

# Primary parotid gland malignant melanoma complicated with lung and bone metastasis; a case report

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## ► Case report

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#These two authors contributed equally to the study.

## ABSTRACT

**Background:** Malignant melanoma of the primary parotid gland (PGMM) is extremely rare, and most of the previous reports are case reports. This study describes the clinical and histological characteristics of a single case of PGMM. **Materials and methods:** The patient was diagnosed following the detection of a mass in the parotid region. Examination of the resected tissue specimens demonstrated cells with copious eosinophilic cytoplasm, significant pleomorphic in the nuclei, and distinct nucleoli. Immunohistochemical analysis was performed to measure HMB45, S-100, SOX-10, and Melan-A markers expression in tumor tissue. The clinicopathological features of a series of parotid gland malignant melanomas were analyzed. **Results:** Despite undergoing surgical intervention, immunotherapy, and targeted therapy, this case occurred distant metastases. The patient survived 2 years and 3 months after surgery due to multiple metastases throughout the body. **Conclusion:** This article reported the clinical characteristics of the case and provided an overview of primary PGMM cases documented over the last three decades.

## INTRODUCTION

Malignant melanoma of the primary parotid gland (PGMM) is exceptionally rare, accounting for 0.68% of all malignant neoplasms in this gland <sup>(1)</sup>. Embryologically, melanocytes originate from neural crest tissue and are not a constituent of normal salivary tissue <sup>(2)</sup>. The bulk of earlier reported cases are likely to be metastatic growth, commonly originating from primary skin cancers of the head and neck <sup>(3)</sup>. Despite its rarity, malignant melanoma is known for its aggressive behavior, characterized by early metastasis and a poor prognosis. Currently, PGMM presents a significant diagnostic challenge due to its uncommon occurrence and diverse clinical and radiographic presentations. Timely detection, accurate diagnosis, and prompt treatment are crucial in managing this highly aggressive soft tissue malignancy.

This study described the clinicopathological, and immunohistochemical features and treatment of a primary PGMM, with a particular focus on treatment options. This report details a case of primary PGMM in a 57-year-old man presenting with a hard subauricular mass is described. Besides, we examine a series of cases concerning clinical presentation, diagnosis, management, and outcomes that may

provide new insights into recognizing this uncommon tumor.

## MATERIALS AND METHODS

The tissue specimens from the patient case were preserved in formalin and then embedded in paraffin, with the resultant paraffin blocks being accessible for additional scrutiny. The case was assessed and diagnosed by pathologists. The Institutional Ethics Committee Office of Hospital approved the study (No. 2020037; date: 2020.05.26). The patient provided informed consent for the dissemination of the present case report and related images.

### Case presentation

A 57-year-old man was admitted to the hospital, having noticed a firm mass beneath his left ear 20-day prior. Physical examination revealed a 2 cm diameter mass in the left parotid region, which was firm and mobile, with no evident signs of spontaneous pain or tenderness and slightly compressibility. The patient presented significant risk factors for cancer. One month before admission, an ultrasound of the left parotid region detected a solid hypoechoic nodule. Preoperative laboratory

tests, including complete blood count, electrolytes, urinalysis, and liver and kidney function tests, were all within normal limits. Based on the clinical examination, laboratory results, and radiological findings, the tumor was initially considered benign, and thus no fine needle aspiration cytology (FNAC) examination was performed.

A partial parotidectomy was conducted with a 1.5 cm incision around the tumor. During the procedure, the mass was found encapsulated within parotid tissue, with no lymph nodes detected in the surrounding area. The excised specimen was circumscribed, firm, and had a smooth surface, measuring 4.0 cm × 3.5 cm × 1.0 cm. The surgery was free of complications, and the facial nerve remained intact. Postoperative pathological diagnosis confirmed malignant melanoma. Further questioning and investigation revealed no prior history of melanoma or non-melanoma skin cancer, and a thorough skin examination showed no black plaques or primary tumors. The patient also denied childhood sun expose and family history.

