Cytodiagnosis of unusual metastases in parotid gland

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Documentation of metastatic lesions in the parotid gland diagnosed by fine-needle aspiration Abstract cytology (FNAC) is limited in the cytopathology literature. The metastases within the parotid masquerades clinically as primary neoplasm of parotid. The authors of present case report intent to highlight the importance of FNAC in the diagnosis of metastases in parotid. These diagnoses enable the search for the locations of unknown primaries. The nodules within the parotid masquerading as primary neoplasm have undergone FNAC in five cases. The cytomorphological interpretation of the smears was performed. The diagnosis on cytology was compared with subsequent histological evaluation of the suggested primary neoplasm. FNAC in the five cases revealed the following cytodiagnosis: metastases of ductal carcinoma (2), melanoma (1), deposits of small cell carcinoma (1) and metastases of clear cell renal cell carcinoma (RCC) (1). There was complete concordance when these cytodiagnoses were compared with histological evaluation from the suggested sites of primaries as well-differentiated ductal carcinoma of the breast (2), melanoma of the scalp (1), small cell carcinoma of the lung (1) and clear cell RCC of the kidney (1). The metastases within the parotid can masquerade as primary neoplasm. The cytomorphological patterns and features of metastases are similar to that of their primary neoplasm. Therefore, FNAC over the nodules within the parotid unsuspected for metastases provides valuable information to search for primary neoplasm.

Keywords: Fine-needle aspiration cytology, metastases, parotid gland

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INTRODUCTION

Metastases to parotid are rare. Therefore, secondary neoplasms of parotid on many occasions remain unsuspected in patients asymptomatic of primary. There are several reports in the literature describing the secondary neoplasms of the parotid gland. These reports published in literature described wide range of primaries metastasizing to parotid.^[1-15]

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The most common metastases reported in parotid because of anatomic proximities and lymphatic anastomosis are from the oral cavity.^[1] However, the many other primary malignant tumors arising in supraclavicular and infraclavicular areas have been quoted to metastasize to parotid,^[1-15] which includes more commons such as melanoma, breast carcinoma, small cell carcinoma lung, follicular carcinoma thyroid, adenocarcinoma from gut and renal cell carcinoma (RCC) and others.

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The reports of diagnosis of secondary neoplasm of parotid by fine-needle aspiration cytology (FNAC) are rare.^[2-4,7,8,12,14] Nonlymphomatous tumors metastasizing to parotid is a rare diagnostic encounter on FNAC when clinical suspicion of it is missing due to nonreport of any primary in the case.

The present article reports the five cases of cytopathological diagnosis of unusual metastases in parotid which clinically masqueraded as the primary neoplasm of parotid when no known primary was yet detected. The report of metastases of FNAC in these cases prompted clinicians to search for suggested primary. These cases later underwent pathological assessment of the detected primary that confirmed the original diagnosis of metastases offered on FNAC.

This was an unusual event in the practice of cytopathology and therefore worthy of sharing with medical fraternity.

MATERIALS AND METHODS

Five cases were drawn from cytological audit of last 7 years from the Division of Cytopathology, Department of Pathology, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences (Deemed to be University), Sawangi (Meghe), Maharashtra, India.

These five cases reported in the article never complained of the primary to the treating physicians or surgeons at the time of physical examination. The primary remained unsuspected till the diagnosis of metastases to parotid was made.

These patients reported to the clinical outpatient department (OPD) of general surgery, otorhinolaryngology and oromaxillofacial surgery to seek consultation of the progressively increasing painful nodular swelling in the parotid which was causing disfigurement.

These patients underwent ultrasonography (USG)-guided FNAC of nodular swelling in parotid by the standard procedure.^[16] FNAC aspirates of these nodular swellings were wet and dry fixed to be stained by Papanicolaou and Giemsa stain, respectively.

Assessment of cytomorphological features differentiating between the primary and secondary malignant neoplasm of parotid was performed. The diagnostic cytomorphology was reported by the relevant standard text and references.^[2-4,7,8,12,14,17]

The cases of squamous cell carcinoma metastasizing to the parotid from known primary in the head and neck area have been excluded from reporting in this article.

RESULTS

The abridged description about five cases for their clinicopathological data is described in Table 1. The following are the details of the cases.

