CASE REPORT
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Primary Lymphoepithelial Carcinoma of Parotid Gland: Inadequate Preoperative Assessment Resulting in Extensive Surgery

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ABSTRACT

Parotid lymphoepithelial carcinoma is extremely rare, and makes up only 0.4% of cases among the anaplastic variant of salivary gland carcinoma. We present a 63-year-old man who had progressive enlarging right neck swelling for one year. He sought treatment in another centre and underwent superficial parotidectomy, following an ultrasound assessment of the mass that was suggestive of a benign parotid tumour. There was no fine needle aspiration cytology or other radiological imaging performed prior to the surgery. However, the surgeon encountered difficulty intraoperatively and abandoned the surgery. The incisional biopsy of the tumour was reported as lymphoepithelial carcinoma. He then presented to us with the progression of the residual parotid malignant tumour. CT and MRI showed a locally aggressive parotid tumour that had infiltrated the subcutaneous tissue, external auditory canal, facial nerve, and multiple ipsilateral metastatic cervical lymph nodes. Subsequently, the patient underwent total parotidectomy with facial nerve sacrifice, lateral temporal bone resection and ipsilateral modified radical neck dissection. The surgical site defect was reconstructed with anterolateral thigh myocutaneous free flap. Concurrent static facial reanimation with fascia lata sling was performed. The patient received adjuvant chemoradiation following the surgery. The extent of the local infiltration by the tumour and the resulting surgery could have been reduced if the tumour had been properly assessed and excised at the initial stage. A complete preoperative assessment of a parotid mass is essential to avoid misdiagnosis, unexpected intraoperative finding and delay in definitive treatment.

Keywords: Fine needle aspiration, parotid carcinoma, salivary gland carcinoma, lymphoepithelial carcinoma, myocutaneous free flap, facial reanimation

INTRODUCTION

Salivary gland malignancies represent about 6% of all head and neck carcinomas. Among these neoplasms, parotid tumours consist of about 85% of all salivary gland neoplasms, in which about 15% are malignant (1). One rare variant of poorly-differentiated salivary gland carcinoma is lymphoepithelial carcinoma (LEC) that is characterised by extensive lymphoid infiltration in the stroma, mimicking the histopathological features of undifferentiated nasopharyngeal carcinoma (NPC). In fact, this variant was first reported in nasopharynx in 1921 by Schminke (2). Later, in 1952, Godwin found benign lymphoepithelial lesions in salivary glands of about 11 patients, which subsequently became the first case series in the league (3). Primary salivary gland LEC are extremely rare, composing only 0.4% of all malignant salivary gland tumours, and parotid glands are the most commonly occurring sites (4). Besides the salivary glands, LEC tumours have been reported in the literature to exist in other head and neck regions such as tonsil, floor of mouth, sinonasal cavity and larynx, as well as other organs such as lungs, stomach, breast, uterus, bladder and skin (5).

Similar to NPC, primary salivary gland LEC have a notable geographical and demographic propensity, occurring more

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often among Asians from south eastern China and Japan, and the natives of Arctic region (6). It is postulated that the Epstein–Barr virus (EBV) has a close association with salivary gland LEC, especially in EBV-endemic areas (6). Meanwhile in the non-endemic regions, although EBV is mostly not present in the LEC tumours, the diagnosis of these rare tumours cannot be excluded totally (6). A primary salivary gland LEC must be differentiated from metastatic undifferentiated NPC by nasal endoscopic examination and radiological imaging.

Hereby, we present a rare case of primary parotid gland lymphoepithelial carcinoma that was misdiagnosed as a benign salivary gland tumour. This resulted in tumour progression, delay in treatment and a more extensive surgery. We emphasise the importance of a complete pre-operative assessment and investigation in a parotid tumour, especially when it is suspicious for malignancy.

