

Unusual Metastatic Malignant Lesions Involving the Parotid Region: A Cytopathological Case Series

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ABSTRACT

Background: The parotid gland is predominantly affected by benign neoplasms; however, a broad spectrum of malignant lesions may present as parotid or periparotid masses. Secondary involvement of the parotid gland by metastatic malignancies and hematolymphoid neoplasms may closely mimic primary salivary gland neoplasms. Fine-needle aspiration cytology (FNAC) serves as a valuable initial diagnostic modality for recognizing these unusual secondary lesions and is important for guiding appropriate ancillary investigations, identifying the primary tumor, and facilitating subsequent clinical management. **Materials and Methods:** We retrospectively reviewed unusual malignant lesions diagnosed on cytological specimens from the parotid at a tertiary oncology centre. Clinicopathological details, cytological diagnosis, available immunohistochemical findings and correlation with histopathological specimens from other anatomical sites were reviewed where ever available. **Results:** Seven unusual malignant lesions involving the parotid region were identified. The patients ranged in age from 42 to 72 years, with a mean age of 55.9 years. Five patients were male and two were female. The lesions comprised four cases of metastatic squamous cell carcinoma, one case of metastatic neuroblastoma, one case of metastatic gastrointestinal stromal tumor (GIST), and one case of plasmablastic multiple myeloma with extramedullary parotid involvement. **Conclusion:** Fine-needle aspiration cytology (FNAC) is a rapid, safe and minimally invasive first-line investigation for any masses. It can identify unusual cytomorphological patterns, when combined with cell-block preparation and targeted immunohistochemistry—help establish tumor lineage. Combined with clinical and radiological correlation, FNAC can guide the search for a primary tumor, avoid unnecessary surgery and facilitate appropriate management.

Keywords: *parotid gland; fine-needle aspiration cytology; metastatic carcinoma; squamous cell carcinoma; neuroblastoma; gastrointestinal stromal tumor; extramedullary plasmablastic disease; cytopathology*

INTRODUCTION

The parotid gland is the most frequently involved major salivary gland and encompasses a diverse spectrum of benign and malignant neoplasms. Although primary salivary gland tumors constitute the majority of parotid lesions, secondary malignant involvement is an important diagnostic consideration. Large cytopathological series have demonstrated that metastatic tumors constitute an important proportion of malignant parotid lesions. Squamous cell carcinoma and melanoma are among the most frequent metastatic malignancies, particularly from head and neck and cutaneous primary sites. [1-4]

The present study describes a series of unusual malignant lesions involving the parotid diagnosed primarily by cytological evaluation, with emphasis on the diagnostic spectrum and the importance of clinicopathological correlation.

MATERIALS AND METHODS

This was a retrospective descriptive case series conducted in the Department of Pathology, Kidwai Memorial Institute of Oncology, Bengaluru for a duration of one year from May 2025 to May 2026.

Cases diagnosed as metastatic malignant lesions involving the parotid were identified from the

cytopathology records. The available clinical details, age, sex, anatomical site, cytological diagnosis, immunohistochemical findings and histopathological correlation were retrieved from the laboratory records. Where available, the cytological diagnosis was correlated with histopathological examination.

Case Selection and Diagnostic Evaluation

Cases of unusual malignant lesions involving the parotid region were retrospectively identified from the cytopathology records of the Department of Oncopathology, Kidwai Memorial Institute of Oncology, Bengaluru, during the study period from May 2025 to May 2026. Seven cases were included in this descriptive case series. The review included available clinical details, demographic characteristics, imaging findings, cytomorphological features, cell-block findings, immunohistochemical results, and histopathological correlation, wherever available. The

final diagnoses were established by integrating the available cytological findings with clinical history, radiological findings, immunohistochemistry, and histopathological or hematological investigations, as applicable.