Patient 1

A 45-year-old female presented to the general surgery OPD with nodular swelling in the right parotid region. The examination of the nodule revealed firm-to-hard consistency with restricted mobility. The swelling was single in the preauricular area. FNAC was carried out. Smears revealed a typical ductal cell carcinoma cytomorphology that showed the cytoarchitecture of sheets and ductal placements of malignant ductal cells. The background showed tumor necrosis and malignant diathesis. The diagnosis of metastases of well-differentiated ductal carcinoma was offered [Figure 1] with advice to search for primary in the breast. On examination, ipsilateral breast revealed 2 cm lump in the upper inner quadrant. The lump underwent FNAC followed by tru-cut biopsy. The offered diagnosis on these investigations was of well-differentiated ductal carcinoma. The patient later underwent the surgical management for the lump in the right breast.

Patient 2

A 56-year-old female came with the chief complaints of deep nodular swelling in the left parotid region. The examination of the nodule revealed firm to hard in consistency with restricted mobility. The swelling was solitary. FNAC was carried out. Smears revealed discohesive cell sheets with internal attempted ducts. The cells carried hyperchromatic pleomorphic nuclei with irregular chromatin and infrequent nucleoli. The nuclei of the cell sheets showed rare mitosis. The background was hemorrhagic with dissociated malignant cells. The diagnosis of metastases of well-differentiated ductal carcinoma was presented [Figure 2] with advice to search for primary in the breast. On examination, left breast revealed 1.5 cm lump in the upper outer quadrant. The lump underwent FNAC followed by tru-cut biopsy. The offered diagnosis on these investigations was of well-differentiated ductal carcinoma. The patient later underwent surgical management for the lump in the left breast.

Patient 3

A 68-year-old male complained of superficial but nodular swelling in the right parotid region. The patient complained of pain in ear and the swelling. The swelling measured 3 cm in diameter with restricted mobility and showed erythematous skin over it. The examination of ear, nose and throat was reported to be normal. The patient was

Table 1: Clinicopathological features in five patients				
Patient number/ gender/age	Lesion in parotid (metastatic site)	FNAC diagnosis	Primary site/cytohistological diagnosis	
1/45 years/female	Deep nodular swelling in the right parotid	Metastatic ductal carcinoma	Right breast/ductal carcinoma	
2/56 years/female	Deep nodular swelling in left parotid	Metastatic ductal carcinoma	Left breast/ductal carcinoma	
3/68 years/male	Superficial nodular swelling in right parotid	Metastatic deposits of melanocarcinoma	Scalp/melanocarcinoma	
4/48 years/male	Deep nodular swelling in left parotid	Metastatic small cell carcinoma lung	Left lung/small cell carcinoma	
5/65 years/male	Deep nodular swelling in right parotid	Clear cell renal cell carcinoma	Right kidney/clear cell renal cell carcinoma	

FNAC: Fine-needle aspiration cytology



Figure 1: Metastases of ductal carcinoma breast (WD) (fine-needle aspiration cytology) malignant cells in ductal configuration, (Pap stain, \times 40)

advised to be assessed by USG-guided FNAC. The aspirate revealed dissociated to polygonal cells carrying centrally placed hyperchromatic nuclei with rounds prominent nucleoli. Few of the cells showed bi-nucleation. The cytoplasm of these cells carried granules of altered hue. The background showed infrequent melanin containing macrophages [Figure 3]. Cytodiagnosis of melanoma was made with advice to search for primary of melanoma. The re-examination showed 1 cm size of brown-colored tumorous lesion uncomplained by the patient. This primary lesion of the scalp underwent FNAC followed by excision revealing similar diagnosis of melanoma on both occasions.

Patient 4

A 40-year-old habituated to chronic smoking complained of deeply placed nodular swelling in the left parotid region which pained during mastication of food. Bimanual examination of the swelling revealed of nodule on intraoral examination. The nodule was of 2 cm, firm in consistency. The nodule underwent USG-guided FNAC. The smear made of aspirate revealed predominantly small cell population placed in nests, pseudoglandular configuration and ill formed rosettes. The nuclei were of high N: C ratio, hyperchromatic which pepper salt chromatin. Cells show



Figure 2: Metastases of ductal carcinoma breast (WD) (fine-needle aspiration cytology) malignant ductal cells in sheets with cellular discohesion and attempted internal ducts, (Pap stain, ×40)

absent to scant blue cytoplasm with plentiful background presence of bruised and fragile nuclei [Figure 4]. These cytomorphological features guided to report the diagnosis of metastases of small cell carcinoma. The advice to search small cell malignant tumor in the head, neck and lung was given. Computed tomography (CT) revealed the presence of tumor mass in the left lung with a few satellite nodules on the same side of gland. A percutaneous transthoracic FNAC was carried under CT guided. The material obtained was processed for cytopathology and histopathology by cell block. The results of both the investigative techniques revealed the diagnosis of small cell carcinoma lung (Oat cell type).

