Hidden in plain sight: Intraparotid lymph nodal metastases on computed tomography

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Learning objectives

• To discuss relevant embryology of parotid gland and its lymphatic drainage pattern.

• Enumerate various malignancies and their possible routes of intraparotid lymph nodal metastases.

• To discuss computed tomographic features of intraparotid lymph nodal metastases.
Background

Parotid gland is unique among all salivary glands owing to the presence of intraparotid lymph nodes. This anatomic nodal arrangement renders parotid gland particularly vulnerable to local and distant metastatic deposits. Intraparotid lymph nodal metastases are uncommon and poorly recognized entity. Presence of nodal metastases especially the parotid lymph nodes suggests poor prognosis in head and neck malignancy, often precluding an optimal locoregional disease control and necessitating modification of surgical technique to avoid future recurrence.

Through this article we aim to discuss relevant embryology of parotid gland, lymphatic drainage patterns of head and neck lymph nodes, various causes of intraparotid lymph nodal metastases and computed tomographic features of the same.
Findings and procedure details

Embryology of parotid glands

The parotid anlagen is first to develop at 4-6\textsuperscript{th} week of embryonic life. The same embryogenetic basis is shared by all the salivary glands. The parenchyma of the salivary gland develops from proliferation of oral epithelium i.e. primitive stomodeum (Fig.1) and stroma consisting of capsule and septa, may be of mesodermal or neural crest origin. The salivary gland development follows a chronological order (parotid-submandibular-sublingual) barring an event of encapsulation. The parotid gland is the last to acquire its investing fascia thus leading to its delayed encapsulation. Lymphatic channels develop after encapsulation of submandibular and sublingual gland but before the parotid encapsulation, resulting in entrapment of lymph nodes in parotid parenchyma. Epithelial buds enlarge, elongate and branch initially forming solid structures. Subsequent branching of the glandular mass leads to arborization. Each branch terminates in one or two solid end bulbs. Elongation of the end bulb follows and lumina appears in their centers, transforming the end bulbs into terminal tubules. These tubules transform into various acini and ducts at the stage of terminal differentiation (Fig.2).

Anatomy

The parotid glands are situated in the preauricular region, at the posterior border of mandible. The facial nerve after exiting the skull base through stylomastoid foramen passes through parotid gland dividing it into superficial and deep lobe (Fig. 3 & 4). The superficial lobe, overlies the lateral surface of the masseter, and is defined as the part of the gland lateral to the facial nerve. The deep lobe is medial to the facial nerve and located between the mastoid process of the temporal bone and ramus of mandible. The Stenson's duct is formed at the anterosuperior border of the parotid gland travelling parallel and 1cm below the zygoma over the masseter muscle. It turns sharply medial at the anterior border of masseter muscle and passes through the buccinators muscle, buccal mucosa and into the oral cavity opposite the maxillary second molar. The arterial blood supply is through external carotid artery and its terminal branches. The venous drainage is through retromandibular vein\textsuperscript{1}.

Lymphatic drainage
There are total 15-20 parotid and periparotid lymph nodes. These are grouped as extraglandular and intraglandular\textsuperscript{2, 3}. The extraglandular lymph nodes are either preauricular or infraauricular. Majority of intraglandular parotid lymph nodes are found along the course of and lateral to retromandibular vein.\textsuperscript{4} Around 4-7 lymph nodes are present in superficial and 1-2 nodes are present in the deep parotid lobe\textsuperscript{5}. The intraparotid lymph nodes drains eyelids, orbits, conjunctiva nose, cheek, middle ear, Eustachian tube, upper lip and infratemporal fossa (Fig.5). Extraglandular and intraglandular lymph nodes are considered as single functional unit with efferent lymphatics draining to superior deep cervical lymph nodes\textsuperscript{6}.

Location-wise lymphatic drainage pathways of head and neck have been enumerated in Fig 6,7&8.

Normal lymphatic pathway could be easily interrupted even by minor surgical procedure, irradiation or in presence of massive cervical lymph nodal metastases\textsuperscript{7, 8}. Three routes of tumor metastases from the primary sites to the parotid lymph node can be considered: direct invasion, lymphatic spread, and hematogenous dissemination. The lymphatic routes for tumor spread to the intraglandular parotid nodes is via a) retropharyngeal nodes b)indirectly through periparotid extension to nodes superficial or deep to the parotid capsule adjacent to parotid parenchyma. c) through retrograde extension from massive metastasis in the neck due to obstruction of the normal lymphatic drainage pattern.