RESULTS

Seven malignant lesions involving the parotid region were identified during the study period. The patients ranged in age from 42 to 72 years, with a mean age of 55.9 years. Five patients were male and two were female. Metastatic squamous cell carcinoma constituted the largest group, accounting for four of seven cases (57.1%). The remaining cases comprised one metastatic neuroblastoma, one metastatic gastrointestinal stromal tumor, and one case of plasmablastic multiple myeloma with extramedullary parotid involvement, each accounting for 14.3% of the series.

Table 1. Clinicopathological profile of the cases

Case No.	Age (years)	Sex	Cytological Diagnosis	Final Diagnosis
C6808/26	42	Male	Metastatic small round cell tumor	Metastatic neuroblastoma
C7252/26	50	Male	Spindle cell neoplasm	Metastatic gastrointestinal stromal tumor (GIST)
C7078/26	51	Male	Squamous cell carcinoma	Metastatic squamous cell carcinoma
C7071/26	62	Female	Squamous cell carcinoma	Metastatic squamous cell carcinoma
C5525/26	72	Male	Squamous cell carcinoma	Metastatic squamous cell carcinoma
C8702/26	59	Male	Squamous cell carcinoma	Metastatic squamous cell carcinoma
C5527/26	55	Female	Plasmablastic neoplasm	Plasmablastic multiple myeloma with extramedullary parotid involvement

Case 1: Extramedullary plasmablastic disease

A 64-year-old woman presented with persistent low back pain. MRI of the spine revealed multiple suspicious vertebral lesions suggestive of metastatic disease. PET-CT demonstrated an FDG-avid nodule in the left thyroid lobe, along with multiple FDG-avid osteolytic lesions involving the axial and appendicular skeleton. In view of the thyroid lesion and widespread skeletal abnormalities, metastatic thyroid carcinoma was initially suspected. The patient underwent total thyroidectomy, and histopathology confirmed follicular variant papillary thyroid carcinoma. The skeletal lesions were presumed to represent metastatic deposits, and she subsequently received radiotherapy and radioactive iodine therapy.

Two months later, she developed a rapidly progressive swelling in the left parotid region. Imaging revealed a large soft-tissue mass measuring 10.4 × 8.6 × 7.8 cm, with infiltration of the left mandibular ramus and maxilla. FNAC of the mass showed numerous plasmacytoid cells arranged singly and in sheets. The cells exhibited eccentric nuclei, abundant cytoplasm, and plasmablastic morphological features.(Fig 1)

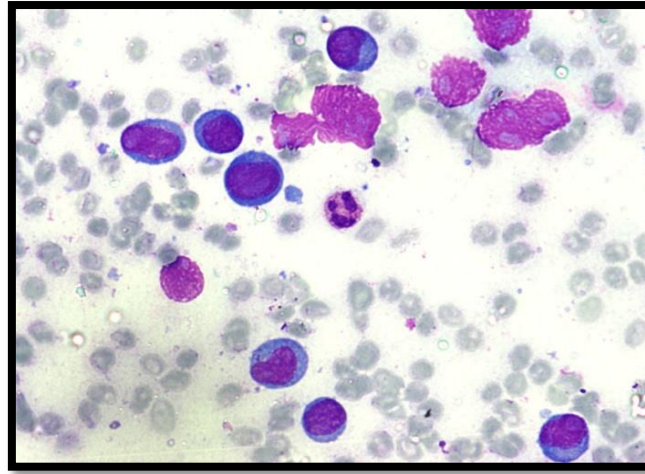


Figure1 FNAC of left parotid region swelling showing plasmacytoid cells (MGG 10X)