CASE REPORT

A 63-year-old male with no comorbidity was referred from another medical centre for further management. He presented with right neck swelling at the parotid region for one year, which was painless and progressively increasing in size. Otherwise, there was no significant ear, nose or throat symptom. He was an ex-smoker (30 years previous) and an occasional alcohol consumer. He sought treatment in a medical centre and a neck ultrasonography was performed. He was told by the treating surgeon that the features were of a benign parotid gland tumour. There was no cytological investigation or other radiological imaging performed. The patient subsequently underwent right superficial parotidectomy. However, intraoperatively, the surgeon found that the tumour had involved the deep lobe of the parotid gland, with no clear plane around the facial nerve. It was difficult to excise the tumour while preserving the facial nerve. The surgeon decided to take an incisional biopsy of the tumour instead and discontinued the surgery. The histopathology of the tumour was later reported as lymphoepithelial carcinoma with the presence of intraparotid metastatic lymph nodes.

The patient was subsequently referred to our centre for further management. At 3 weeks after the first surgery, the parotid swelling had further increased in size. Examination showed a well-healed modified Blair incision at the right side, with a palpable right parotid mass with firm to hard consistency measuring 4 x 3 cm. The mass was fixed to the underlying structures and part of the overlying skin was tethered to the tumour. There was a palpable right level IV cervical lymph node measuring 2 x 1 cm. The facial muscles supplied by the right buccal and marginal mandibular branches of the facial nerve were weak, which the patient noticed after the parotid surgery. White light endoscopic examination of the nasopharynx revealed no mass and image enhanced endoscopy showed no abnormal mucosal lesion. A second histopathology reading of the biopsy specimen showed malignant cell infiltration in the salivary gland, arranged in syncytial islands and trabeculae pattern. The malignant cells displayed pleomorphic, vesicular nuclei, prominent nucleoli and eosinophilic cytoplasm, and were strong and diffusely positive for CK AE1/AE3 on immunohistochemistry study. Abundant lymphocytic cell infiltrates were seen in between the malignant cells, highlighted by a mixture of CD20 positive B-cells and CD3 positive T-cells. Residual salivary gland tissue was seen at the periphery. An EBV-encoded RNA in-situ hybridisation study (EBER ISH) was negative. These features are consistent with an undifferentiated carcinoma, favouring LEC of salivary gland.

Computed tomography (CT) of the neck showed an ill-defined heterogeneous mass involving both the superficial and deep lobes of the right parotid gland, measuring 2.9 x 4.0 x 4.1 cm (Figure 1a, b). The tumour extended medially, causing mild

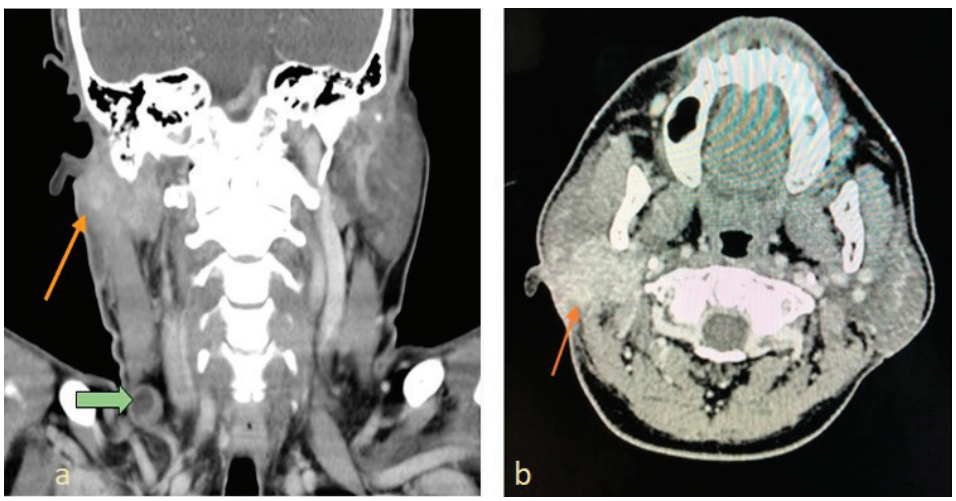

Figure 1: (a) Coronal CT scan shows an irregular shape contrast-enhanced right parotid tumour (thin arrow) with poor demarcated margin. The tumour is encroaching the soft tissue near the pinna and the stylomastoid foramen. An enlarged level IV lymph node with central necrosis is seen (thick arrow). (b) Axial CT scan shows ill-defined heterogeneous mass (arrow) involving both the superficial and deep lobes of the right parotid gland, and is seen extending medially, causing mild effacement of the parapharyngeal space