Once the tumor has metastasized to a parotid area lymph node, it has access to the lymphatic plexus, parotid parenchyma, parapharyngeal space, and the facial nerve after breaching the nodal capsule. Therefore it can be concluded that parotid lymph nodal metastasis behaves in identical way to a high-grade parotid neoplasm like primary squamous cell carcinoma\textsuperscript{9}. Malignancy has proclivity to metastasize to first echelon lymph nodal group. For face, conjunctiva, infratemporal fossa, preauricular region, frontal, temporal and parietal scalp, parotid area lymph nodes are first echelon lymph nodes (Fig 9).

Common group of malignancy from primary tumour zones to have parotid lymph nodal metastases have been enumerated in Figure 10.

**Computed tomography of parotid lesions:**
Due to varying degree of stromal fat and exclusive serous saliva, the CT density of parotid gland is always almost lower than the surrounding musculature (Fig 11). This fibrofatty nature due to intraglandular fat content provides ideal contrast for evaluation of mass lesions. When the density of parotid gland diminishes and approaches that of muscle, diagnostic dilemma may be confronted in parotid mass evaluation. Also chronic recurrent infection or inflammatory process like recurrent parotitis can reduce the available contrast (Fig 12). Anatomically the facial nerve divides parotid gland into superficial and deep parotid lobe, however it is not readily discernible on computed tomography. A smoothly marginated retromandibular vein, measuring less than 1 cm is constantly visualized at the junction of the superficial and deep lobes just posterior and slightly lateral to the ramus of the mandible and can be used as a surrogate marker for facial vein within the gland. Majority of intraparotid lymph nodes lying lateral to retromandibular vein are labelled to be within superficial lobe and those lying medially are labelled as deep parotid lymph nodes (Fig 11).

The role of computed tomography for salivary gland tumour evaluation is limited. Metastatic parotid lymph nodes either appear single or multiple, well circumscribed, solid or necrotic, with mild to moderate post contrast enhancement. Mostly an ipsilateral locoregional malignancy from primary tumour site is identified. The parotid lymph nodal metastases may occur in isolation or in presence of enlarged cervical lymph nodes. CT imaging features of parotid lymph nodal metastases vary according to the primary malignancy and no specific CT imaging features allows for their accurate differentiation.

A) Cutaneous squamous cell carcinoma:

Cutaneous squamous cell carcinoma comprise 20% of all skin cancer of the head and neck. Rowe et al. reported an extensive review of the literature on cutaneous SCC of the face, ear, and lip.

Following risk factors were identified for increase in local recurrence and regional metastasis:

- Lesion diameter >2cm.
- Depth of invasion > 4mm.
- Poor differentiation on histopathology.
- Past treatment.
- Location (ear, lip, scalp, scar or non sun exposed area).
- Perineural invasion.

Lymphatic spread of head and neck cutaneous SCC often involves parotid lymphatics first and subsequently cervical area lymph nodes.
The current American Joint Committee on Cancer (AJCC) staging system for cutaneous SCC metastatic to regional lymph nodes fails to adequately describe the extent of disease. Therefore, O’Brien et al. have recently proposed a new staging system (Fig 13) that separates parotid gland from cervical lymph node involvement and is superior prognostic indicator than AJCC staging system as confirmed by multicenter study.\(^\text{11}\)

B) **Basal cell carcinoma.**

Of nonmelanoma skin cancers, approximately 80% are basal cell carcinoma. It is known to be a locally aggressive tumour and metastasize late, in contrast to squamous cell carcinoma. Lymphatic spread is most common route in 70% of cases, though hematogenous spread is also present.

In 1951 Lattes and Kessler proposed the following criteria for diagnosis of metastatic basal cell carcinoma:

- Primary tumour arising from the skin and not from the mucous membrane or other glands.
- Metastatic nodule must be confined to lymph node or distinct from the primary tumour.
- Identical histomorphology of primary and metastatic nodule.
- Features of squamous cell carcinoma must be absent.

The incidence of metastasis is reported to be 2% for tumours larger than 3 cm, 25% for tumours larger than 5 cm and 50% for those more than 10 cm.\(^\text{13, 14}\) Majority of metastatic basal cell carcinoma arises from facial region, an area known to have high vascularity.