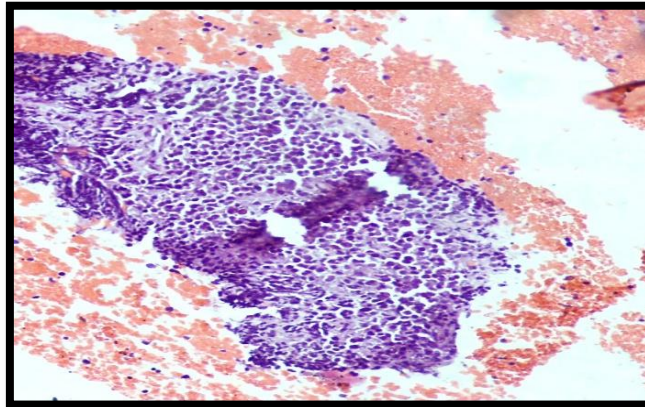


Figure 2 Cell block on FNAC of left parotid swelling showing sheets of plasmacytoid cells (H&E 10X)

Immunohistochemistry showed positivity for EMA(Fig 3), CD138(Fig 4), and MUM1, with a Ki-67 proliferation index of approximately 80%.

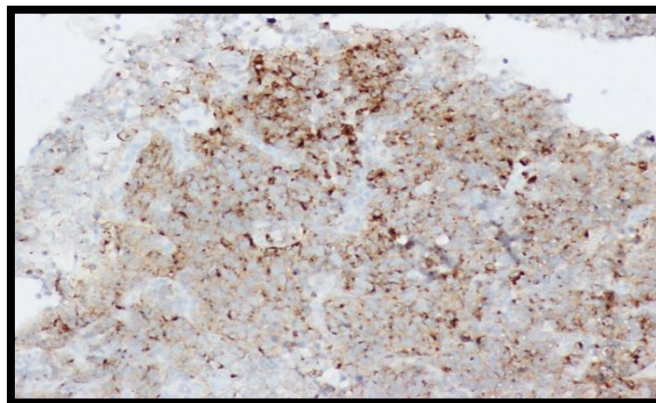


Figure 3 Cell block immunohistochemistry: EMA shows cytoplasmic and membranous positivity (10X)

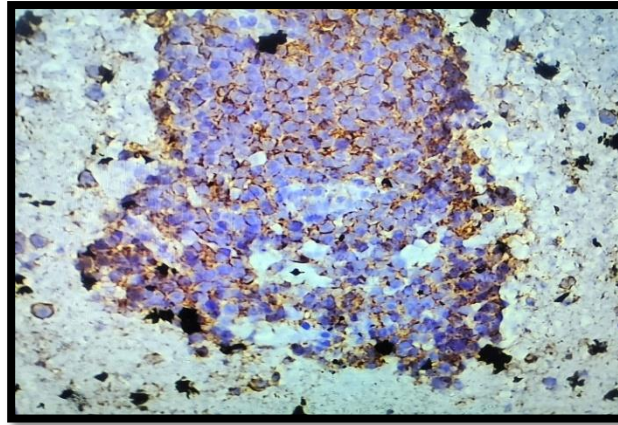


Figure 4 Cell block immunohistochemistry: CD138 shows membranous positivity (10x)

The tumor cells were negative for cytokeratin, LCA, CD20, PAX5, PAX8, TTF1, p63, and other lineage specific markers. These findings supported a high-grade plasma-cell neoplasm with plasmablastic morphology. Subsequent biopsy confirmed the cytological impression and demonstrated strong c-MYC expression. Laboratory investigations revealed anemia, elevated serum creatinine, and an M-spike on serum protein electrophoresis.

Immunofixation demonstrated monoclonal IgG lambda gammopathy. Bone marrow aspiration revealed approximately 58% plasma cells, including plasmablasts and binucleate forms. The final diagnosis was plasmablastic multiple myeloma with extramedullary parotid involvement, occurring synchronously with follicular variant papillary thyroid carcinoma.

This case illustrates the diagnostic value of FNAC, cell-block preparation, and immunohistochemistry in distinguishing extramedullary myeloma from metastatic thyroid carcinoma.