effacement of the parapharyngeal space. The tumour extended superiorly to the floor of the right external auditory canal. There was no direct involvement of the masticator space, pterygoid muscles, paravertebral muscles, internal jugular vein or carotid arteries. There were multiple enlarged ipsilateral cervical lymph nodes at levels II, III and IV with central necrosis, the largest measuring 1.7 x 2.5 cm at level II. No distant metastases were evidenced in the staging CT scan. Magnetic resonance imaging of the neck showed isointense parotid tumour on T1W1, hyperintense on T2W1 with heterogeneous enhancement post contrast. Areas of restricted diffusion were seen within. There was no clear fat plane seen between the tumour and the sternocleidomastoid muscle and the posterior belly of digastric muscle (Figure 2). Laterally, the tumour had extended to the adjacent subcutaneous fat and skin. The tumour was seen extended medially to the stylomastoid foramen. The facial nerve was thickened with solid enhancement up to the mastoid segment, likely perineural spread of the tumour. There was no abnormal enhancing lesion at the nasopharynx to suggest nasopharyngeal carcinoma.

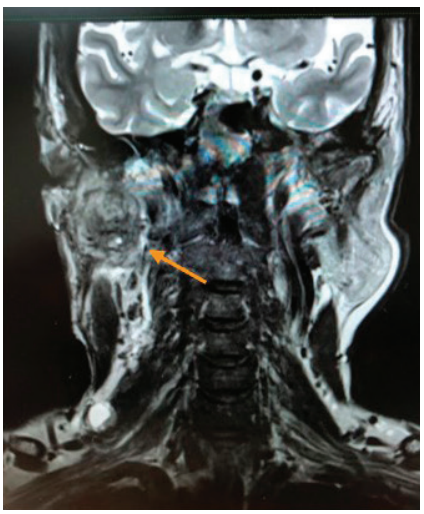

Figure 2: Coronal T2W1 MRI shows the right parotid mass (arrow) with sternocleidomastoid muscle involvement and multiple enlarged ipsilateral cervical lymph nodes.

In view of the aggressive nature of the tumour, the patient was counselled for completion of parotidectomy, modified radical neck dissection, lateral temporal bone resection and free flap reconstruction. He was also informed that the facial nerve would most likely be sacrificed due to perineural tumour spread. The skin adjacent to the tumour was excised due to tumour infiltration, and the skin incision was made to expose the parotid tumour, the neck and the mastoid, with a good cutaneous margin. The tumour was seen engulfing the facial nerve to the stylomastoid foramen, thus making the preservation of facial nerve surgically impossible. The facial nerve was therefore transected and removed together with the tumour. Ipsilateral modified radical neck dissection was performed, and the right sternocleidomastoid muscle and spinal axillary nerve were removed, preserving the internal jugular vein. This was then followed by lateral temporal bone resection, in which the entire tympanic bone, tympanic membrane, incus, malleus, mastoid tip and stylomastoid foramen were removed. Part of the conchal cartilage was excised, preserving the ear pinna. The mastoid segment of the facial nerve was exposed and excised to the second genu. The surgical defect was reconstructed with an antero-lateral thigh myocutaneous free flap. Meanwhile, static facial reanimation was performed in the same setting using tensor fascia lata sling to reduce post-operative facial asymmetry.

