Case Report

Salivary duct carcinoma in the submandibular gland: A rare case report with differential diagnosis

Geerthanaa Muthu, Prasanth Thankappan, Angelin D, Franklin R

Department of Oral and Maxillofacial Pathology, Sree Mookambika Institute of Dental Sciences, Kanyakumari District, Tamil Nadu, India

Abstract

Salivary duct carcinoma (SDC) is a rare and highly aggressive malignant salivary gland neoplasm, accounting for only 0.2% of salivary gland tumours. It predominantly affects the parotid gland and represents a significant concern with limited prevalence (1–1.2 individuals per million). We present a case of a 65-year-old female patient with a clinical history of swelling and pain in the right lower jaw region for six months. Diagnostic investigations revealed a well-defined submandibular gland lesion. Subsequent histopathological and immunohistochemical findings confirmed the lesion to be SDC. This case report emphasises the challenges in diagnosing this aggressive malignancy, which stems from its rarity and resemblance to other neoplasms. It is worth noting that the involvement of the submandibular gland is observed in a mere 12% of SDC cases, while females account for only 25% of the reported instances.

Keywords: HER2/neu, lipomatosis, necrosis, salivary duct carcinoma, submandibular salivary gland

Address for correspondence: Dr. Prasanth Thankappan,Department of Oral and Maxillofacial Pathology, Sree Mookambika Institute of Dental Sciences, Kanyakumari District, Tamil Nadu, India.
E-mail: prasantht2020@gmail.com

Submitted: 07-Nov-2023, **Revised:** 08-Dec-2023, **Accepted:** 09-Dec-2023, **Published:** 11-Jul-2024

INTRODUCTION

Salivary duct carcinoma (SDC) is an exceptionally uncommon and highly aggressive salivary gland tumour, accounting for merely 0.2% of salivary gland tumours, as classified by the World Health Organization, with an estimated prevalence of around 1–1.2 individuals per million, firm, solitary, painful swelling in the right submandibular region for 6 months, measuring 5×5 cm in size at its greatest dimension, with a tender and painful right submandibular lymph node [Figure 1].[1] SDC mainly arises in the parotid gland (over 85% of cases) and occasionally in the submandibular gland (8–12% of cases), rarely affecting minor salivary glands. Contrast enhanced computerised tomography showed a well defined, peripherally enhancing septated hypodense lesion in the deep lobe of the right submandibular gland [Figure 2]. It predominantly affects males, typically in their seventh and eighth decades. The high-grade variant is especially concerning due to its aggressive nature, spreading locally through lymphatic and blood vessels, leading to a poor prognosis.[2-4]

CASE REPORT

A 65-year-old female patient presented with a complaint of a firm, solitary, painful swelling in the right submandibular region for 6 months, measuring 5 × 5 cm in size at its greatest dimension, with a tender and painful right submandibular lymph node. Contrast-enhanced computerised tomography showed a well-defined,

Access this article online

Quick Response Code:

Website: https://journals.lww.com/JPAT/

DOI: 10.4103/jomfp.jomfp_476_23

How to cite this article: Muthu G, Thankappan P, Angelin D, Franklin R. Salivary duct carcinoma in the submandibular gland: A rare case report with differential diagnosis. J Oral Maxillofac Pathol 2024;28:311-4.

peripherally enhancing septated hypodense lesion in the deep lobe of the right submandibular gland. An incisional biopsy of the lesion was performed under general anaesthesia, and specimens were sent for further histopathological examination.

Microscopic examination of haematoxylin- and eosin-stained soft tissue sections revealed the presence of cuboidal and polygonal neoplastic epithelial cells with a moderate amount of eosinophilic cytoplasm-forming islands and sheets that show cribriform arrangement in the connective tissue stroma [Figure 3a]. These neoplastic cells exhibited pleomorphism in both cellular and nuclear aspects, along with the presence of mitotic figures. Solid aggregates of cells with central comedo-type necrosis were also noted [Figure 3b]. Capsular invasion and extracapsular spread were observed in certain areas involving muscle fibres. Salivary gland acini showed oncocytosis and lipomatosis [Figure 4a]. The connective tissue stroma showed areas of hyalinisation, haemorrhage, extravasated red blood cells and focal chronic inflammatory infiltrate. Immunohistochemical analysis showed negative expression of androgen receptor (AR) [Figure 5], human epidermal growth factor receptor 2 (HER2/neu) [Figure 4b] and tumor protein 63 (p63). Based on the clinical, radiographic and histological findings, SDC was diagnosed.