Patient 5

A 65-year-old male patient sort medical advice for complains of hematuria, lump in abdomen and shortness of breath along with a nodular swelling in the right parotid. The patient was provisionally diagnosed of lump in the abdomen probably malignant arising from right kidney. Meanwhile, his workup for other complains was being carried out, nodule in the right parotid underwent FNAC. It revealed the tubular structures of cuboidal epithelial cells in isolation or within the sheets



Figure 3: Metastases of melanocarcinoma (fine-needle aspiration cytology) dissociated round to polygonal melanocytes showing prominent nucleoli, binucleation and cytoplasmic fine melanin pigments, background shows melanin containing macrophages (Giemsa stain, ×40)

of cells. The cells carry low-grade malignant nuclei but revealed vacuolated clear appearing cytoplasm with little granularity in a few. Background of smear shows fine vesicles of lipids with few loops of endothelial cells due to consideration to his clinical presentation, a diagnosis highly suspicious of metastases of clear cell RCC was offered [Figure 5]. The patient underwent multiple investigations. FNAC from the sites of renal mass and suspected metastatic nodule of the left lung revealed the cytomorphology consistent with RCC and metastases of RCC in the lung, respectively.

Superficial parotidectomy was performed in one case of melanoma. The other cases (n = 2) of metastatic ductal carcinoma breast underwent excision of the nodule within the parotid. The cases diagnosed with metastases of small cell carcinoma and RCC underwent medicinal management (chemotherapy). All five cases showed complete concordance between cyto-histological diagnoses.

DISCUSSION

A study of Franzen *et al.*^[1] analyzed metastases to parotid gland and have concluded that the secondary neoplasia in the parotid gland is increasingly frequent. This study has observed that the frequent cancer metastasizing to the parotid gland was squamous cell carcinoma (79%) arising in oropharynx and the primaries which were above the clavicle. This study collected data from surgical specimen and did not mention about their encounters with the diagnosis of secondary neoplasm by FNAC. The presently reported cases in this article are other than that of squamous cell carcinoma. The metastatic lesions of



Figure 4: Metastases of small cell carcinoma lung (fine-needle aspiration cytology) nested population of small to intermediate size cell with high N: C, nuclei show pepper salt chromatin and significant nuclear fragility (Giemsa stain, ×40)

squamous cell carcinoma as observed at our place were excluded from reporting as the primary were known to us.

The comprehensive study of Lussier *et al.*^[2] comprising of 40 cases of nonlymphmatous tumors metastasizing to major salivary gland diagnosed on FNAC too has described squamous cell carcinoma as one of the frequent metastases. This study chiefly described the metastatic lesions of squamous cell carcinoma, melanoma, rhabdomyosarcoma, retinoblastoma and breast carcinoma. The other metastases diagnosed on FNAC within the salivary gland were papillary carcinoma thyroid and case of lacrimal gland carcinoma. However, except for one, the rest of the cases in their study had known primary. The distribution of the primary that has metastases to salivary gland was mostly arising from above the clavicle except for the four cases of carcinoma of breast and a case of carcinoma thyroid.

Upon the comparison of the primary, reported in the present article except for one, rest of the primaries was detected to be coming from below clavicular organs. The present study suggested to search for unknown primary upon the diagnosis of the metastases which is contrary to the observations of Lussier *et al.* were known except one.