The histopathology finding showed a lobulated unencapsulated tumour infiltrating the parotid gland parenchyma. The neoplastic cells were polygonal to spindle-shaped in solid

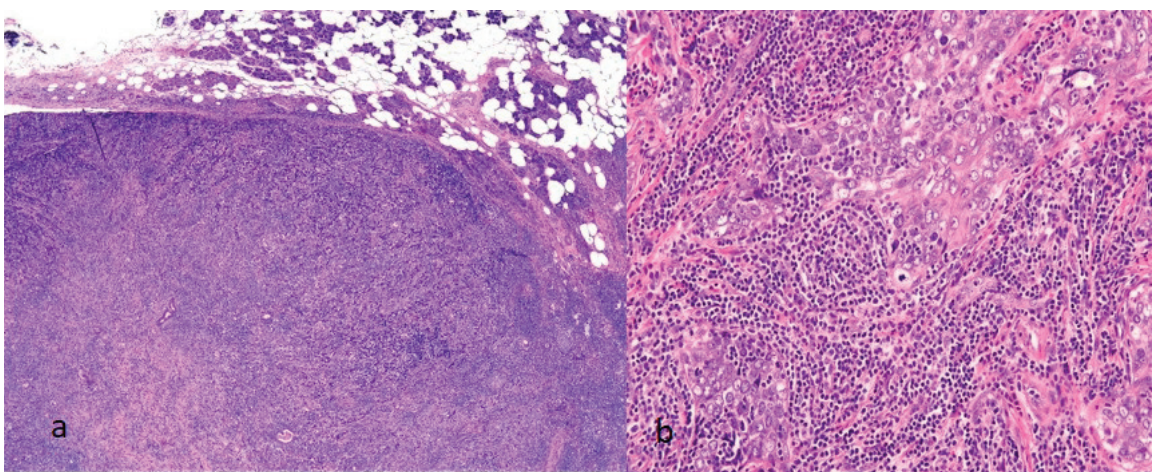

Figure 3: (a) The tumour is composed of malignant cells infiltration in syncytial islands and trabeculae amongst benign lymphoid component. A normal salivary gland tissue is seen at upper part of the image (Hematoxylin & Eosin, 4x). (b) Higher magnification showed that the malignant cells exhibit pleomorphic, vesicular nuclei, prominent nucleoli, and moderate amount of lightly eosinophilic cytoplasm with indistinct cellular borders. There are abundant lymphocytic infiltrates in between the malignant cells (Hematoxylin & Eosin, 20x).

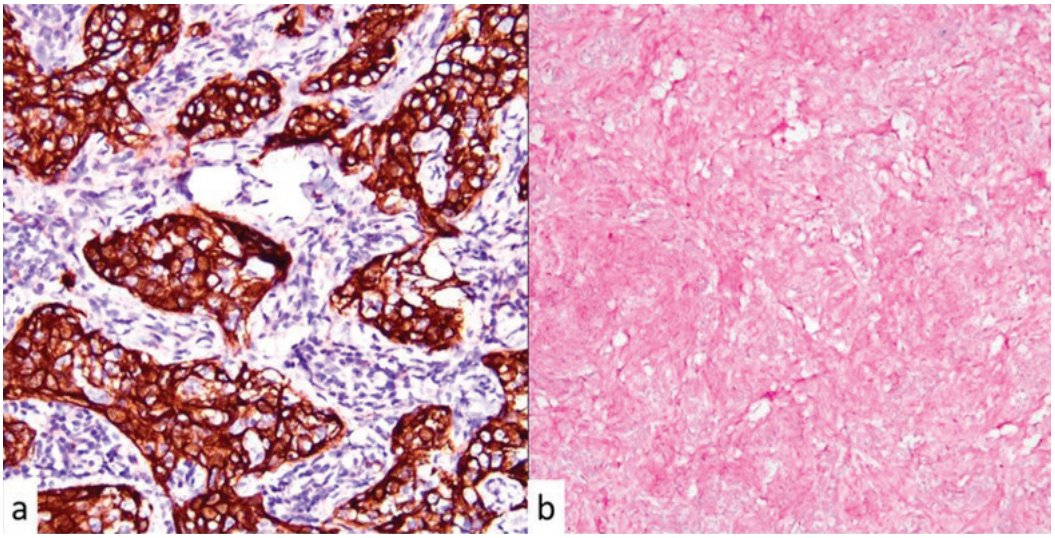

Figure 4: (a)The malignant epithelial cells are diffusely positive (brown staining) to pancytokeratin CKAE1/AE3, in contrast to the negative staining within the lymphoid component, (20x) while (b) the Epstein Barr Virus-encoded RNA in-situ hybridization study (EBER ISH) is negative (10x).