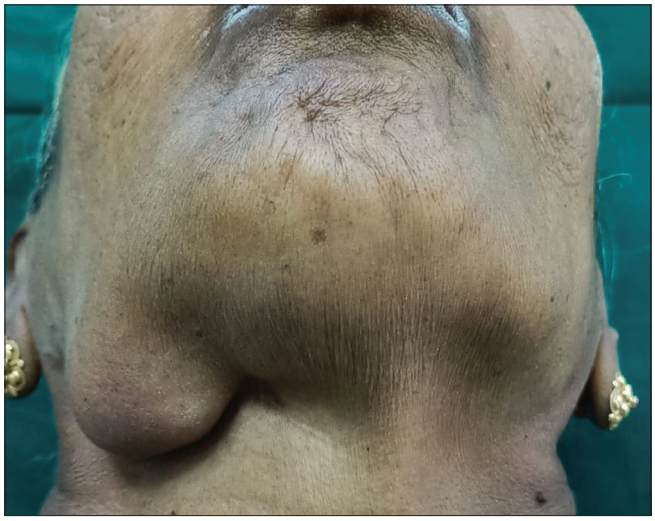

Figure 1: Clinical photograph showing a solitary and firm swelling in the right submandibular region

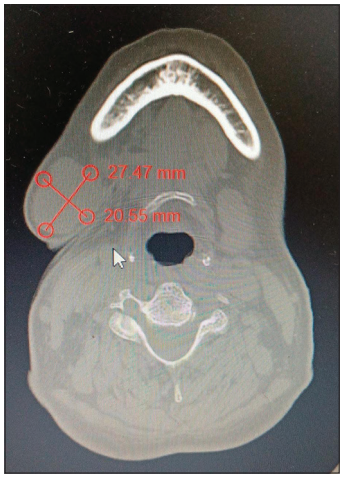

Figure 2: Contrast-enhanced computerised tomography showing a well-defined, hypodense lesion in the deep lobe of the right submandibular gland

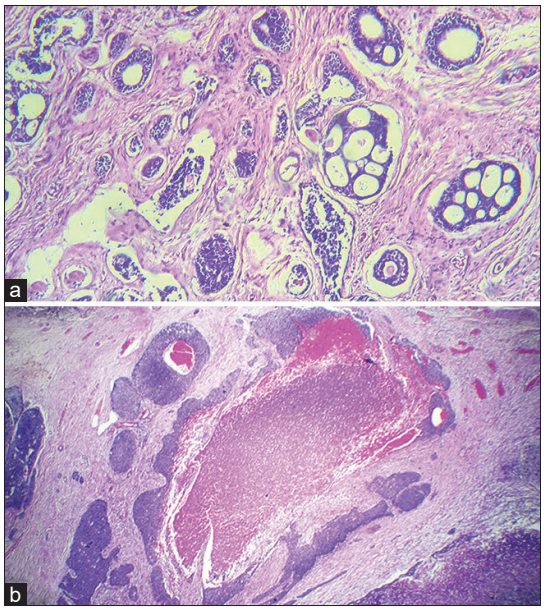

Figure 3: (a) Neoplastic cells forming a cribriform pattern in the connective tissue stroma (H & E; 100×). (b) Solid aggregates of cells with central comedo-type necrosis (H & E; 100×)

