculated the patients with EMC containing a high-grade transformation component have been older than typical EMC patients. The most frequent site was the parotid gland, followed by the submandibular gland and palate. The lymph node and distant metastases were respectively reached up to 40% and 20%. Only one patient had confirmed mortality. The current patient alive 4 years with no recurrence after surgery. However, the EMC is generally regarded as a low-grade malignancy, the local recurrence rate is estimated to be 30%, and the distant metastases are extremely rare in only 4.5%,[1] so the data has been shown to be more aggressive than typical EMC with a high propensity for cervical lymph node and distant metastases. Though the reported cases are limited and follow-up is insufficiency and short, the poor prognosis suggest the patients of EMC with HGT should be necessary with more radical treatment than typical EMC, including wider excision, neck dissection and even adjuvant radiation therapy.[4]

In conclusion, the EMC with HGT is extremely rare and the authors described a rare case of EMC with HGT arising in the parotid gland. According to the analysis, it is more aggressive and worse prognosis, so it is significant to accurately diagnose the EMC with HGT to avoid inappropriate treatment. More studies are needed in order to deeply understand the clinical and histopathologic features of the EMC with HGT.

Table 1

Clinicopathologic summary of 22 cases of EMC with HGT.

	Age/sex	Location	Size, cm	HGT component(s)	HGT component staining	Follow-up
Simpson et al[11]	103/female	Submandibular	6 × 5 × 3	Epithelial	Patchy+ cytokeratin, HMFG and CEA S100−, Desmin-CAM5.2+, HHF35− S100−	Recurrence 18 months with nodal metastasis, alive at 30 months
Fonseca and Soares[10]					Cytokeratin+,CAM5.2+, MSA−, S100−	N/A
Alos et al[12]	69/male	Parotid	7	Epithelial	All stains negative	Died within 3 months, liver Metastasis
	88/female	Parotid	11 × 8 × 6	Epithelial (adenocarcinoma)		Nodal metastasis at 1 year, alive no NED at 6 years
	78/male	Parotid	4 × 3 × 2	N/A (undifferentiated carcinoma)	Cytokeratin+, CAM5.2+, MSA-, S100 focally+ Vimentin+, S100−, cytokeratin-	Alive with no recurrence at 7 months
				Epithelial	p53+	Recurrence 7 months, alive at 25 months
	66/female	Palate	8 × 6 × 5.5	(adenocarcinoma)	p53+	N/A
Manuel et al[13]				Pleomorphic sarcoma	N/A	N/A
	68/female	Parotid	4 × 3	Epithelial	N/A	N/A
Seethala et al[7]				Epithelial		N/A
	N/A	N/A	N/A	Myoepithelial	Cytokeratin AE1/AE3+, CAM5.2+, EMA+, S100−,	
	N/A	N/A	N/A	Epithelial and myoepithelial	HHF35−, GFAP−, SMA-, p53+	Nodal metastasis at presentation,
	N/A	N/A	N/A	Epithelial	CK 5/6 weakly+, p63+, CK14+, CK7−, Actin-, S100+	alive at 2 years
Kusafuka et al[14]	N/A	N/A	N/A		Cytokeratin AE1/AE3+, EMA+,S100−, SMA−, p63−	
	70/male	Parotid	6.8 × 4.7 × 7		N/A	N/A
Niederhagen[15]				Myoepithelial		
Sarode[16]					S100 focally+, CK14+, HMWK+ (squamous areas), LMWK + (ducts)	Nodal metastasis at presentation,
	89/female	Parotid	3 × 2.5	Epithelial (poorly differentiated)	p63+	alive at 7months
Roy et al[17]				Likely epithelial and myoepithelial		N/A
	70/male	Parotid	3 × 2 × 2	Likely epithelial and myoepithelial	CK-, AE1/AE3+, negative for p63 and calponin	
					N/A	Nodal metastasis at presentation,
				Likely epithelial and myoepithelial		alive at 2 years
	82/male	Parotid	N/A			
				Epithelial	Cytokeratin AE1/AE3+, p53+ in both components; S100+,	Alive with disease at 3 years,
	74/female	Parotid	10		p63+, SMA+ in myoepithelial component only SMA	peritoneal, liver, and brain
				Epithelial (salivary duct carcinoma)	partially+,S-100 partially +,P63+	metastases
Yang and Chen[4]				Epithelial and myoepithelial		Pulmonary metastases at 15 months
Kainuma et al[18]	59/female	Parotid	11			Alive with no recurrence at 16 months
Baker et al[2]				myoepithelial		Nodal metastasis at presentation, alive at 7 months
	60/female	Submandibular	3.4 × 3			
						Alive with recurrence at 10 years
	74/male	Parotid	N/A			
Suzuki et al[8]						
	85/female	Submandibular	4.4 x 3.5			
	81/male	Parotid	5.5 × 3.4 × 4.5			
Aydin et al[19]	46/female	Parotid	4 × 5	Differentiated adenocarcinoma	N/A	Alive with no recurrence at 3years
Current case	77/female	Parotid	3.5 × 3.0 × 1.5	Pleomorphic sarcoma	All stains negative	Alive with no recurrence at 4 years

EMC = epithelial-myoepithelial carcinoma, HGT = high-grade transformation

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