Case Report
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Sebaceous carcinoma of submandibular gland presenting with upper-airway obstruction: a case report and review of the literature

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ABSTRACT

Sebaceous carcinoma (SC) of the salivary gland is a very rare tumor mostly occurring in the parotid gland. It is extremely rare in the submandibular gland. Only four cases of submandibular gland SC have been reported worldwide in the medical literature available in English. We presented the first case of submandibular gland SC in our environment. A 55-years-old male farmer presented to our facility with a 10-year history of progressive, painless left submandibular mass that worsened 4 months prior to presentation associated with dysphagia to solid, muffled voice, weight loss, and upper-airway obstruction. He had emergency tracheostomy and biopsy of the left submandibular mass. The histopathological examination of the mass confirmed SC. He was referred for radiotherapy but reportedly died a few weeks later while still preparing for radiation therapy.

Key words: Sebaceous carcinoma, submandibular gland, upper-airway obstruction

INTRODUCTION

Salivary glands are exocrine glands that produce serous, mucous, or mixed salivary secretions through a ductal system. They are divided into major (parotid, submandibular, and sublingual glands) and minor salivary glands. Sebaceous glands are holocrine adnexal components of the skin, usually found in close association with hair follicles (1,2) They are predominantly found around the periocular region, most especially the eyelid (1-5). They could also be found in the normal salivary glands, parotid glands (11%–28%), and submandibular glands (6%) (1-6). However, malignant changes in these glands are extremely rare (1-7). The sebaceous carcinoma (SC) of the salivary gland occurs more in the parotid than in the submandibular and sublingual glands (1-7). The parotid gland is the second most frequent site for SC in the head and neck region (3-7). Tumors of the salivary glands are uncommon, complex, and heterogeneous, with varying clinical and histological presentations (8).

Patients with submandibular gland malignancies often present with either a slow or rapidly growing mass in the submandibular triangle of the neck, with or without pain (5,6,8,9). Clinically, they appear firm, lobulated, fixed to the skin, or deeper structures, and may be associated with paralysis of the marginal mandibular branch of the facial nerve, lingual nerve, or hypoglossal nerve (6,8). The exact diagnosis is made via a histopathological examination (8). Because of the rarity of the SC of the submandibular gland, we observe a paucity of data on its etiology, pathogenesis, and management modalities.

In this study. we reported a case of SC of the submandibular gland presenting with the upper-airway obstruction, which necessitated emergency tracheostomy.

CASE PRESENTATION

IMM was a 55-year-old male farmer who was referred to our clinic with a 10-year history of left-sided,

progressive, painless submandibular swelling, which worsened 4 months prior to presentation. There was associated dysphagia to solid, muffled voice, weight loss, and features of upper-airway obstruction. The physical examination showed a chronically ill middle-aged man in obvious respiratory distress. The neck examination revealed a huge left submandibular swelling that crossed the midline, measuring 10 x 8 cm^2, firm, and fixed to the underlying structures but not attached to the skin. Multiple, firm, matted, level II–V ipsilateral cervical lymphadenopathies were observed, the largest being 7 x 4 cm^2 (Fig. 1a). On the contralateral side, multiple, firm, matted, level II and III cervical lymphadenopathies were observed, the largest being 3 x 4 cm^2 (Fig. 1b). No cranial nerve palsy could be seen. The indirect laryngoscopy revealed a huge mass at the base of the tongue, which was more toward the left side, obscuring the view of the laryngeal inlet. The pooling of purulent discharge was also noted in the hypopharynx. The assessment was made for a malignant left submandibular tumor (Stage IVb: T3N3aMx).

Computed tomography (CT) scan of the neck revealed a huge ill-defined heterogeneous predominantly isodense mass in the submandibular region bilaterally but more on the left, extending superiorly to the floor of the mouth with a mild displacement of the tongue (Fig. 2a). Posteriorly, it extended to the oropharynx and hypopharynx, as well as the upper half of the larynx, compressing and obliterating the airway at that level (Fig. 2b). The osteolytic destruction of the hyoid bone was also noted. Multiple, discrete, oval-shaped masses of varying sizes, with some having a hypodense area of fluid density and some having peripheral curvilinear calcifications, were observed, all presenting at the lateral aspect of the neck as well as submandibular and parotid region bilaterally (representing lymphadenopathy) (Fig. 3). The minimal heterogeneous contrast enhancement of the mass was noted. The thyroid gland was displaced and distorted.