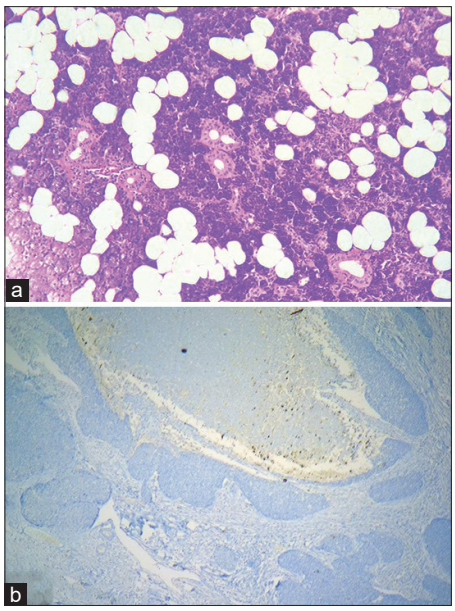

Figure 4: (a) Salivary gland acini showing oncocytosis and lipomatosis (H & E; 100×). (b) Immunohistochemical analysis showed negative expression of HER2/neu (H & E; 100×)

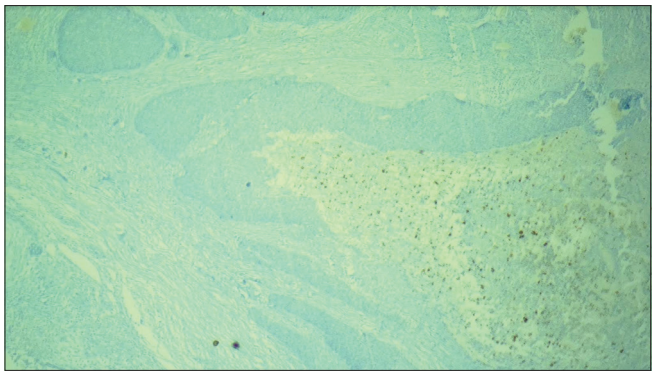

Figure 5: Immunohistochemical analysis showed negative expression of the androgen receptor (H & E; 100×)

Fine-needle aspiration cytology of the right submandibular lymph node revealed no evidence of metastasis. Computed tomography (CT) scan of the abdomen and chest did not reveal metastasis. Using a submandibular approach, a submandibular skin incision was created, followed by blunt dissection, and the right submandibular salivary gland and the right submandibular (level 1b) lymph node were excised. Solid aggregates of cells with central comedo-type necrosis were also noted [Figure 3]. The post-surgical histopathologic findings were in accordance with the features stated earlier. The postoperative radiation therapy comprised 45 Gy delivered in 25 fractions using the salivary gland acini showed oncocytosis and lipomatosis [Figure 4] external beam radiation therapy (EBRT) technique, with each fraction administering 1.8 Gy.

DISCUSSION

SDC is a highly aggressive malignancy, frequently diagnosed at advanced stages, and can arise either de novo or as carcinoma ex pleomorphic adenoma. The molecular features of SDC include HER2 amplification and mutations in genes, such as Tumor protein 53 (TP53) and Phosphatidylinositol-4,5-bisphosphonate 3-kinase catalytic subunit alpha (PIK3CA). Intriguingly, SDC may display genetic alterations typically linked to other salivary gland carcinomas. SDCs possess a moderately low tumour mutational burden comparable to certain organ-specific cancers and maintain microsatellite stability. This intricate genetic landscape of SDC necessitates tailored therapeutic strategies.[5] Historically, SDC has exhibited a propensity for male predominance and a preponderance of cases involving the parotid gland. The present case of SDC in the submandibular gland of a female patient is one of the exceedingly infrequent cases of its nature.[6,7]

Although SDC was initially described in 1968 by Kleinsasser *et al*., it gained official recognition by the World Health Organization in 1991. SDC often exhibits papillary, cribriform growth patterns, along with pleomorphism and necrosis. SDC also presents rare variants, such as papillary or micropapillary, sarcomatoid, mucinous, oncocytic and basaloid morphologies.[8] In the present case, necrosis, cribriform growth pattern, pleomorphism and oncocytosis served as critical diagnostic indicators. Furthermore, a low-grade variant can resemble other carcinomas, such as low-grade acinic cell carcinoma or mammary analogue secretory carcinoma.[8]