Case 2: Neuroblastoma involving the parotid region

A 42-year-old man presented with a preauricular swelling since 3 months. Ultrasonography of the parotid region revealed a well-defined focal lesion involving the parotid gland measuring 2.3x2x1cm. The

lesion demonstrated heterogeneous echotexture with internal vascularity on Doppler evaluation. No definite features of a benign salivary gland neoplasm were identified.

Patient underwent USG guided FNAC and cytological examination of the lesion revealed a malignant small round-cell neoplasm (Fig 5), which was initially reported as a metastatic small round-cell tumor. At the time of the initial cytological evaluation, the patient's relevant clinical history was not available. On subsequent review of the medical records, it was noted that the patient had undergone resection of a scalp lesion two years earlier, which had been diagnosed as neuroblastoma.

In the absence of this clinical history, the cytomorphological differential diagnosis included lymphoblastic lymphoma, neuroendocrine carcinoma, rhabdomyosarcoma, Ewing sarcoma/primitive neuroectodermal tumor, and metastatic neuroblastoma. In view of the previous diagnosis and morphology of small round blue cell, targeted immunohistochemical evaluation was performed on cell block exhibiting similar morphology (Fig 6) tumor cells demonstrated nuclear positivity for PHOX2B (Fig 7), supporting neural crest differentiation and confirming metastatic neuroblastoma involving the parotid region.

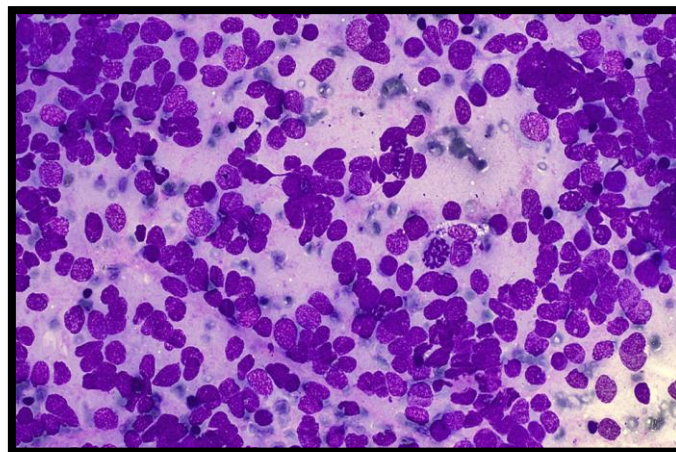


Figure 5 Cellular smear composed of small round cells in focal clustering and dispersed singly, Focal pseudorosette-like arrangement against eosinophilic background. (40x)

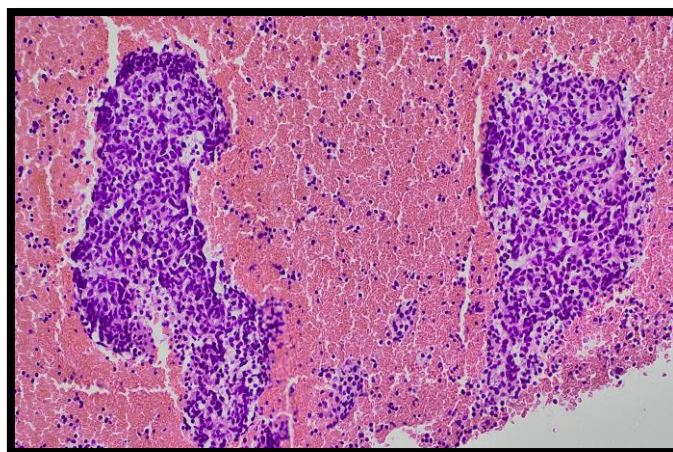


Figure 6: Multiple tissue fragments with scattered aggregates of small round cells, H&E 20X