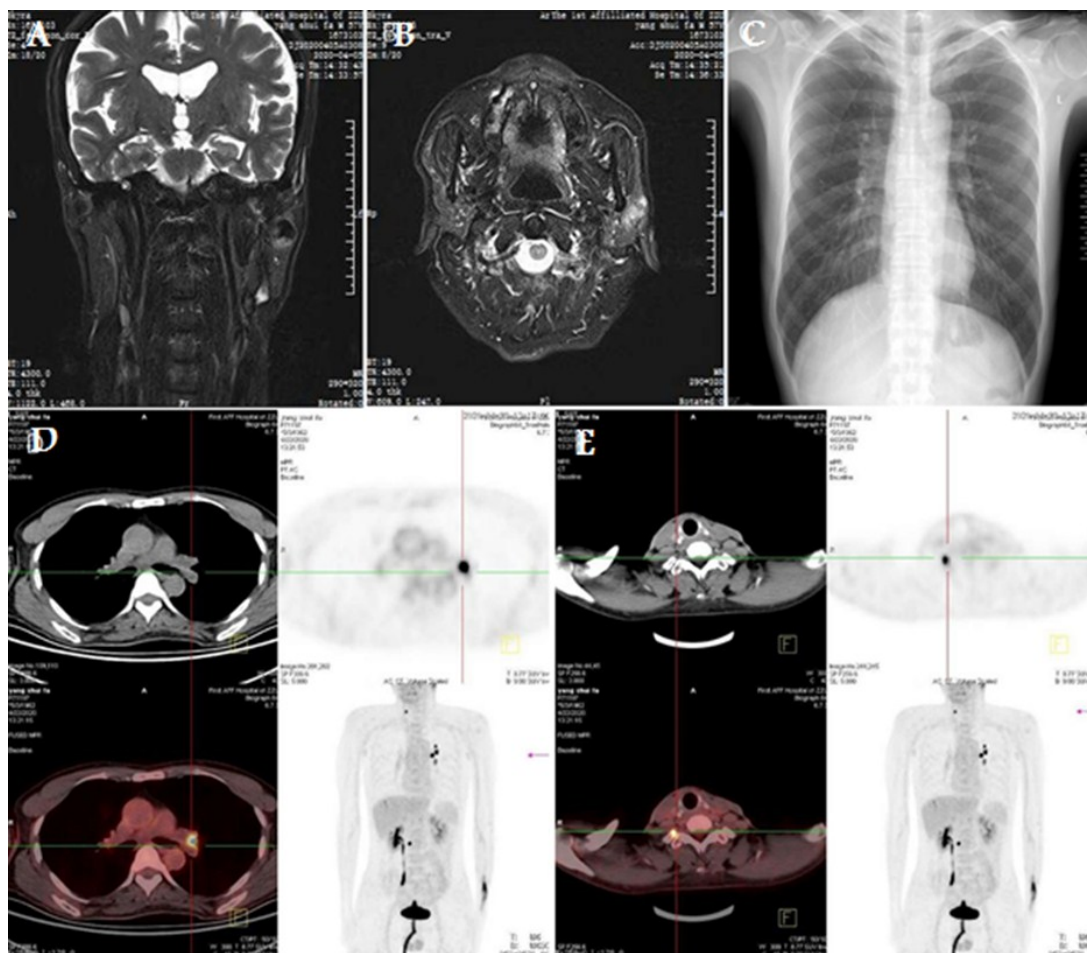
#### **Hematoxylin-eosin (HE) staining and immunohistochemical analysis**

Sections (4 µm thick) were prepared and stained

with hematoxylin-eosin (Solarbio, Beijing, China) to visualize endothelial markers during surgery treatment. Consecutive sections placed on positively charged slides were subjected to immunohistochemical methods (Beyotime, Shanghai, China) by the conventional avidin-biotin-peroxidase complex (ABC) technique.

#### **Imaging characteristic**

Magnetic resonance imaging (MRI) of the maxillofacial region revealed a mass in the left parotid region. The boundary is clear, the envelope is complete, and representative images are shown in figure 1A and B. If there is a sufficient quantity of melanin, it can manifest as high signal intensity on T1-weighted MRI scans, which is uncommon in other cancers. Moreover, the chest radiograph revealed no obvious abnormalities (figure 1C). Postoperatively, the patient underwent 18F-FDG PET-CT examination, which revealed multiple enlarged lymph node shadows in the left hilum, with a standard uptake value (SUV) of about 18.1, and the larger shadow was about 1.1 cm × 1.5 cm. A radioactive concentration was observed in the first rib on the right, with an SUV of about 24, indicating metastasis to the left lung hilar and right first rib (figure 1D, E).