In most cases, over 90% show AR expression. Identifying 'AR-negative SDC' like in the present case requires carefully ruling out other possibilities.[5] SDC possesses specific histopathological characteristics, including an infiltrative growth pattern, solid or cribriform arrangements, necrosis and perineural invasion. It is vital to distinguish it from other tumours, such as breast ductal carcinoma, high-grade mucoepidermoid carcinoma, metastatic melanoma, myoepithelial carcinoma and cystadenocarcinoma due to its underlying biological nature and shared characteristics.[9] Even though they share a close resemblance, in the present case, the clinical history and breast cancer indicators serve to distinguish it from breast ductal carcinoma. The absence of epidermoid and goblet cells and negative p63 expression rule out high-grade mucoepidermoid carcinoma. Both SDC and oncocytic carcinoma exhibit oncocytosis; however, oncocytoma lacks an intraductal pattern. The absence of myoepithelial cells differentiates this case from myoepithelial carcinoma. Metastatic melanoma exhibits melanin pigment and melanocytic features, which are absent in this case. In the current case, there is an absence of the cystic presentation typically associated with cystadenocarcinoma. Although HER2 expression was negative in this case and is not exclusive to SDC, it is advisable to assess the status of HER2 to provide guidance for treatment strategies. Trastuzumab and hormone therapy are options for targeting cancer cells in HER2-positive SDC cases.[5]

Surgical resection is the main therapeutic approach followed by postoperative radiation therapy to optimise patient outcomes, with elective neck dissection recommended for nodal metastases and T3–T4 patients without nodal metastasis. Postoperative radiation therapy is advised regardless of tumour size and margin status. SDC is associated with a high mortality rate (77%) and common occurrences of local recurrence (35–66%), lymph node metastasis (66%) and distant metastasis (50–70%).[10] In the present case, surgical excision followed by radiation therapy yielded a good prognosis after a follow-up period of one year.

CONCLUSION

SDC represents a high-grade malignancy associated with invasive behaviour. Diagnosing SDC remains a challenge, given the underlying biological nature and overlapping features with other salivary gland tumours. This case report highlights the importance of histopathology in the identification and therapy of SDC. Early diagnosis, multidisciplinary approach and regular follow-up are crucial to addressing the complex nature of this malignancy and improving patient outcomes.

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 initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Kantamani D, Bandaru SS, Miatech JL, Stagg MP. Salivary duct carcinoma: Case reports and brief review of the literature. Case Rep Oncol Med 2021;2021:2672772.
2. Sepulveda I, Trivaz Rodriguez F, Monsalvez C, Compan A, Ulloa JP. Salivary duct carcinoma of submandibular gland. J Med Cases 2019;10:354-8.
3. Anwer AW, Faisal M, Adeel M, Waqas O, Abu Bakar M, Qadeer S, *et al*. Clinicopathological behaviour and treatment-related outcome of rare salivary duct carcinoma: The Shaukat Khanum Memorial Cancer Hospital experience. Cureus 2018;10:e3139.
4. Hsu CC, Li WY, Chu PY. Salivary duct carcinoma of the supraglottis with a distinct presentation. A case report and literature review. Medicine (Baltimore) 2018;97:e0095.
5. Nakaguro M, Tada Y, Faquin WC, Sadow PM, Wirth LJ, Nagao T. Salivary duct carcinoma: updates in histology, cytology, molecular biology, and treatment. Cancer Cytopathol 2020;128:693-703.
6. Wakely Jr PE. Salivary duct carcinoma: A report of 70 FNA cases and review of the literature. Cancer Cytopathol 2022;130:595-608.
7. Kusafuka K, Sato Y, Nakatani E, Baba S, Maeda M, Yamanegi K, *et al*. The implicated clinical factors for outcomes in 304 patients with salivary duct carcinoma: Multi-institutional retrospective analysis in Japan. Head Neck 2022;44:1430-41.
8. Schmitt NC, Kang H, Sharma A. Salivary duct carcinoma: An aggressive salivary gland malignancy with opportunities for targeted therapy. Oral Oncol 2017;74:40-8.
9. Simpson RHW. Salivary duct carcinoma: New developments—morphological variants including pure *in situ* high-grade lesions; Proposed molecular classification. Head Neck Pathol 2013;7(Suppl 1):48-58.
10. Fletcher C. Diagnostic Histopathology of Tumors. 4th ed. Philadelphia: Saunders; 2013;1:336-7.