



## High-Grade Mucoepidermoid Carcinoma *Ex* Metastasizing Pleomorphic Adenomas in the Parotid Gland and Parapharyngeal Space: a Case Report and Literature Review

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### Case Report

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Pleomorphic adenoma is the most common benign neoplasm of the salivary glands. Its three malignant variants include carcinoma ex pleomorphic adenoma, carcinosarcoma, and metastasizing pleomorphic adenoma. Among the subtypes of carcinoma ex pleomorphic adenoma, high-grade mucoepidermoid carcinoma has rarely been reported. Additionally, metastasizing pleomorphic adenoma is rare. We report the imaging findings of a high-grade mucoepidermoid carcinoma ex metastasizing pleomorphic adenoma of the parotid gland and parapharyngeal space in a 42-year-old man.

**Keywords:** High-grade mucoepidermoid carcinoma ex metastasizing pleomorphic adenomas; Carcinoma ex pleomorphic adenoma; Metastasizing pleomorphic adenoma; Adenoma, pleomorphic; Carcinoma, mucoepidermoid; Magnetic resonance imaging

### INTRODUCTION

Pleomorphic adenoma (PA) is the most common benign neoplasm of the salivary glands (1). Among its malignant variants, carcinoma ex PA (that is, carcinoma in pre-existing PA), carcinosarcoma, and metastasizing pleomorphic adenoma (MPA), the latter two types are extremely unusual.

There are few reports on mucoepidermoid carcinoma (MEC) arising from PA (2-7). Theoretically, mucoepidermoid carcinoma ex metastasizing pleomorphic adenoma (MEC ex MPA) is possible. However, MEC ex MPA has not been reported in the English literature.

Herein, we report a unique case of MEC ex MPA of the parotid gland and parapharyngeal space without previous surgical treatment of the primary PA.

### CASE REPORT

A 42-year-old man was referred to the department of otorhinolaryngology / head

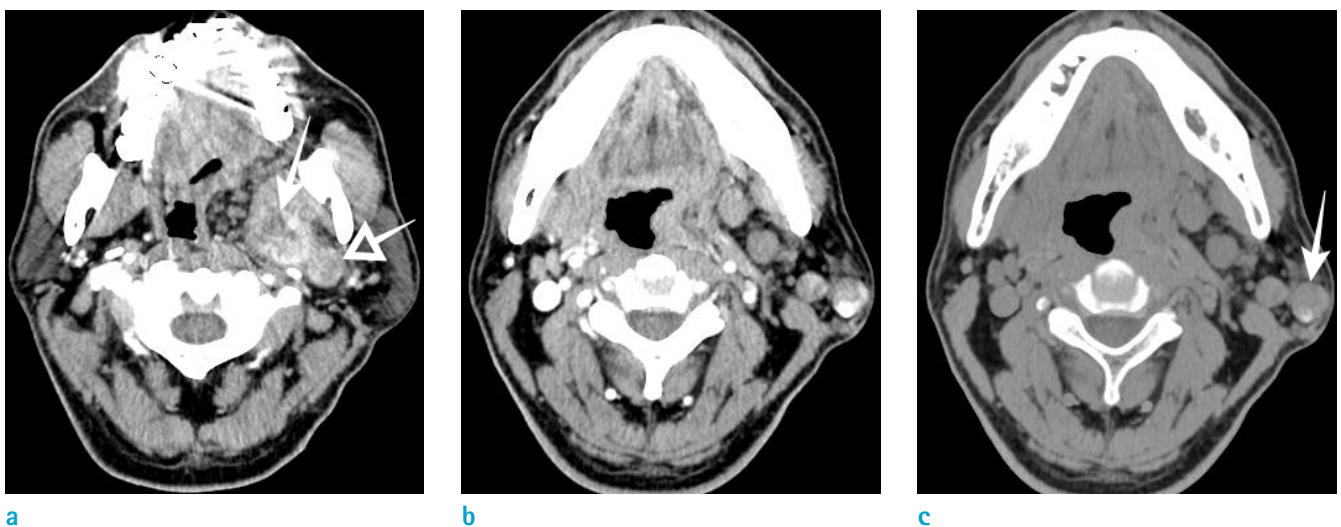
and neck surgery at our institution for an incidental left parapharyngeal-space mass detected by brain magnetic resonance imaging (MRI). The patient had previously undergone neck surgery for a benign lipoma. The patient had an asymptomatic mass in left neck level II. The remainder of the head and neck examination was unremarkable. The laboratory data were within the normal ranges.