sheet and nests with large round to oval vesicular nuclei, in the background of non-neoplastic lymphoid stroma and entrapped glands (Figure 3a, b). Perineural invasions were prominent. The malignant cells were positive for pancytokeratin (Figure 4a). The Epstein Barr Virus-encoded RNA in-situ hybridization study (EBER ISH) was negative (Figure 4b). There were metastases in 23 out of 95 lymph nodes with extranodal extension seen. The resected facial nerve fibre was infiltrated by malignant cells but the proximal end was tumour free. The resected cartilaginous and bony external ear canal showed no evidence of malignant infiltration. These findings were consistent with a parotid gland lymphoepithelial carcinoma with lymph node metastases and facial nerve involvement.

The patient made an uneventful recovery. The facial expression was acceptable to the patient with House-Brackmann grade IV (Figure 5a, b). A second stage facial reanimation surgery is planned later after the patient completes the oncological treatment. He subsequently received adjuvant chemo-radiotherapy 8 weeks post-surgery.

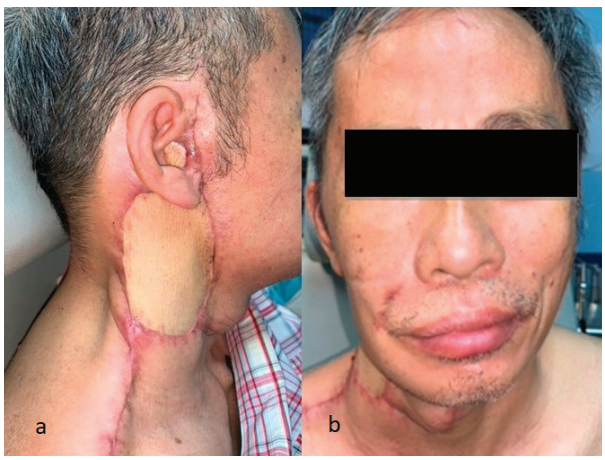

Figure 5: (a) and (b) House Brackmann Grade IV facial nerve function at rest

DISCUSSION

LEC of salivary glands is a rare tumour that primarily involves the parotid gland. It commonly presents in adults aged 30 to 50 years, with female preponderance (ratio 3:2). Parotid LEC mostly presents itself with a rather rapidly growing mass. It is often painless, but pain or discomfort may be present in some patients. About 10-20% of patients with parotid malignancies commonly present with facial nerve palsy (7). This facial nerve dysfunction implies that the tumour has already infiltrated the nerve and it is a negative prognostic factor. On the contrary, the surgery involving facial nerve sacrifice does not show better survival rate in these patients nor a better tumour control (8).

These features of enlarging, painful parotid mass and facial nerve involvement should alarm clinicians and raise the suspicion of a malignant tumour (7). In our case, the patient initially presented with a painless parotid swelling with no facial palsy. The cause of facial palsy that developed after the first surgery could not be ascertained, either iatrogenic or due to tumour infiltration. However, the facial nerve involvement by the tumour was proven whereby the facial nerve was thickened and enhanced in radiological imaging and malignant infiltration was evident in the postoperative facial nerve histopathology examination.

A retrospective analysis done in Poland on patients who were treated for parotid carcinoma reported that cases with worse prognosis were from the patients with preoperative facial nerve palsy and patients with initial diagnosis of pleomorphic adenoma (9). In another case series of salivary duct carcinoma, it was reported that the factors contributing to disease-specific

survival and the overall survival are lower grade of tumours, early stages of I and II, smaller size of tumours (≤3 cm) and absence of metastasis to neck nodes (9).