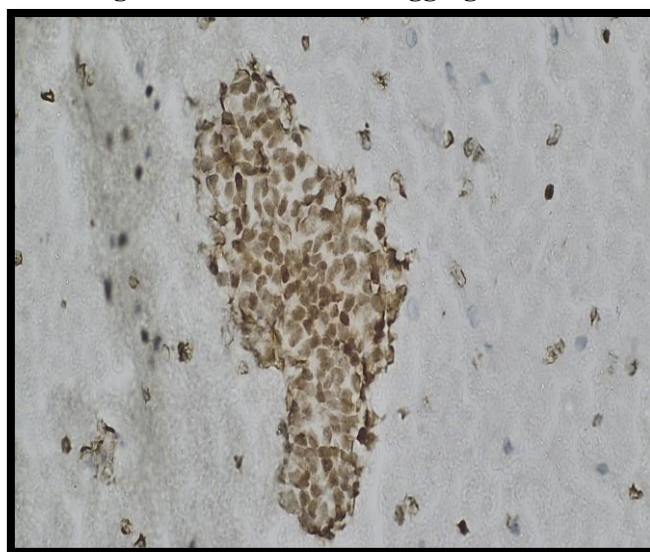


Figure 7: PHOX2B exhibiting nuclear positivity in tumour cells, 20X

This case highlights the diagnostic challenges in cytology posed by small round-cell neoplasms at unusual sites and emphasizes the importance of obtaining a complete clinical history. It also underscores the utility of targeted immunohistochemistry, particularly PHOX2B, in establishing the diagnosis of metastatic neuroblastoma when the clinical history is initially unavailable.

Case 3: Gastrointestinal stromal tumor involving the parotid

A 50-year-old man presented with a parotid swelling of 7 months' duration. Ultrasonography revealed a deep-seated mass lesion in the parotid gland measuring $4.5 \times 2.0 \times 1.0$ cm, for which ultrasound-guided fine-needle aspiration cytology (FNAC) was performed.

The patient was a known case of gastrointestinal stromal tumor (GIST) of the caecum, diagnosed at an outside institution approximately 1.5 years previously. Six months prior to the current presentation, he was found to have a liver lesion measuring $5.6 \times 6.3 \times 3.0$ cm. Ultrasound-guided FNAC of the hepatic lesion was performed at our institution and showed cytomorphological features consistent with metastatic GIST.

Cytological examination and cell block of the parotid lesion revealed a spindle-cell neoplasm comprising dispersed and loosely cohesive groups of spindle cells (Fig 8&9). The cells showed elongated nuclei with relatively uniform nuclear contours and scant to moderate cytoplasm. In the absence of the patient's clinical history, the differential diagnosis for a spindle-cell neoplasm involving the parotid region would include pleomorphic adenoma with prominent spindle-cell areas, myoepithelioma, schwannoma, solitary fibrous tumor, leiomyosarcoma, and metastatic mesenchymal neoplasms.

Although the history of GIST raised the possibility of metastatic involvement, the unusual site of presentation necessitated confirmation by immunohistochemistry. The parotid lesion demonstrated immunoreactivity for DOG1 (Fig 10) and CD117, with a staining profile concordant with that of the previously diagnosed GIST. These findings, in conjunction with the cytomorphology and clinical history, established the diagnosis of metastatic GIST involving the parotid gland.

Metastatic GIST involving the parotid gland is an exceptionally uncommon presentation. This case highlights the importance of integrating

cytomorphological findings with radiological features, previous pathology, and clinical history when evaluating unusual spindle-cell lesions of the parotid region. Recognition of the patient's prior diagnosis of

GIST, followed by appropriate immunohistochemical confirmation, was crucial in establishing the metastatic nature of the lesion and avoiding misclassification as a primary parotid spindle-cell neoplasm.