Contrast-enhanced computed tomography (CT) and MRI revealed a well-defined mass measuring  $3.2 \times 2.6$  cm with heterogeneous enhancement in the left parapharyngeal space (Figs. 1, 2). There were multiple small ovoid to round heterogeneously enhancing nodules in the left parapharyngeal space, contiguous with the deep lobe of the parotid gland, infraparotid area, and left neck levels IB and II (Figs. 1, 2). Several nodules in the left infraparotid area and level II were calcified (Fig. 1). The mass and nodules in the left parapharyngeal space displaced the left parapharyngeal fat and the left oropharyngeal and nasopharyngeal walls in the medial direction (Figs. 1, 2). The largest mass in the left parapharyngeal space exhibited an inhomogeneous intermediate to high signal intensity on T2-weighted images, with a non-enhancing central portion suggesting cystic change (Fig. 2). The other nodules also expressed similar signal intensities, including various degrees of cystic changes (Fig. 2). On diffusion-weighted imaging, the largest mass in the left parapharyngeal space

expressed central high and peripheral low signal intensities on apparent diffusion coefficient (ADC) mapping images, suggesting central necrosis and hypercellular components, respectively (Fig. 2). Other nodal mass and nodules in left level IB-II with cystic changes also exhibited foci of low signal intensities on ADC mapping images (Fig. 2). Considering the intermediate T2 signal intensities, diffusion restriction areas, and multiple satellite nodules, carcinoma ex pleomorphic adenoma with metastases and multiple co-existing intraparotid pleomorphic adenomas were suggested.

We did an excisional biopsy on a left neck level II mass. The histopathological diagnosis of the biopsy was benign pleomorphic adenoma. The patient then underwent tumor resection surgery using a transcervical-transparotid approach under general anesthesia. We could not do a complete excision of the parotid masses, because the gland appeared to be replaced by miliary solid nodules. We also could not completely excise the numerous satellite nodules in left level II.

The final diagnosis was high-grade MEC arising from MPAs. Histopathologically, multiple nodules and masses in the left parotid gland, left parapharyngeal space, and left neck level I and II showed unequivocal features of malignancy along with benign PAs. The largest parapharyngeal mass appeared to be intracapsular high-

