Case report

Master of mimicry: Rare primary cutaneous anaplastic large cell lymphoma presenting as fungating parotid tumor—case report and review

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A B S T R A C T

Introduction: Primary cutaneous anaplastic large cell lymphomas (PC-ALCL) are rare. They fall within non-Hodgkin's lymphomas spectrum. Commonly misdiagnosed, this malignancy involving the skin has favorable prognosis. To the best of our knowledge, this is the first reported case of PC-ALCL involving the parotid gland. This clinical presentation can mislead surgeons. We highlight this diagnostic conundrum.

Case presentation: A 73-year-old gentleman presented with two painless, ulcerating nodules over the right pre-auricular and angle of the mandible. Prior to that, he had right pre-auricular swelling that enlarged over a year. Skin nodules erupted few weeks before seeking treatment. Computed Tomography scan reported homogenously enhancing masses at posterior part of parotid gland's superficial lobe with diffuse lobe enlargement and no regional lymphadenopathy. A hypodense lesion at the liver indicated metastasis. Biopsy revealed PC-ALCL. He responded well to chemotherapy.

Discussion: PC-ALCL commonly presents as solitary nodules that can ulcerate over the head and neck region. Reports of PC-ALCL involving the eyelids, lips, and breast were found in our literature review. Multifocal lesions occur in 20% of cases. Malignant parotid tumors are aggressive and require parotidectomy which carry the risk of facial nerve injury. Treatment of PC-ALCL however, is local excision and radiotherapy for solitary lesions; and chemotherapy for those with extracutaneous spread. The 5-year survival rate is 90% in PC-ALCL. Conclusion: PC-ALCL is a master of mimicry. To prevent serious morbidity, awareness regarding this entity as a differential diagnosis compared to the common malignant parotid tumors need to be raised.

1. Introduction

Cutaneous T-cell lymphomas are notoriously challenging to diagnose. This spectrum of lymphomas are divided into 7 categories, including primary cutaneous CD30 positive lymphoproliferative disorders, which are characterized by skin-homing T-cells [1]. These disorders are further classified into lymphomatoid papulosis (LyP) and primary cutaneous anaplastic large cell lymphoma (PC-ALCL) [1,2]. 9% of all cutaneous T-cell lymphomas are PC-ALCL [3]. Its rarity compounds mismanagement and literature is rife with reports of misdiagnosis [4–7].

PC-ALCL presents heterogeneously. It can present as solitary or multifocal nodules that may ulcerate with spontaneous regression; or extracutaneous dissemination with or without nodal and systemic involvement [2,3,7,8]. Good prognosis is reported, with 5- and 10-year survival rates more than 90% [1–3,7,8]. In extracutaneous PC-ALCL,
systemic chemotherapy is first line therapy [2,3,7,9]. Recently, task forces have sought to establish diagnostic criteria and management guidelines for these lymphoproliferative disorders [3]. However, due to confusion with cutaneous malignancies and systemic lymphomas, they are often treated with unnecessarily aggressive and inappropriate therapies [4,5,7,8]. To our knowledge, this is the first case of PC-ALCL with involvement of the parotid gland clinically and on imaging. When PC-ALCL masquerades as a malignant parotid tumor, this results in a diagnostic and therapeutic conundrum. Surgeons unfamiliar with this rare lymphoproliferative disorder may be misled into performing a parotidectomy. We aim to raise awareness regarding this entity as a rare differential diagnosis to malignant parotid tumors. Highlighting this case will help in preventing surgeons from performing unnecessary procedures that carry with it the serious surgical morbidity such as facial nerve injury.

2. Presentation of case

A 73-year-old gentleman presented with two fungating lesions over the right pre-auricular and angle of the mandible. A year ago, he developed a right pre-auricular swelling that slowly increased in size without pain, facial weakness, or asymmetry. Two months prior to seeking treatment, a fungating mass erupted over the pre-auricular region, followed by another over the angle of the mandible. He sought treatment at a general practitioner’s clinic and was prescribed multiple courses of oral antibiotics. The friable masses frequently bled on contact and did not resolve. He was then referred to our university hospital for further investigation. He denied other skin lesions and other medical illness or previous surgeries. He denied fever, epistaxis, weight loss or family history of malignancies. He is an ex-smoker who quit smoking twelve years ago.