C) **Malignant melanoma.**

About one-third of cutaneous malignant melanoma arises in the head and neck. Cutaneous melanoma are second most common malignancy after squamous cell carcinoma to metastasize to parotid gland, accounting for almost 40% of cases. The direct spread is a possibility but uncommon event. Lymphatic spread is deemed as most common route. Studies have shown that melanoblasts can exist in intralobular duct of the parotid gland and serve as origin for primary melanoma, but still the metastases out number the primary parotid melanoma substantially. The facial, oral and anterior oropharyngeal melanoma commonly metastasize to the submandibular lymph nodes and
gland. In contrast to cutaneous melanoma, oral malignant melanoma are aggressive and more infiltrative in growth, with majority of them presently with cervical lymph nodes at the time of initial presentation. Low rate of occult metastasis are noted in patients with stage I disease according to Clark levels. With stage II and higher, the number of occult metastasis increases significantly and therefore elective treatment should be considered. Distant metastasis are more often found in malignant melanoma than in squamous cell carcinoma when concomitant parotid lymph nodes metastases are present.

Parotid metastases from a primary melanoma of unknown origin have been described in the literature\textsuperscript{15,16}. Interestingly melanoma of unknown site presenting with enlarged cervical and parotid lymph nodes have better survival rates than the known primary\textsuperscript{17} (Fig 14).

D) Oral squamous cell carcinoma

Direct lymphatic connections may exist between the parotid gland and the oral cavity or the oropharynx. Alternatively, parotid metastases may result from retrograde or aberrant lymphatic drainage occurring secondary to disruptions in normal lymphatic drainage due to extensive neck disease\textsuperscript{18}.

The pattern of parotid node metastasis may differ with the histologic diagnosis of the particular oral carcinoma and its natural history(Fig 15). The risk of parotid node involvement increase with an increased number of cancer-positive cervical lymph nodes. The involvement of three or more positive cervical nodes could be a risk factor for parotid node metastases.

E) Nasopharyngeal carcinoma

Nasopharynx do have intercommunication to parotid lymph node and can potentially present with parotid metastases. Nasopharyngeal carcinoma metastasize to parotid lymph node through three routes i) via lateral retropharyngeal lymph nodes to the parotid gland tissue (ii) via superior deep cervical lymph nodes; and (iii) via parotid gland tissue involvement. Nasopharyngeal cancer can also invade the parotid gland tissue directly by way of the peripharyngeal space\textsuperscript{19}.

F) Lymphoma
Secondary parotid involvement by systemic lymphoma is more common than primary tumour, occurring 1% to 8% of lymphomas, mostly with high-grade, diffuse large-cell lymphoma (Fig 16 a & b). Increased incidence is also seen in patients with Sjogren's disease. The prognosis is usually poor because of the high-stage and high-grade tumor. The computed tomographic appearance varies with the pathologic distribution of the disease. Intraparotid lymph nodal metastases are homogeneous and may enhance slightly on post contrast study. A diffuse infiltration into parotid parenchyma is suggested by either poorly defined margins or involvement of the entire gland. Nodal lymphoma needs to be differentiated from MALToma, a task possible only through histopathology and immunochemistry.

F) Distant metastases

Distant parotid metastases from infraclavicular malignancies are rare amounting to 0.16-0.4% of total number of cases\textsuperscript{20}. Reports have shown unilateral parotid metastases from lung carcinoma, renal carcinoma, ductal breast carcinoma, malignant melanoma, rhabdomyosarcoma of the lower limb, testicular seminoma, and Merkel cell carcinoma\textsuperscript{20}.

These tumours can metastasize to the parotid gland through thoracic duct, Batson's paraspinal venous plexus or by bypassing pulmonary vascular filtration. Those metastasizing through hematogenous route usually infiltrates parotid parenchyma more than the parotid lymph nodes. Parotid lymph nodal metastases is usually the late manifestations of distant primaries and suggests an advanced disease.

Most common CT differential when considering nonnecrotic intraparotid lymph nodal metastases should include reactive intraparotid lymph node (Fig 17), Warthin’s tumour (Fig 18) and pleomorphic adenoma. The pleomorphic adenoma shows prominent post contrast enhancement (Fig 19a) when the tumor size is around 1-2cm, becoming less marked and sometimes showing delayed enhancement at larger sizes (Fig 19b). Warthin’s tumour shows feature of bilaterality, location in the tail region of parotid and greater tendency to undergo cystic changes (Fig 20a, b & c). Benign lymphoepithelial lesion, small parotid abscess, epidermal cyst can mimic necrotic lymph nodal metastases besides cystic variety of Warthin’s tumour (Fig 21 a, b & c).

A preoperative FNAC of the parotid mass plays an important role in the treatment decision-making process. It is necessary for definitive diagnosis since it offers a good sensitivity and specificity. Due to profound impact on the course of disease and for being an independent prognostic factor in disease specific outcome, early detection and definitive treatment of parotid bed metastases is of utmost importance. The management of parotid metastasis usually involves a combined modality treatment...
including parotidectomy, ipsilateral neck dissection and postoperative irradiation to avoid recurrence and improve better locoregional control of the disease.
**Fig. 1:** Schematic illustration showing origins of the parotid gland, submandibular gland and sublingual gland from the epithelial lining of the primitive stomodeum.