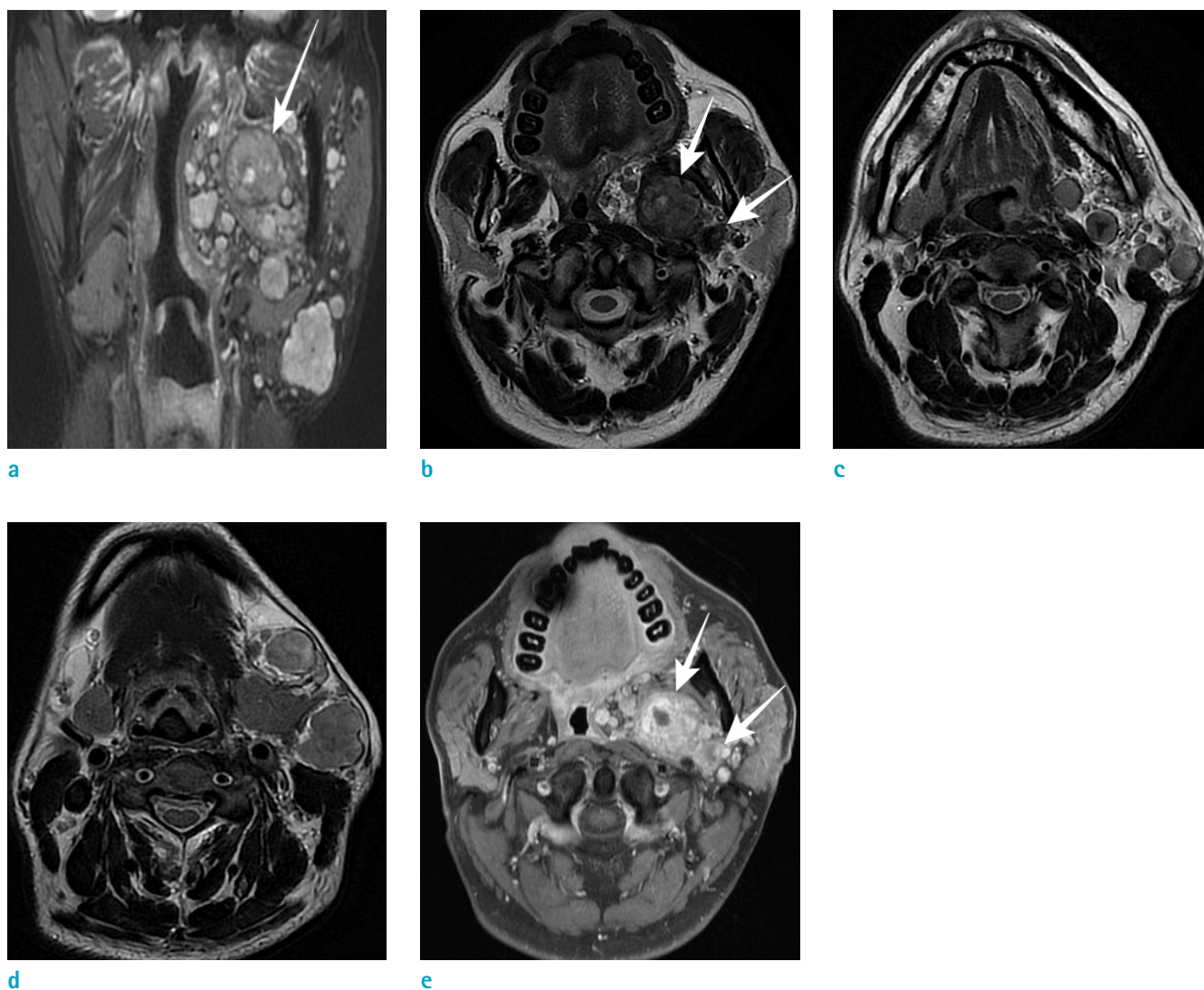


**Fig. 1.** High-grade mucoepidermoid carcinoma ex metastasizing pleomorphic adenomas arising in the left parotid gland and left parapharyngeal space in a 45-year-old man. (a) The axial contrast-enhanced CT image showed a well-defined mass in the left parapharyngeal space, measuring  $3.2 \times 2.6$  cm with heterogeneous enhancement and cystic change (arrow), contiguous with a heterogeneously enhancing mass in the deep lobe of the left parotid gland (empty arrow). (b) On the axial contrast-enhanced CT image, the larger nodules in the left neck level II and infraparotid area presented heterogeneous enhancement. (c) The axial non-contrast-enhanced CT showed calcification in a nodule in the left infraparotid area (arrow).