On admission, physical examination revealed two ulcerating, fungating lesions, 2 × 3 cm over the pre-auricular region and 3 × 2 cm over the angle of mandible (Fig. 1A, B) with an enlarged parotid gland. These findings were independently corroborated by clinical assessments of a consultant professor in plastic and reconstructive surgery with more than ten years of experience as well as two plastic and reconstructive surgeons (less than five years’ experience). No evidence of facial nerve palsy and no regional lymphadenopathy detected. Naso-endoscopy and oropharyngeal assessment was negative of suspicious lesions. Head and Neck Computed Tomography (CT) scan reported exophytic, homogenously enhancing masses with ulceration at the posterior part of right parotid gland’s superficial lobe, measuring 1.9 cm × 3.0 cm × 2.6 cm. Diffuse enlargement of superficial right parotid gland (4.8 cm × 2.5 cm × 5.4 cm) and poor fat plane with overlying subcutaneous tissue reported by two independent radiologists with more than ten years’ experience (Figs. 2 and 3). CT Thorax, Abdomen and Pelvis revealed a hypodense enhancing lesion at segment IVa liver measuring 2.5 cm × 2.9 cm. Ultrasonography later indicated liver metastasis.

While awaiting tissue biopsy, another fungating lesion appeared over the angle of the mandible. Wedge biopsy under local anesthesia of all lesions (4 sites) was performed by a plastic and reconstructive surgeon (more than three years’ experience). Histopathological examination revealed diffuse intradermal infiltration of large pleomorphic malignant lymphoid cells with irregular (wrath-like and kidney shaped) nuclei and large nucleoli with moderate to abundant cytoplasm. There were many neutrophils in the background (Fig. 4). Tumor cells were positive for CD30, CD4, CD5, EMA, and CD25. They were CD3, CD8, CD20 and ALK-negative (Fig. 5). No evidence of epidermatropism seen. Unfortunately, other immunohistochemistry (IHC) staining such as CLA (cutaneous lymphocyte-associated antigen) was unavailable in our center. Repeated wedge biopsy 6 months later by a different plastic surgeon yielded similar results. Correlating these findings with his clinical presentation and imaging, a diagnosis of PC-ALCL with extracutaneous involvement of the parotid gland was determined.

Multiagent chemotherapy with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) was started as initial therapy. However, after 2 cycles of CHOP, there was no response and lesions increased in size. The patient was then started on intravenous brentuximab vedotin. The lesions are responding, and he is satisfied with the treatment as well as his continued follow-up. This work is reported in line with the SCARE 2020 criteria [10].

3. Discussion

PC-ALCL is an infamous master of mimicry. Its diagnosis relies mostly on clinical judgement [7,8]. With PC-ALCL’s rarity, only recently have authors attempted to establish diagnostic and management gold standard [2,3]. PC-ALCL has been mistaken for a variety of dermatological diseases. Literature reports misdiagnosing PC-ALCL as labial herpes, breast-implant-associated ALCL (BIA-ALCL), cutaneous malignancies, discoid lupus erythematosus, reactive diseases with cutaneous
infiltrates that express CD30 positivity such as scabies; as well as other neoplastic diseases such as cutaneous B-cell lymphomas [4,5,7,11]. Further confusion exists in differentiating entities within the spectrum of lymphoproliferative disorders such as LyP [3].

Our patient initially presented with a vague swelling over the parotido-masseteric region without cutaneous lesions. Fungating lesions erupted a year later. This deviates from the commonly reported clinical course of PC-ALCL in the literature [2,3,7,8]. The diagnostic criteria from latest recommendations are based on clinical and histologic findings [3]. In diagnosing parotid gland malignancies, fine needle aspiration or ultrasound guided core biopsy are performed [12]. However in PC-ALCL an incisional biopsy or punch biopsy of 4 mm is the recommended biopsy technique [3]. This patient had three fungating, ulcerating lesions and due to cutaneous involvement of suspiciously malignant tumor, a wedge biopsy was performed instead. The biopsy was adequate for tissue analysis. In centers with limited IHCs and lack of supportive molecular ancillary tests, correlating histopathological findings with clinical presentation is crucial. There was loss of CD3 expression, which occurs in ALCL [13]. Hence, the need to include other T-cell IHC markers such as CD2, CD5, CD4, CD8, CD7 and CD25. These tumor cells were also highly proliferative, evidenced by Ki67 immunoreactivity. CD30 positivity was strong and homogenous in all neoplastic cells, differentiating the case from other entities such as LyP. There was no longstanding history of recurrent skin lesions and absence of epidermatropism, excluding transforming mycosis fungoides into ALCL. Poorly differentiated metastatic carcinoma was excluded with findings of negative CK, AE1 and AE3 marker (not shown). Other additional IHCs supporting ALCL were perforin, EMA, MUM1(not shown) and ALK, which are often negative in PC-ALCL [13]. CLA is an important IHC to establish a primary cutaneous origin but was unavailable in our center. Finally, what differentiated between extracutaneous PC-ALCL from systemic ALCL with skin involvement in our case was the exclusion of lymph node spread.