Abdominopelvic ultrasound showed features of bilateral renal parenchymal disease with a complex left renal cyst. The chest radiograph was normal. The complete blood count and electrolyte, urea, and creatinine were normal, but the erythrocyte sedimentation rate was raised (126 mm/h). The fine-needle aspiration cytology (FNAC) of the left cervicomandibular swelling yielded scanty hemorrhagic aspirate on macroscopy. At the same time, the microscopic examination showed a moderately cellular smear composed of a few clusters of epithelial cells that were mildly pleomorphic, having round to oval nuclei and moderate cytoplasm, numerous polymorphs, and few lymphocytes. These features indicated the possibility of malignancy.

The patient had an emergency tracheostomy under general anesthesia, and a surgical biopsy of the left submandibular was performed. An 18G nasogastric tube was passed for feeding. The immediate postoperative condition was satisfactory.

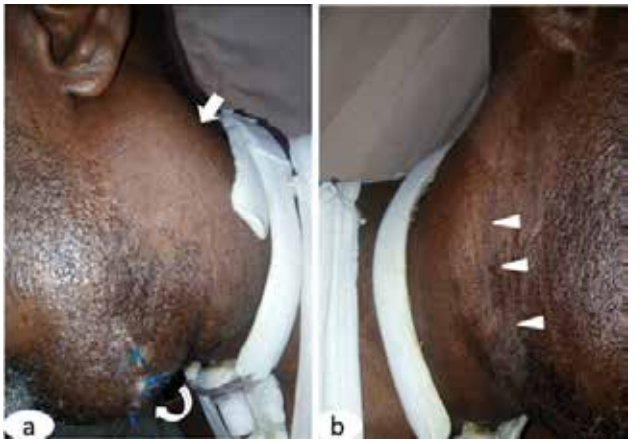

Figure 1 (**a**) Multiple levels II–V left cervical lymphadenopathy (straight arrow) and submandibular region fullness *(curved arrow)*. (**b**) Multiple levels II and III right cervical lymphadenopathy *(arrowheads)*.

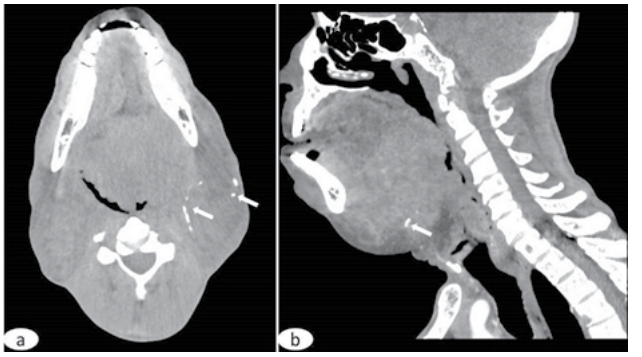

Figure 2 (**a**) Axial and (**b**) sagittal CT scan of the neck showing a huge ill-defined heterogeneous predominantly isodense mass in the bilateral submandibular region more to the left and extending superiorly to the floor of the mouth. Curvilinear calcifications were also observed *(arrows)*.

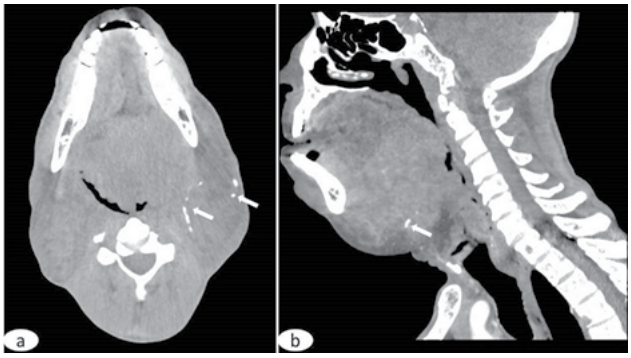

Figure 3 (**a**) Coronal and (**b**) sagittal CT scan of the neck showing multiple, discrete, oval masses of varying sizes in the lateral aspect of the neck and submandibular regions bilaterally, with some having hypodense area of fluid density *(arrows)* and others showing peripheral curvilinear calcifications *(arrowheads)* representing lymphadenopathy.