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**Fig. 2:** Schematic illustration showing various stages in development of a salivary gland.

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**Fig. 3:** Schematic diagram showing anatomical relationship of neurovascular bundle to parotid gland.
Fig. 4: Schematic diagram showing division of parotid gland by facial nerve into superficial lobe (outer) and deep lobe (inner) and relationship to retromandibular vein.
**Fig. 5:** Diagrammatic representation of lymphatic drainage pattern of head and neck. The parotid lymph nodes drains the eyelids, orbits, conjunctiva nose, cheek, middle ear, eustachian tube, upper lip and infratemporal fossa (shaded region) with efferent to deep cervical group of lymph nodes.

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<table>
<thead>
<tr>
<th>Location</th>
<th>Afferent</th>
<th>Efferent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occipital</td>
<td>Occipital region of scalp</td>
<td>Deep cervical lymph nodes</td>
</tr>
<tr>
<td>Retroauricular</td>
<td>Posterior part of the temporoparietal region, the upper part of the cranial surface of the auricula or pinna, and the back of the external acoustic meatus</td>
<td>Deep cervical lymph nodes</td>
</tr>
<tr>
<td>Parotid</td>
<td>Intraglandular: Root of the nose, the eyelids, the frontotemporal region, the external acoustic meatus and the tympanic cavity, possibly also the posterior parts of the palate and the floor of the nasal cavity. Extraglandular: Nasal part of the pharynx and the posterior parts of the nasal cavities.</td>
<td>Deep cervical lymph nodes</td>
</tr>
<tr>
<td>Buccal</td>
<td>Cheek over buccinators muscle</td>
<td>Submandibular or parotid lymph nodes</td>
</tr>
<tr>
<td>Submandibular</td>
<td>Medial palpebral commissure, the cheek, the side of the nose, the upper lip, the lateral part of the lower lip, the gums, and the anterior part of the margin of the tongue.</td>
<td>Deep cervical lymph nodes</td>
</tr>
<tr>
<td>Submental</td>
<td>Anterior tongue, the medial inferior lip, the medial inferior gingivae and teeth, and the chin</td>
<td>Submandibular group or to deep cervical nodes</td>
</tr>
<tr>
<td>Anterior cervical</td>
<td>Skin, superficial tissue of the front of the neck</td>
<td>Deep cervical lymph nodes</td>
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**Fig. 6**: Table.1 Lymphatic drainage pattern of superficial lymph nodes of head.
<table>
<thead>
<tr>
<th>Location</th>
<th>Afferent</th>
<th>Efferent</th>
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<tbody>
<tr>
<td>Anterior Cervical nodes</td>
<td>Found in association with the anterior jugular vein. They drain lymph from the skin of the anterior neck, below the hyoid bone.</td>
<td>Deep nodes on either side of the neck</td>
</tr>
<tr>
<td>Posterior cervical nodes</td>
<td>Found in the posterior triangle. These drain lymph from the lateral and posterior skin of the neck</td>
<td>Transverse cervical (supraclavicular) nodal group</td>
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**Fig. 7:** Table 2 Lymphatic drainage pattern of superficial lymph nodes of neck.

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<table>
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<tr>
<th>Location</th>
<th>Afferent</th>
<th>Efferent</th>
</tr>
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<tbody>
<tr>
<td>Deep cervical nodes</td>
<td>Collects lymph from the other groups of the head and neck. Superior deep cervical nodes typically drain to inferior deep nodes.</td>
<td>Efferent vessels from inferior deep cervical nodes typically collect into a single jugular trunk. This unites with the thoracic duct on the left prior to entering the brachiocephalic vein. On the right, the jugular trunk usually empties directly into the brachiocephalic vein.</td>
</tr>
<tr>
<td>Retropharyngeal nodes</td>
<td>Predominately from the pharynx, including the fauces.</td>
<td>Deep cervical lymph nodes</td>
</tr>
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**Fig. 8:** Table 3 Lymphatic drainage pattern of deep cervical lymph nodes.

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Fig. 9: Illustration showing primary tumour zones of head and face metastasizing to parotid lymph nodes.