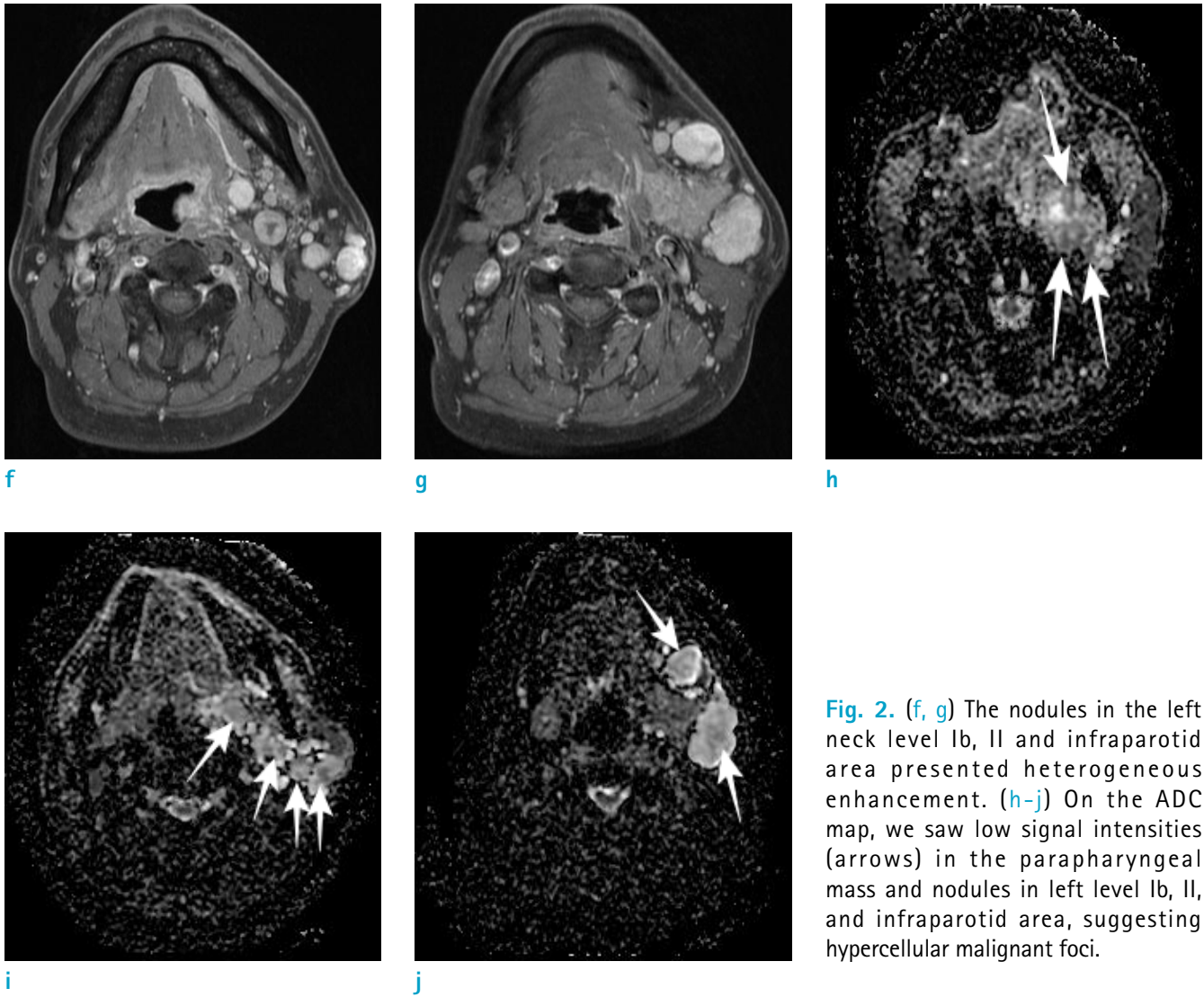
grade carcinoma ex PA, which was consistent with predominantly high-grade MEC (making up about 95% of the mass) and partly high-grade salivary-duct carcinoma (making up about 5% of the mass) (Fig. 3). One nodule in the parotid gland revealed a high-grade MEC ex PA. A nodule in left neck level II was intermediate-grade MEC ex MPA. Other nodules in left neck levels I, II were mostly MPA mixed with several reactive lymph nodes.

On postoperative F-18 fluorodeoxyglucose positron

emission tomography/computed tomography, we found no other metastatic lesions. The patient underwent postoperative radiation therapy for two months. After treatment, the patient was regularly followed up. On follow-up CT done five months after surgery, there was a 2.7-cm remnant tumor in the left parapharyngeal space. The patient underwent CT and MRI every three months after radiation treatment. He has been stable for 1.5 years.



**Fig. 2.** MRI of the patient. (a, b) On the coronal fat-saturated T2-weighted image and the axial T2-weighted image, the largest mass in the left parapharyngeal space (arrows) exhibited inhomogeneous intermediate to high signal intensities. (a-d) Multiple nodules in the left parapharyngeal space, parotid gland, left neck level Ib, II, and infraparotid area also expressed similar inhomogeneously intermediate to high signal intensities. (e) On the axial contrast-enhanced T1-weighted image, the largest mass in the left parapharyngeal space (arrows) showed heterogeneous enhancement with a non-enhancing central portion, suggesting cystic change.