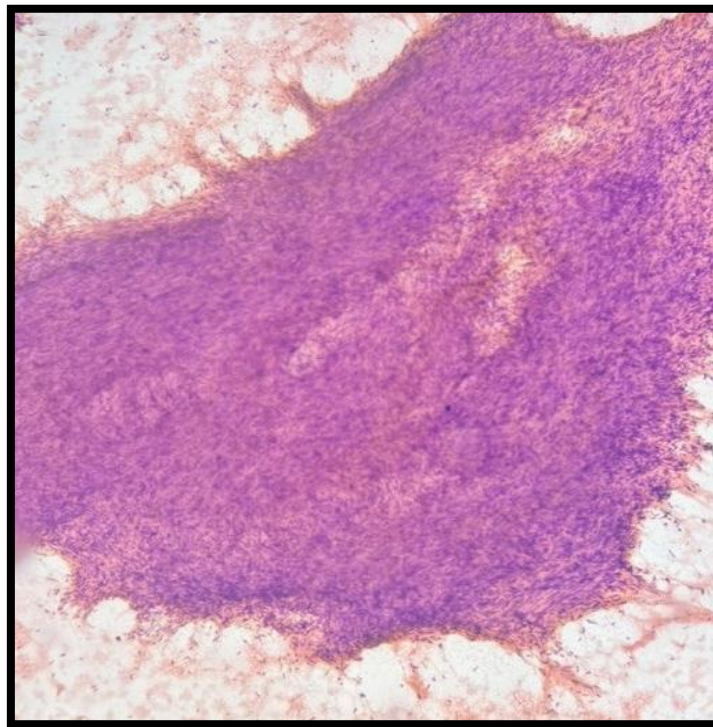


Figure 8: Bland spindle cells arranged in fascicles, H&E 20x

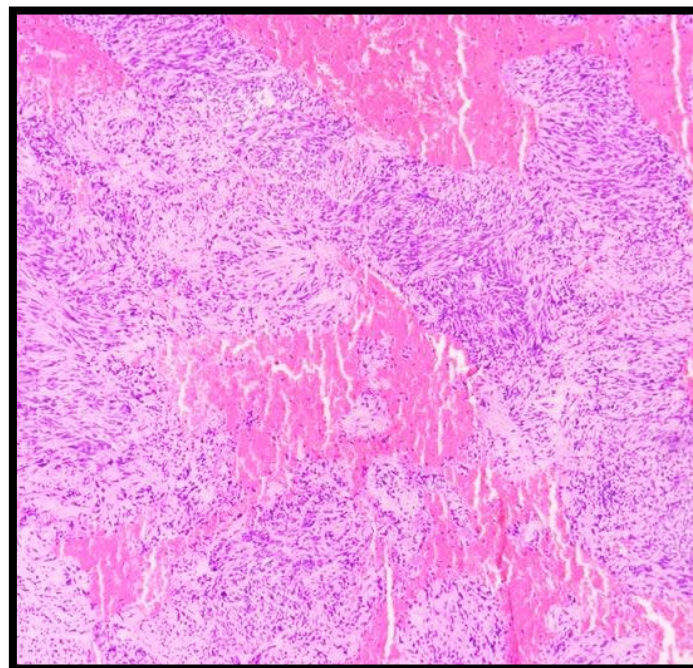


Figure 9: Cell block: Spindle cells arranged in fascicles, with faintly eosinophilic cytoplasm in a syncytial pattern with elongated nuclei with inconspicuous nucleoli, 20x