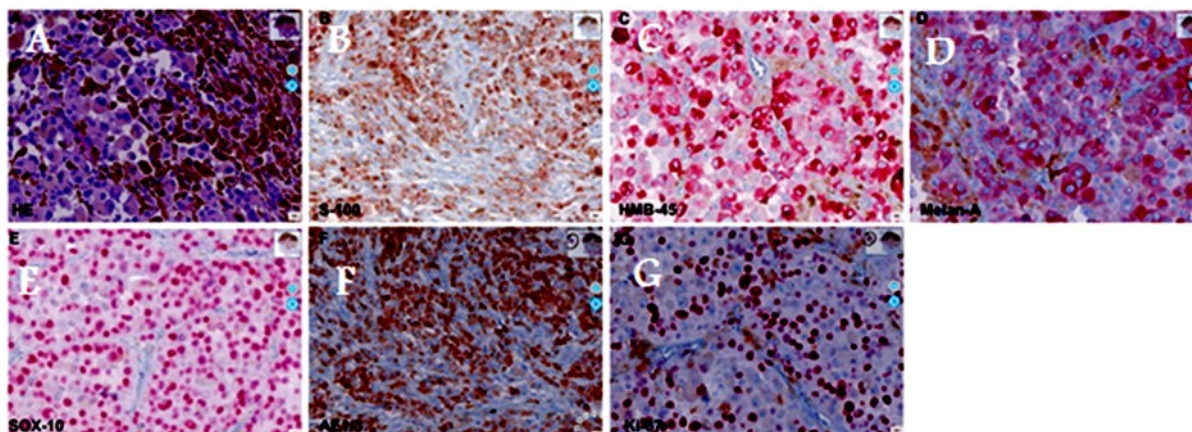


**Figure 1.** Examination images of a case of primary parotid gland malignant melanoma. (A&B) The patient's preoperative MRI was coronal and horizontal planes. (C) Patient's preoperative chest CT. (D&E) Postoperative PET-CT results.

### Pathological features

The tumor comprises mainly diffusely organized cells with rich eosinophilic cytoplasm, giant pleomorphic nuclei, conspicuous nucleoli, and some cells with marked melanin pigmentation (figure 2A). Immunohistochemical analysis revealed positive cytoplasm for S-100 (figure 2B), HMB-45 (figure 2C),

and Melan-A (figure 2D), along with positive nuclei for S-100 (figure 2B), and SOX-10 (figure 2E). The cells were negative for epithelial markers, such as AE1 and AE3 (figure 2F). Ki-67 staining revealed 40% of positive cells (figure 2G). Thus, the malignant melanoma was confirmed.



**Figure 2.** HE staining and immunohistochemical images of the tumor (magnification 40×). (A) HE staining of the operative specimen section. Tumor cells are positive for S-100 (B), HMB-45 (C), Melan-A (D), and SOX-10 (E). Tumor cells are negative for AE1/3 (F) and Ki-67 (G).

### Treatment and follow-up

Following the pathology diagnosis of malignant melanoma, the patient received a combination of immunotherapy and targeted therapy. Treatment included oral vemurafenib (480 mg twice daily) along with pembrolizumab (2 mg administered every three weeks). The patient survived for 2 years and 3 months post-surgery but died in July 2022 due to widespread metastases.

## DISCUSSION

Identifying malignant melanoma histologically is frequently straightforward, especially when pigmentation or an in situ component is evident. However, many melanomas lack diagnostic histological characteristics. Immunohistochemistry analysis revealed positive cytoplasm for S-100, HMB-45, and Melan-A, positive nuclei for S-100, and negative for AE1/3(F) and Ki-67.

In the present case, the patient developed lung and bone metastases. The exact timing of the metastases remain unclear due to the limitations of preoperative chest radiography. Additionally, chest radiography lacks sufficient sensitivity in detecting mediastinal lymph node metastases, chest wall, and mediastinal invasion, and necessitates chest CT screening.