**Fig. 2.** (f, g) The nodules in the left neck level Ib, II and infraparotid area presented heterogeneous enhancement. (h-j) On the ADC map, we saw low signal intensities (arrows) in the parapharyngeal mass and nodules in left level Ib, II, and infraparotid area, suggesting hypercellular malignant foci.

**DISCUSSION**

PA can undergo malignant transformation into three forms: Carcinoma ex PA, carcinosarcoma (true malignant mixed tumor), and MPA (1). The latter two are extremely rare, with MPA accounting for 1% of malignant PAs (1). MEC arising from PA has been rarely reported and is tentatively accepted as carcinoma ex PA, with 11 cases in the English literature (2-7). MPA is histologically indistinguishable from PA, but it produces distant secondary tumors (1). It occurs due to iatrogenic causes, particularly during surgical resection with seeding of disrupted tumor cells into the bloodstream (1). The mechanism behind MPA is poorly known. Seeding of disrupted tumor cells during surgery was not the only mechanism for metastasis. We

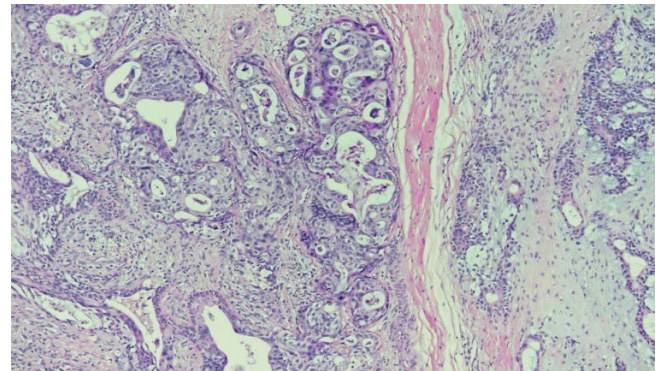
report a rare case of high-grade MEC ex MPA without previous surgical treatment of the primary PA.

Carcinoma ex PA has several histological variants, likely due to the heterogeneity among precursor PAs (8). PA can transform into MEC, because there are close phenotypic and ultrastructural resemblances between the intermediate cells of MEC and the myoepithelial cells of PA. Moreover, we found common karyotypic alterations in both tumors, suggesting the link between them (6). As seen in our case, carcinoma can arise from MPA, including the MEC subtype. Czader M et al. (9) suggested the possibility that MPA and carcinoma ex PA may show metachronous development in the underlying benign PA in the process of developing into different tumor entities in the common biologic pathway (9-11).

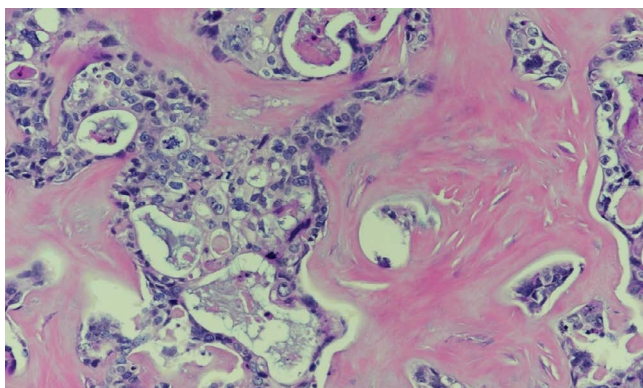




a



b



c

**Fig. 3.** On gross pathological examination, (a) the cut surface of the left parapharyngeal mass showed a conglomerate of well-circumscribed pearly white miliary nodules consisting of histopathologically discrete pleomorphic adenomas. Microscopic examination demonstrated non-invasive high-grade carcinoma ex pleomorphic adenoma composed (b) predominantly of high-grade mucoepidermoid carcinoma (H&E,  $\times 100$ ) and (c) partly of salivary duct carcinoma (H&E,  $\times 400$ ). H&E = Hematoxylin and Eosin stain

Few cases of MEC ex PA have been reported (2-7) (Table 1). Among these, eight involved high-grade MEC ex PA (2, 6, 7). There were two low-grade and one intermediate-grade tumors (3-5). Nine out of 11 cases were located within the parotid gland. One case (2) presented as a mass within the left parapharyngeal space, contiguous with the deep lobe of the parotid, and metastatic MEC in the left neck level II lymph node. One case was associated with recurrent PA (6). In our case, there were high-grade MEC ex MPA in the parapharyngeal space, contiguous with the mass in the deep lobe of the parotid gland. We observed intermediate-grade MEC in the metastatic masses in the left neck level II. Our case was unique, because MPA was not associated with recurrent PA after surgery. MEC has been commonly observed in the main mass in the parapharyngeal space and in metastatic masses in the ipsilateral parotid gland and

lateral neck.