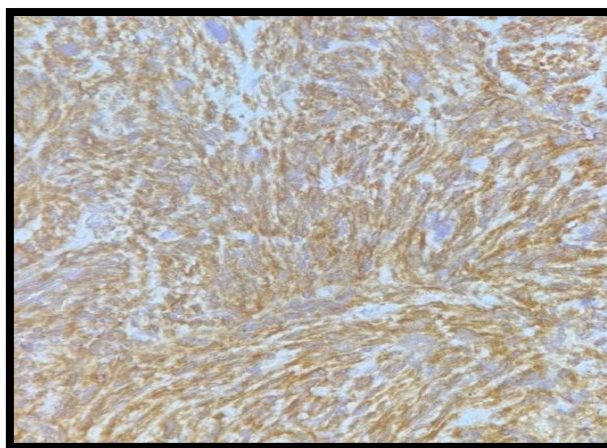


Figure 10: IHC done on cell block, DOG1 positivity, 40x

Cases 4 to 7: Metastatic squamous cell carcinoma

Four cases of metastatic squamous cell carcinoma (SCC) were identified, representing the largest diagnostic group in the series. The patients were aged 49–72 years. Ultrasonography of the parotid region demonstrated mass lesions varying in size from 2.2x2.1x2cm largest to 1x1.5x0.8cm smallest involving the parotid gland, corresponding to the clinically palpable lesions, and these were subsequently evaluated by fine-needle aspiration cytology.

Two cases had a documented prior history of squamous cell carcinoma involving the buccal mucosa, which had been diagnosed histopathologically three and five years earlier, respectively. In these cases, the cytological findings were interpreted in conjunction with the known clinical history and previous histopathological diagnosis.

The remaining two cases were initially diagnosed on cytology as squamous cell carcinoma, with the possibility of a primary versus metastatic lesion being considered. As primary squamous cell carcinoma of the parotid gland is rare and represents a diagnosis of exclusion, further clinical and radiological evaluation was performed. Subsequent evaluation identified lesions involving the base of the tongue, establishing the parotid lesions as metastatic SCC.

On cytology, metastatic SCC may show malignant squamous cells occurring singly and in cohesive groups, with variable degrees of keratinization, dense cytoplasm, nuclear pleomorphism, irregular nuclear contours, and a necrotic background. Depending on the degree of differentiation, these findings may overlap with those of primary salivary gland malignancies exhibiting squamoid differentiation. Therefore, correlation with the clinical history, imaging findings, and identification of a primary lesion at another anatomical site are essential for distinguishing metastatic SCC from a primary parotid malignancy.

These cases highlight the importance of considering metastatic disease in squamous-cell lesions of the parotid region, particularly given the rarity of primary squamous cell carcinoma of the parotid and the

potential for cytomorphological overlap with other salivary gland neoplasms.

DISCUSSION

The present case series highlights the diverse spectrum of metastatic malignant lesions that may present as a parotid. Although primary salivary neoplasms are common in this region, metastatic, hematolymphoid, and mesenchymal malignancies should also be considered when the cytological findings are atypical.

Metastatic squamous cell carcinoma (SCC) was the predominant diagnosis in our series, accounting for four of seven cases (57.1%). This finding is comparable with larger published studies, in which SCC represents one of the most frequent metastatic malignancies involving the parotid gland [1–4].

The parotid contains numerous intraparotid and periparotid lymph nodes that drain the scalp, face, external ear, and upper aerodigestive tract, making it particularly susceptible to metastatic disease [17,18].

Two SCC cases in the present series had a previous history of buccal mucosal carcinoma diagnosed three and five years earlier.

In the remaining two cases, SCC was first identified by cytology, while the primary site was initially uncertain. Subsequent evaluation revealed a base-of-tongue lesion in one patient, confirming metastatic rather than primary parotid SCC. Because primary parotid SCC is exceptionally rare, metastatic disease should be excluded before assigning a primary salivary origin [19].

Cytologically, metastatic SCC may show malignant squamous cells singly and in cohesive groups, with variable keratinization, dense cytoplasm, nuclear pleomorphism, irregular nuclear contours, and necrotic background. These findings may overlap with those of primary salivary tumors showing squamoid differentiation. Therefore, cytological interpretation must be integrated with clinical examination, imaging, and evaluation of the skin and upper aerodigestive tract. The neuroblastoma case was particularly unusual compared with previously published reports, which have predominantly involved infants and children with

primary parotid, adrenal, or paraspinal tumors [5,11–14].

In contrast, our patient was a 42-year-old adult with metastatic disease from a scalp primary. Correlation with clinical history and targeted immunohistochemistry, including PHOX2B and neural markers, was essential for diagnosis. Parotid involvement by plasma-cell neoplasms is also rare.