To our knowledge, 12 reports of primary PGMM have been published during the past 30 years (1993-

2024), with a predominance of single cases (1, 2, 4-6). Table 1 encapsulates a summary of the previously documented cases that included comprehensive details regarding age, sex, treatment, prognosis, and pathology (2, 4, 5, 7-14). The average age of patients is 51.67 years, but it can happen to anyone from the ages of 13 to 80 years. Tumor size was known in 7 of 12 patients, with a maximum tumor diameter of 2 cm to 15 cm. While not all patients had quickly developed tumors, four did, except for one, and they were all accompanied by excruciating pain. All patients' facial nerves continued to operate normally. All patients were treated surgically with neck dissection procedures. Ten patients experienced the occurrence of local or distant metastases, of which, four formed nodules in the regional neck, and six suffered distant metastases (including two lung, two brain, and three bone metastases) developed elsewhere in the body. Follow-up information showed the survival times ranging from 1 to 15 months, only two patients had no evidence of died (2, 4-6). Despite advancement of therapy of PMGG, majority patients had a short survival time. Some authors advocated combined therapy (surgery + adjuvant immunotherapy + chemotherapy + radiotherapy) (1), while others have not gained any benefits from combination (12). Although the patient underwent surgery, immunotherapy and targeted therapy, the survival time is 2 year and 3 months, which benefits are still limited.



**Table 1.** The situation of 12 patients with primary malignant melanoma of the parotid gland

Authors	Age (year)	Sex	Case history (month)	Location	Pain	pathology	Treatment	metastasis	Follow-up
R T Woodward <i>et al.</i> <sup>(12)</sup>	51	female	9	left	No	MM	superficial parotidectomy +left radical neck dissection +chemotherapy + radiotherapy	cerebral	Died
Barbieri M <i>et al.</i> <sup>(10)</sup>	64	female	18	left	No	MM	total left parotidectomy +radical neck diffection	bone	Died
Tsutsumida A <i>et al.</i> <sup>(9)</sup>	63	female	24	left	No	MM	total left parotidectomy + radiotherapy	Lung+brain+lymph nodes	Died
N Gao <i>et al.</i> <sup>(7)</sup>	37	male	2	left	Yes	AMM	total left parotidectomy	Widespread	Died
Bangerter M <sup>(8)</sup>	55	male	< 1	right	/	MM	parotidectomy	Lymph node	-
Karpowicz MK <i>et al.</i> <sup>(11)</sup>	45	male	2	right	yes	MM	right total parotidectomy + radiotherapy	bone	Died
Apparau D <i>et al.</i> <sup>(5)</sup>	13	male	6	right	yes	MM	wide local excision + radiotherapy	Lymph node	Died
Chaouki A <i>et al.</i> <sup>(4)</sup>	27	female	8	left	no	MM	total parotidectomy with neck dissection+ radiotherapy	generalized visceral metastases	Died
Sultana M <i>et al.</i> <sup>(2)</sup>	60	female	42	Left	yes	AMM	Parotidectomy + chemotherapy	masseter muscle, left upper buccal mucosa, left cervical, right supraclavicular lymph nodes, multiple active skeletal metastases	Died
Zhao Q <i>et al.</i> <sup>(1)</sup>	60	male	10	left	no	MM	Surgery + immunotherapy + Chemotherapy + radiotherapy	No	-
Yan M <i>et al.</i> <sup>(13)</sup>	77	male	1	left	no	MM	total parotidectomy + immunotherapy	multiple active metastases	Died
Zebbakh H <i>et al.</i> <sup>(14)</sup>	68	male	2	right	no	MM	total right parotidectomy	Bone + lung	-

MM: Malignant melanoma; AMM: amelanotic malignant melanoma; /: no relative information; -:no evidence of died.

## CONCLUSION

This report highlights the clinicopathological features of the case. Considering the aggressive and early metastatic nature of this tumor, further advancements in personalized treatment for malignant melanoma will be critical in the future.

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**Ethical consideration:** The study protocol was approved by The Ethics Committee of The First Affiliated Hospital of Zhengzhou University and followed the principles outlined in the Declaration of Helsinki.

**Author contribution:** S. Q, R. L and M.L. S designed the research study. D. Z, M.G. L and G.H. L performed the research. S. Q and R. L analyzed the data. S. Q and R. L wrote the manuscript. M.L. S contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

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