The particular imaging findings for MEC ex PA have not been reported. The imaging findings of carcinoma ex PA are nonspecific and undifferentiated from those of other benign and malignant salivary-gland tumors (12), and we assume that the imaging features of high-grade MEC ex PA may not differ from those of carcinoma ex PA. On MRI, PAs exhibit various signal intensities because of their cytomorphologic and architectural diversity. Thus, it is challenging to differentiate PAs from low-grade malignant tumors in the absence of an irregular margin or infiltration into the surrounding tissue (12, 13). In our case, there were multiple lobulated heterogeneous masses and nodules in the left parapharyngeal space, parotid gland, and neck levels IB and II, resembling the imaging findings of the recurrent PA after surgical resection. On MRI, intermediate T2 signal intensities

**Table 1. Clinicopathologic Data on Eleven Patients with Histologic Mucoepidermoid Carcinoma Arising from Pleomorphic Adenoma**

Reference	Age/Sex	Location	Histopathologic grade	Treatment	Follow up
Stanley 1990 (3)	53/M	Parotid gland, superficial lobe	Low	Surgery	Alive, disease-free, 8 years
Jacobs 1994 (4)	32/F	Parotid gland, superficial lobe	Low	Surgery	Alive, disease-free
Pitman 1995 (5)	28/F	Parotid gland, deep lobe	Intermediate	Surgery	N/A
Klijanienko 1998 (6)	57/M	Submandibular gland	High	Surgery	Alive, disease-free 1 year
	45/F	Parotid gland	High	Surgery	Lost to follow-up
	57/M	Parotid gland	High	Surgery, radiotherapy	Lost to follow-up
	75/M	Parotid gland	High	Surgery, radiotherapy, chemotherapy	Dead of disease, 1 year
	68/M	Parotid gland	High	Surgery	Alive, disease-free, 7 years
	62/F*	Parotid gland	High	Surgery, radiotherapy	Lost to follow-up
Pollack 2014 (2)	71/M	Parotid gland, deep lobe	High	Surgery	Alive, disease-free, 2 years
Daniel 2014 (7)	62/F	Lacrimal gland	High	Surgery	Recurrent, after the end of two and a half years
Our case 2021	42/M	Parotid gland, parapharyngeal space	High	Surgery, radiotherapy	Alive, stable disease status after one and a half years

\*This patient had a history of recurrent pleomorphic adenoma.

and decreased ADC values were shown in the main mass in the left parapharyngeal space and larger nodal masses. The low signal intensity on T2WI (14) and low ADC value could provide clues to diagnose the malignant foci of carcinoma ex PA (12).

Complete surgical excision is the mainstay of treatment for benign and malignant parotid-gland tumors (8). For low-grade or early-stage malignant tumors, the treatment consists of surgical excision alone (8). High-grade tumors are typically treated by wide surgical excision with lymphadenectomy and adjuvant radiotherapy (2). Chemotherapy is generally reserved for palliation or advanced disease (8). The survival of MPA patients was not documented clearly. However, multiple metastases, which are fatal, indicate a poor prognosis (1). In most cases, the treatment of choice for MPA was total resection. Improved survival has not been documented in cases treated with radiotherapy alongside surgery (1).

In conclusion, we reported the CT and MRI findings of high-grade MEC ex MPA of the parotid gland and parapharyngeal space. This was the first report in the English literature. Achieving a preoperative radiologic diagnosis for carcinoma ex PA was challenging, but MRI findings, including T2 signal intensity and diffusion-

weighted imaging, provided clues to diagnose the malignant foci of carcinoma ex PA arising from PA.

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