The 20 cases reported by González-Pérez et al. refer specifically to parotid extramedullary plasmacytoma. The present case is distinctive because it showed a large plasmacytic/plasmablastic parotid lesion in parotid region which lead to further analysis of patient where in we saw there was anemia and bone marrow was also involved by plasma cells hence the patient with multiple myeloma and synchronous follicular-variant papillary thyroid carcinoma was diagnosed. This case emphasizes the importance of considering plasma-cell neoplasms in patients with osteolytic lesions, anemia, renal dysfunction, and monoclonal gammopathy. It also illustrates the potential morphological overlap between plasmablastic plasma-cell neoplasms and plasmablastic lymphoma and need to correlate with hematological and immunological work up to differentiate between the two [6-10].

The metastatic GIST in our series represents an exceptionally unusual spindle-cell lesion of the parotid region. Unlike most GIST metastases, which involve the liver and peritoneum, this case presented at an unusual head-and-neck site [15,16].

The diagnosis was established through correlation with the patient's known gastric GIST and hepatic metastasis, together with CD117 and DOG1 positivity. This finding emphasizes that a parotid spindle-cell lesion may represent metastatic disease and should not automatically be classified as a primary salivary or soft-tissue tumor. Overall, the present study demonstrates the value of fine-needle aspiration cytology as a minimally invasive triage technique, when combined with interventional radiology like USG guided FNAC the yield will be better. Cytology can identify malignancy and suggest an unusual lineage, while cell-block preparation and targeted immunocytochemistry help establish the final diagnosis. Accurate classification requires integration of morphology, immunophenotype, clinical history, and radiological staging.

Recognition of these uncommon lesions prevents misdiagnosis, avoids inappropriate surgery, and facilitates appropriate

Limitations

The present study has certain limitations. The small sample size and retrospective, single-centre design limit the generalizability of the findings. The cases represent an uncommon and selected spectrum of malignant lesions involving the parotid region and may not reflect the overall distribution of parotid malignancies. Furthermore, the availability of clinical

information, immunohistochemical findings, and histopathological correlation varied among cases. Despite these limitations, the series highlights the importance of integrating cytomorphology with clinical history, imaging, and targeted immunohistochemistry for the evaluation of unusual malignant lesions involving the parotid region.

CONCLUSION

Fine-needle aspiration cytology (FNAC) is a useful initial diagnostic tool for evaluating unusual malignant lesions involving the parotid region. Recognition of atypical cytomorphological features, combined with careful assessment of clinical history, radiological findings, cell-block preparation, and targeted immunohistochemistry, can help establish the diagnosis and distinguish metastatic or systemic malignancies from primary salivary gland neoplasms. This case series highlights the importance of a multidisciplinary diagnostic approach in identifying uncommon lesions, guiding further investigations, and facilitating appropriate clinical management. However, the findings should be interpreted in view of the small sample size and retrospective, single-centre design.

DECLARATIONS

Ethics Approval and Consent to Participate

The study was retrospective and involved a review of existing clinical and cytopathology records. Ethics committee approval or exemption status should be stated in accordance with the institutional requirements.

Consent for Publication

The status of consent for publication of clinical details and cytopathological images should be confirmed and stated in accordance with institutional policy.

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Use this statement only if accurate.

Conflict of Interest

The authors should declare any conflicts of interest. If none exist, state: "The authors declare no conflict of interest."

Author Contributions

All authors' contributions to study conception, data collection, pathological evaluation, manuscript preparation, critical revision, and final approval should be specified according to their actual contributions.

Data Availability

The data supporting this case series are available from the corresponding author upon reasonable request, subject to institutional policies and patient confidentiality requirements.

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AI Use Disclosure

The authors declare that no generative artificial intelligence tools were used to generate or substantially modify the scientific content of this manuscript.

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