The study of Emanuelli *et al.*^[3] reported 11 cases metastasizing to parotid by FNAC from nonhead and neck tumors. These 11 cases were distributed for their primaries as follows: lung (8), breast (1), pancreas (1) and stomach (1). These cases diagnosed on FNAC were followed by USG-guided core biopsy. Eleven cases of their study were divided into three groups:

(i) Parotid metastases was the first clinical manifestation of unknown primary distant tumor



Figure 5: Metastases of clear cell renal cell carcinoma (fine-needle aspiration cytology) Sheet and tubular structures of cuboidal epithelial cells with low-grade malignant nuclei and cytoplasmic fine vacuoles, (Pap stain, ×40)

- (ii) Parotid tumor was metastatic location of known distant tumor
- (iii) Parotid tumor represented the recurrence of previously treated tumor.

Their study had six cases where primary was unknown. The cytodiagnosis of metastases suggested the search of primary which could be localized at lung (small cell carcinoma-2, squamous cell carcinoma-1, large cell carcinoma-1 and adenocarcinoma-1) and pancreas (adenocarcinoma-1). These findings are similar to reported cases of the present study where primaries were unknown. All the secondary in the parotid were from nonhead and neck tumors except for one. The study of Emanuelli *et al.*^[3] has concluded that parotid metastasis can be the first clinical manifestation of a malignant tumor from a distant site and can manifest years after curative intent treatment to which the finding in the present case report agrees.

The reports of Kmeid *et al.*, have reported the cytodiagnosis of metachronous metastasis to the parotid from primary breast carcinoma on FNAC. The authors encountered no difficulty at interpretation of cytomorphology of breast carcinoma as it showed classic cytomorphological features as seen in the aspirates of primary site of breast carcinoma. Similarly, the two cases reported here revealed a classical cytomorphological pattern of well-differentiated ductal carcinoma equivalent to FNAC aspirates of primary site.

Andreadis *et al.* and Emanuelli *et al.*^[3,7] have reported metastasis of malignant melanoma in parotid on FNAC with primary in head-and-neck region as well as distant to it. The reports of these authors face no difficulty at interpretation of malignant melanocytes and therefore the diagnosis as

the cytomorphological pattern were self-explanatory of the diagnosis. The present study reported a case of deposits of melanoma in right parotid where primary was unknown but detected on scalp upon the diagnosis of FNAC.

Isolated parotid metastasis from small cell lung carcinoma has been reported by Wang *et al.*, Emanuelli *et al.* and Lussier *et al.*^[2,3,10] The diagnosis of metastasis was mostly based on the features of typical small cells of high N: C ratio, salt-pepper chromatin placed in small clusters accompanied by nuclear fragility. The foresaid authors faced no difficulty at reporting the metastasis (small cell and squamous cell carcinoma) at FNAC even in the absence of no known primary in the lung.^[3]

Spreafico *et al.*^[12] have reported the diagnosis of RCC in the right parotid by FNAC in a known case of RCC. There are not many reports in literature which describe the diagnosis of RCC metastases in parotid evaluated on FNAC. Our experience of diagnosing RCC (clear cell type) in the kidney by FNAC enabled us to interpret the cytomorphology in this case. The cytomorphology of RCC at metastases is no different from cytomorphology of it at primary site of the kidney. The clinical scenario supported the cytodiagnosis of metastases of RCC.

There are a few studies retrieved from literature which did cytohistology statistics of salivary metastatic tumors. Eneroth *et al.*^[18] reported 23 cytodiagnosed cases of metastases with histological concordance in all cases.

Qizilbash *et al.*^[19] reported 11 cases of metastases diagnosed on cytology with histological concordance without false diagnoses. MacLeod and Frable^[20] cytodiagnosed 21 cases as metastases of which 18 could be confirmed on histopathological examination. Malata *et al.*^[21] in their 11 cases cytodiagnosed as metastases found no false diagnosis on histopathological comparison. Similarly, the present study did not record any erroneous diagnosis on cytohistological correlation.

CONCLUSION

The metastases in parotid are rare. It may be an initial clinical presentation which may masquerade like the primary neoplasia of parotid. It may arise in different clinical settings with known and unknown primaries.

FNAC with its several advantages helps to resolve the dilemma of primary versus secondary malignant neoplasm of parotid. The cytomorphological exhibits of metastatic carcinoma are similar to that of its primary. The parotid

may be a seat of metastases from the primaries originating in the organs above and below the clavicle. The uniqueness to the present case reports is the diagnosis of metastases in a clinical situation where no primary was yet not detected. Rather the diagnosis of metastases to the parotid made on FNAC suggested the clinicians to search for primary malignant neoplasm.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initial s will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest There are no conflicts of interest.

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