Histologically, tissue sections included an epithelial neoplasm comprising a nest and lobule of sebaceous epithelial cells separated by fibrocollagenous stroma (composed of fairly uniform cells with clear cytoplasm surrounded by palisade cells). The palisade cells have round to oval nuclei and eosinophilic cytoplasm, peripherally exhibiting squamous metaplasia (Fig. 4). Frequent mitotic features were observed, which included abnormal forms (3–4 per HPF). The features were consistent with SC.

DISUCUSSION

Sebaceous cells are mostly found in the eyelids; they could also be found on the skin, major salivary glands (mostly in the parotid glands, but infrequently in submandibular and sublingual glands), oral cavity, vallecula, epiglottis, and hypopharynx (1-7,9,10). Tumors of sebaceous cells such as sebaceous adenoma, sebaceous lymphadenoma, SC, and sebaceous lymphadenocarcinoma are very rare (3). They account for less than 0.2% of all major salivary gland tumors.6,9 Though the origin of SC within the major salivary glands is unclear, SC has mainly been reported in the parotid glands, with few cases involving the submandibular glands (1-7,9,10). Through an extensive online search, we found only four cases of SC of the submandibular glands reported in the medical literature available in English: two cases in Japan, 1 in France, and 1 in Korea (6,10-14). The index case was the first to be reported in Nigeria and the continent of Africa.

The clinicopathological characteristics and histogenesis are not fully understood due to the rarity of incidence of SC (3). Human papillomavirus infection, dysregulated cytokine secretion, and mutations in tumor suppressor genes such as p53 might contribute to the development of sporadic cases of SC (4). SC usually arises de novo, but it may also arise from previous lesions, such as nevus sebaceous of Jadassohn (4,15). In the elderly, SC may develop either from benign or malignant epidermal/adnexal neoplasms, such as syringocystadenoma papilliferum, trichoblastoma, sebaceoma, and basal cell carcinoma (4,15). The peak incidence of SC is in the second to the third decade and the seventh to the eighth decade of life with a male to

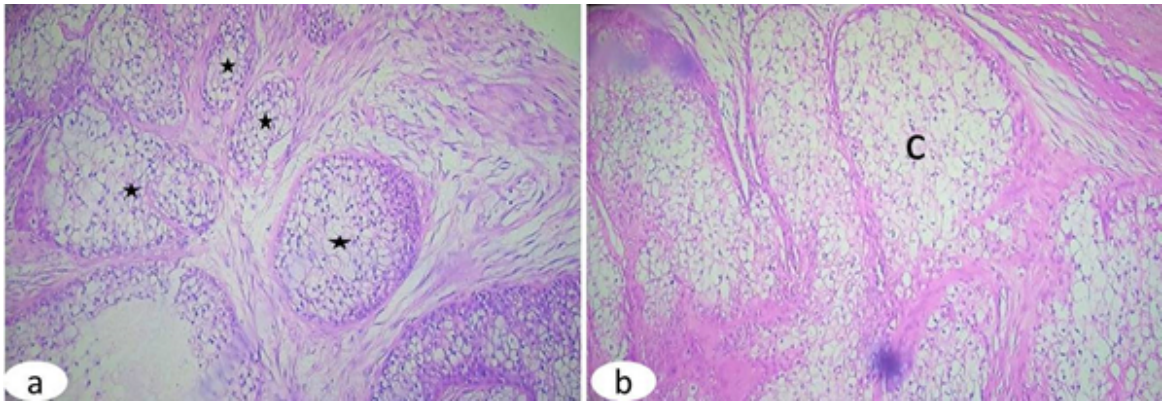

Figure 4 Photomicrograph of (**a**) sebaceous cells arranged in a lobular pattern displaying mild pleomorphism *(asterisks)* [hematoxylin–eosin (H&E) x 100]. (**b**) These sebaceous cells are fairly uniform, having round to oval nuclei with clear eosinophilic cytoplasm *(letter C)* (H&E w 400).

female ratio of 1:1 (4-7,9). Our patient was in his fifth decade of life.