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Table 5 Common malignancies to metastasize to parotid lymph node

- Skin cancer of face and scalp.
  - Nonmelanoma skin cancer.
    - Squamous cell carcinoma.
    - Basal cell carcinoma.
  - Malignant melanoma
- Oral squamous cell carcinoma
- Lymphoma.
- Nasopharyngeal carcinoma.
- Distant primary (rare but have been reported)
  - Breast carcinoma.
  - Lung malignancy.
  - Renal carcinoma.

**Fig. 10:** Table 5. Common malignancies metastasizing to parotid lymph nodes.
Fig. 11: Diagrammatic representation of division of parotid in superficial and deep lobe with respect to retromandibular vein. Majority of intraparotid lymph nodes lie lateral to retromandibular vein. Retromandibular vein can be used as a surrogate marker for facial nerve on CT.

Fig. 12: Non contrast axial CT image at the level of parotids shows loss of fatty attenuation of parotid gland due to recurrent parotitis resulting in reduction of available contrast for depiction of intraparotid lesion.
O’Brien et al system for clinical staging of metastatic cutaneous squamous cell carcinoma involving the parotid gland [12]

<table>
<thead>
<tr>
<th>Parotid</th>
<th></th>
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<tbody>
<tr>
<td>P1</td>
<td>Metastatic node &lt; 3cm</td>
</tr>
<tr>
<td>P2</td>
<td>Metastatic node 3-5cm, multiple parotid nodes</td>
</tr>
<tr>
<td>P3</td>
<td>Metastatic &gt;6cm, disease above facial nerve and skull base</td>
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<table>
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<th>Neck</th>
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<tr>
<td>N0</td>
<td>No clinically suspicious node</td>
</tr>
<tr>
<td>N1</td>
<td>Single ipsilateral lymph node &lt;3cm</td>
</tr>
<tr>
<td>N2</td>
<td>Single node&gt;3cm. Multiple or contralateral node.</td>
</tr>
</tbody>
</table>

**Fig. 13:** O’Brien et al system for clinical staging of metastatic cutaneous squamous cell carcinoma involving the parotid gland.

Fig. 14: Contrast enhanced axial CT image shows a peripherally enhancing, solid, rounded lesion with smooth margins in superficial lobe of left parotid gland (yellow arrow head) subsequently identified as metastases from malignant melanoma of unknown site.

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Fig. 15: Contrast enhanced axial CT images shows large faintly enhancing infiltrating advanced left tonsillar carcinoma (b) Post-operative follow up CT study after 8months shows new left intraparotid lymph nodal metastasis.

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**Fig. 16:** Contrast enhanced axial CT images shows (a) multiple non necrotic right cervical lymph nodes with a large lobulated mass (b) enhancing metastatic right parotid lymph nodal metastases (red arrow heads)

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**Fig. 17:** Contrast enhanced axial CT image at the level of parotid shows features of parotitis in right parotid gland and a subcentimeter sized reactive lymph node (red arrow head) in superficial lobe of left parotid gland.

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Fig. 18: Contrast enhanced axial CT images shows (a) diffuse soft tissue thickening(yellow arrow heads) in left parapharyngeal space due to oropharyngeal malignancy (b) an enhancing oval shaped Warthin’s tumour(red arrow head) in superficial lobe of left parotid mimicking metastatic parotid lymph node.

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Fig. 19: Contrast enhanced axial CT images showing (a) smaller, intensely enhancing pleomorphic adenoma in left parotid (yellow arrow head), indistinguishable from an intraparotid lymph node (b) at larger size the post contrast enhancement of pleomorphic adenoma is less marked and inhomogeneous (red arrow).

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Fig. 20: Contrast enhanced axial CT images showing Warthin’s tumour (a) in bilateral parotid glands (b) in tail region of left parotid lobe (c) with cystic changes in tail of left parotid gland.
Fig. 21: CT images showing (a) a small parotid abscess in left parotid (b) cystic variety of Warthin’s tumour and (c) a lymphoepithelial cyst in left parotid mimicking necrotic intraparotid lymph nodal metastases.
Conclusion

Although metastases to parotid lymph nodes are uncommon, these should always be considered in the differential diagnosis of a parotid mass. As an independent prognostic factor their presence have far reaching implications on disease outcome and necessitates change in treatment decisions. The cutaneous squamous cell carcinoma and malignant melanomas of the head and neck accounts for the predominant number of metastases to the parotid lymph nodes. Computed tomographic features vary according to the underlying primary malignancy and do not allow for definitive imaging differentiation. Further histopathological study is warranted for accurate and definitive diagnosis in the form of preoperative FNAC. Management of parotid is multimodality including parotidectomy, ipsilateral neck dissection and postoperative irradiation.
References