LEC tumours are generally as radiosensitive as their nasopharynx counterparts. Nevertheless, the mainstay of treatment of any parotid gland malignancy is still complete surgical resection, which is followed by adjuvant radiotherapy. The adjuvant therapy is given in LECs as it is rather challenging to achieve adequate positive resection margins (5).

The biggest lesson learnt in this case is misdiagnosing a malignant parotid tumour as a benign tumour, and embarking on surgery without appropriate preoperative evaluation. The use of ultrasound to diagnose a malignant parotid mass has low accuracy (20%), due to the poor sonography characteristics difference between benign and malignant tumours (10). CT scan or MRI are more valuable as they show the extent of the parotid tumour, including the deep lobe involvement and its relation to the major vessels. Most of the parotid LEC are irregular in shape with ill-defined margins, and show heterogeneous signal intensity on plain imaging with no cystic degeneration. The reported accuracy of fine needle aspiration cytology in detecting malignant parotid tumours varies but it is a valuable pre-operative assessment method for subsequent surgical anticipation and proper planning. In a review of 14 cases of LEC, the FNAC result was found to be 78.6% in concordance with the final histology diagnosis (11). The clinical features together with the radiological characteristics of a malignant parotid tumour, typical FNAC results and an absence of nasopharyngeal lesion on nasal endoscopy or CT/MRI with or without nasopharyngeal biopsy would all help in the diagnosis of a parotid LEC.

As mentioned, the mainstay of treatment for parotid LEC is total surgical resection followed by adjuvant radiotherapy, due to its radiosensitivity. Adjuvant chemotherapy is required in the presence of adverse features such as extranodal extension, as seen in this case. Total parotidectomy was performed in our case as the tumour had involved the deep lobe. Ipsilateral modified radical neck dissection was performed, as multiple cervical lymph nodes metastases were evident on clinical examination and radiological imaging. The sternocleidomastoid muscle and the spinal accessory nerve had to be resected due to direct tumour infiltration. Generally, the facial nerve will be preserved in malignant parotid surgery if the nerve is uninvolved. In this case, the patient had normal facial nerve function at presentation. He developed nerve palsy over the buccal and marginal mandibular branches after the first incisional biopsy surgery, but clinically the cause could not be determined (whether iatrogenic or malignant invasion). However, the latter aetiology is favoured since the facial nerve was shown thickened with significant contrast enhancement. Therefore, the facial nerve had to be sacrificed to ensure an oncologic safe tumour resection. On top of that, the extent of surgery was further increased as the tumour had encroached the cartilaginous part of the external auditory canal as well as the mastoid segment of the facial nerve. Thus, lateral temporal bone resection was performed to ensure complete tumour removal and high probability of loco-regional control.

Facial nerve resection must always be followed by reconstruction procedures as it significantly affects the patient's quality of life. Various methods of reconstruction are available, including immediate cable nerve graft interposition, and dynamic and static facial reanimation procedures. This can be done in a single stage or multiple stages. In our case, interposition nerve grafting was surgically difficult as the proximal stump of the facial nerve was in the tympanic segment. Thus, static suspension using fascia lata sling was performed in the same setting. The post-operative facial function was acceptable to the patient. The remaining reanimation procedures can be performed at a later stage after the patient has completed the adjuvant cancer therapy.

CONCLUSION

LEC of the parotid gland is a rare malignant tumour that may require complete resection followed by adjuvant radiotherapy. The surgical resection can be extensive depending on the tumour extension, and in our case, including total parotidectomy, ipsilateral modified radical neck dissection, and lateral temporal bone resection. The surgical defect was reconstructed with an antero-lateral thigh myocutaneous free flap, in addition to the static facial reanimation procedure. The extent of the surgery in this patient could have been less if the malignant parotid tumour had been appropriately assessed during the patient's first presentation with accurate diagnosis and proper surgical planning. We emphasise the importance of complete preoperative assessment of a parotid mass to avoid misdiagnosis and delay in definitive management.

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Peer Review: Externally peer-reviewed.

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Conflict of Interest: The authors have no conflict of interest to declare.

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