Patients with submandibular gland malignancies often present with a slow or rapid growing mass in the submandibular triangle of the neck, with or without pain, and appear clinically as a firm, lobulated mass, which may be fixed to the skin or deeper structures and may be associated with facial nerve (marginal mandibular branch), indicating lingual or hypoglossal nerve paralysis (5-9,15). Our patient presented with a 10-year history of left-sided, painless, progressive submandibular swelling, which worsened 4 months prior to presentation, with associated dysphagia to solid, muffled voice, weight loss, and upper-airway obstruction. This was the only case of the four reported cases of submandibular gland SC that presented with an upper-airway obstruction (which necessitated emergency tracheostomy) likely due to the extension of the mass to the floor of the mouth causing displacement of the tongue, its extension to the oropharynx and hypopharynx, as well as the upper half of the larynx, compressing and obliterating the airway at that level. This could also explain the dysphagia that the patient presented with. The mass extension to the base of the tongue/oropharynx could possibly explain the muffled voice in this patient.

Clinical and radiological examinations are insufficient for diagnosing submandibular gland SC or any other submandibular gland malignancy, thus requiring further histological examination (3,6,16). FNAC, most especially done under ultrasound guidance, has 80% and 97% sensitivity and specificity in differentiating between benign and malignant tumors, respectively (8). However, it has limitations in differentiating the specific malignant subtype and grade of the tumor (3,6,8). Recent studies suggested the role of core needle biopsy as a superior method to FNAC in diagnosing salivary gland malignancies; however, it has the risk of nerve injury, hematoma, and increased pain (6,8,17). Incisional biopsy can be performed primarily on cases of minor salivary gland tumors in the oral cavity, but it is not recommended in major salivary glands due to the risk of nerve injury and tumor seeding.8 Intraoperative frozen section can also be performed, which has a sensitivity and specificity of 90% and 99%, respectively, in differentiating benign from malignant lesions (8). In this patient, the FNAC of the left cervicomandibular swelling showed moderately cellular smear, composed of few clusters of epithelial cells that were mildly pleomorphic, having round to oval nuclei and moderate cytoplasm, numerous polymorphs, and few lymphocytes. The histological findings obtained from the biopsy of the tumor mass showed features consistent with SC. Tumors of the salivary gland are uncommon with diverse histologic types, thus making diagnosis complex and difficult (6,8). H&E staining is still the gold standard diagnostic method, while immunohistochemistry improves the dignosis.6,8,18 The hallmark of diagnosis of SC is the identification of sebocytes,6 consistent with our histopathological findings.

The treatment of choice for submandibular gland SC has not been established due to its rarity and hence the paucity of published data (3,5-7,9). However, the recommended treatment option for salivary gland malignancies is wide surgical excision with negative margins for low-grade tumors (3,5-9). Adjuvant radiotherapy is indicated for advanced malignancies, cervical metastasis, perineural invasion, lymphovascular invasion, extraglandular extension, high differentiations, or positive margins (3,5-9). Primary radiotherapy is usually recommended for unresectable tumors, distant metastasis, and when the patient is a poor candidate for surgery (8). Elective neck dissection should be considered in cases with marked cytologic atypia or when the facial nerve is involved (5,6). Chemotherapy and biological targeted therapy are essentially effective in cases of lymphomas or when providing palliative care, but they are not a standard treatment for salivary gland malignancies (6,8). Comparing the survival outcomes between postoperative chemoradiation and radiotherapy alone in patients who have undergone resection of high-risk salivary gland carcinoma, no significant improvement is observed in its treatment, requiring further clinical studies (6,8,19). No published data is available examining the role of neoadjuvant chemotherapy in the management of salivary gland SC; however, some studies reported its benefit in terms of improving the prognosis and using conservative treatment regimen in advanced-stage or metastatic carcinomas of the salivary glands (6,20). Subsequent concomitant chemotherapy along with radiotherapy was performed with no improvement in the survival rate (6,20). Our patient was referred for radiotherapy due to the advanced stage of the disease (Stage IVb). However, he died while he was being prepared for radiation therapy. The surgery,

if considered in this patient, might include complete tumor resection, partial glossopharyngolaryngectomy with reconstruction, and neck dissection. Salivary gland SC has a survival rate of about 62%, which is lower than the survival rate of SC (84.5%) when arising in the skin and orbit (6,9). SCs rarely metastasize; however, it could possibly recur (6,9).

CONCLUSIONS

SCs of the submandibular gland are very rare tumors, presenting as a slow progressive mass, and could sometimes present with features of upper-airway obstruction necessitating tracheostomy. Surgical excision is the mainstay of treatment for low-grade or early-stage tumors, while advanced-stage tumors may require additional radiotherapy alone or with chemotherapy. Early diagnosis and prompt treatment are crucial for improving the survival rate of the patient.

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