PC-ALCL commonly occurs over the head, neck, trunk and extremities [7,8] in older males with median age of 55–60 years old [3,6,8]. Unfortunately, patients with common parotid gland malignancies fall within similar demographic [14]. Eruption of cutaneous lesions in quick succession over the parotido-masseteric region were highly suggestive of aggressive tumor. If staged according to common salivary gland malignancies prognostic index, the prognosis was poor [14]. This appearance of advanced stage disease might prompt a surgeon to hastily perform a superficial parotidectomy to curb further locoregional spread. When in
fact, PC-ALCL responds well to chemo- and radiotherapy [1-3,9,15] which spares the patient from a parotidectomy that carries the debilitating morbidity of facial nerve injury. Primary lymphomas of the parotid gland are another differential diagnosis. However, extra-nodal parotid gland lymphomas (our patient had no nodal involvements); are extremely rare. Their incidence is 2.1% - 7% of all salivary gland tumors and are almost entirely B-cell instead [16]. Literature was searched systematically with PubMed and Google Scholar, using terms such as “parotid gland”, “primary cutaneous T-cell lymphoma”. Terms were separated by Boolean operators “OR” and “AND”. There were 3 articles that reported parotid gland anaplastic large cell lymphomas however none were PC-ALCL [17]. Parotid gland T-cell lymphomas are very rare and to date 18 cases have been reported in literature; none were PC-ALCL [17-20]. To the best of our knowledge, we report the first case of PC-ALCL with parotid gland involvement detected clinically and on imaging.

PC-ALCL carries good prognosis [1,2,7,8]. PC-ALCL undergoes episodes of relapsing lesions and 25% spontaneously resolve [2,7-9]. Solitary PC-ALCL that do not regress, respond well to radiotherapy [3,9] and can be combined with surgical excision. Complete remission (CR) rates range from 67% to 95% [3,7,9]. Unfortunately, data on appropriate surgical margins are lacking [3]. In multifocal PC-ALCL, some authors recommend multiagent chemotherapeutic agents with doxorubicin-based multiagent chemotherapy with CHOP as first line

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Fig. 4. Biopsy of the tumor shows intradermal tumor infiltration with absence of epidermatropism (H&E, 40x). The inset shows the hallmark cells (yellow arrow) scattered and other anaplastic large cells with the background of heavy infiltration of acute inflammatory cells (majority are neutrophils) (H&E, 400x). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Fig. 5. The immunohistochemistry patterns of the fungating tumor. A: CD3 and B: CD20, only positive in the background reactive T and B cells respectively (×40); C: CD30, strong and homogenous in all of the tumor cells (×40); D: CD5, and E: CD4, T cell markers that are positive in the neoplastic cells (perforin was positive in some of these cells, not shown) (×100); F:CD8 background cytotoxic T cells (×40); G: ALK totally negative (×40); H:CD25 (×100); I:EMA, strong and highlighted the Golgi body (×100).
therapy [3]. Multifocal PC-ALCL with extracutaneous involvement, as in our case, occurs in 5%–13% [1–3]. Limited data exists on managing PC-ALCL with extracutaneous involvement. Some authors advocate CHOP as first line; others combine chemotherapy (CHOP) with CD30 targeted monoclonal antibodies (brentuximab vedotin) [8] or brentuximab vedotin alone [15], all with good outcomes. However, more prospective trials are needed to establish management guidelines [3].

4. Conclusion

PC-ALCL is rare. This rarity compounds the confusion in diagnosis and complicates management. Clinical and histopathological findings are important in establishing diagnosis. PC-ALCL with evidence of parotid involvement on clinical and imaging findings can confuse surgeons who rarely manage these lymphoproliferative disorders. Surgeons should be aware of this entity as a rare differential diagnosis for parotid tumors.

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Ethical approval

This paper was exempted by the Institutional Review Board of the Hospital of University of Sciences Malaysia and performed in accordance with the principles of the Declaration of Helsinki.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.  

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Declaration of competing interest

All authors have nothing to declare.

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