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CASE REPORT

Sclerosing odontogenic carcinoma – what we know so far

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Abstract

Sclerosing odontogenic carcinoma (SOC) was described in 2008 and is recognised as a malignant odontogenic tumour in the World Health Organisation classification of head and neck tumours. Nine cases have been reported including six in the mandible and three in the maxilla. After initial controversy over whether SOC was a variant of an odontogenic tumour or a separate entity, it is now established as a distinct entity with an infiltrative and invasive pattern but is usually a diagnosis of exclusion as other odontogenic neoplasms should be ruled out first. They are low-grade tumours most commonly exhibiting perineural and soft tissue invasion, but distant metastases have not been reported. Treatment varies from radical resection, neck dissection and radiotherapy to enucleation or curettage with no adjuvant treatment. There has been one reported recurrence, occurring eight months after curettage, which was treated with segmental mandibular resection, but no incidences of disease-related mortality. We report a case of SOC initially treated as an odontogenic fibroma by enucleation. Once the diagnosis of SOC was confirmed, local excision without neck dissection or radiotherapy was undertaken. The patient remains disease-free, suggesting local excision might be sufficient treatment. Treatment standardisation cannot be possible without more reported cases.

Introduction

Sclerosing odontogenic carcinoma (SOC) is a little known entity among the tumours of dental origin since its recognition in 2008[1]. To date, only nine cases have been reported worldwide therefore approaches to treatment have been extrapolated from similar tumours[1–5]. Surgical management of carcinomas typically involves wide excision with neck dissection and adjuvant radiotherapy to achieve disease control but this approach could represent overtreatment in low-grade odontogenic malignancies. The patients with SOC described so far presented with non-specific, painless swellings, (which may have been present for several years) or were asymptomatic suggesting that these are indolent tumours that do not require radical surgery.

Seven subtypes of malignant odontogenic tumours are listed in the WHO Classification of head and neck tumours (five carcinomas, sarcomas and odontogenic carcinosarcomas) and SOC has been included as a distinct entity in the most recently published classification[6]. SOC can show features similar to other odontogenic carcinomas, benign fibro-osseous lesions and benign odontogenic tumours (i.e. odontogenic fibromas), making the diagnosis challenging[4,7,8].

The histopathology of these tumours is well documented in previous case reports but treatment has varied between conservative resection, wide local excision and segmental mandibulectomy with or without neck dissection and post-operative radiotherapy. We report the tenth case of SOC and the first one with a particular focus on the treatment dilemma these tumours pose from a surgical point of view.

Case description

Background

A 43-year-old fit and well female was referred by her General Dental Practitioner (GDP) with an incidental finding of a radiolucency in the right anterior maxilla apical to the upper right lateral incisor, canine and first premolar on an orthopantomogram. She was asymptomatic but had a cleft in the palate adjacent to the roots of these teeth (Fig. 1), which had been present for many years. There was evidence of a radiolucency on an OPT taken by another GDP 16 years earlier but other than routine dental treatment no further investigation or intervention had been provided.

Initial investigations and treatment

A computerised tomography (CT) scan showed the lesion to be well demarcated but with erosion of the roots of the adjacent teeth and extension superiorly into the floor of the nose and maxillary sinus (Fig. 2A,B). The lesion appeared partially corticated, with expansion of the palatal bone and resorption of surrounding structures.

An incisional biopsy demonstrated fibrous tissue with small nests of odontogenic epithelium, some of which showed clearing which in places was surrounded by a dense zone of hyalinisation. The histological appearance was consistent with an odontogenic fibroma. However, the resorption of the tooth roots was unusual and the hyalinised collagen raised the possibility of a SOC. At this stage, there was no evidence of perineural infiltration or invasion of the adjacent soft tissue in the initial biopsy specimen.

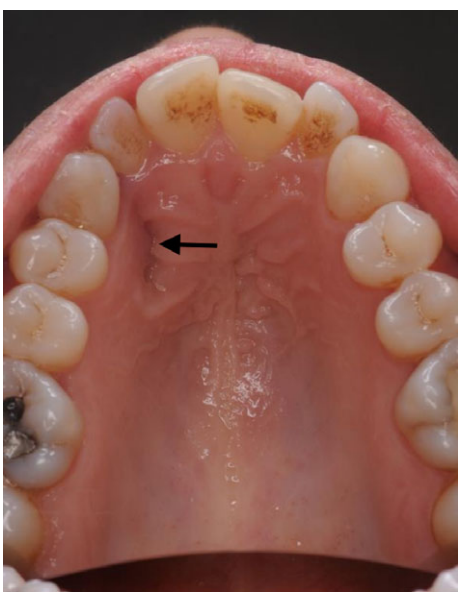

Figure 1 Intra-oral photograph showing the cleft in the anterior right hard palate caused by the lesion (arrow).

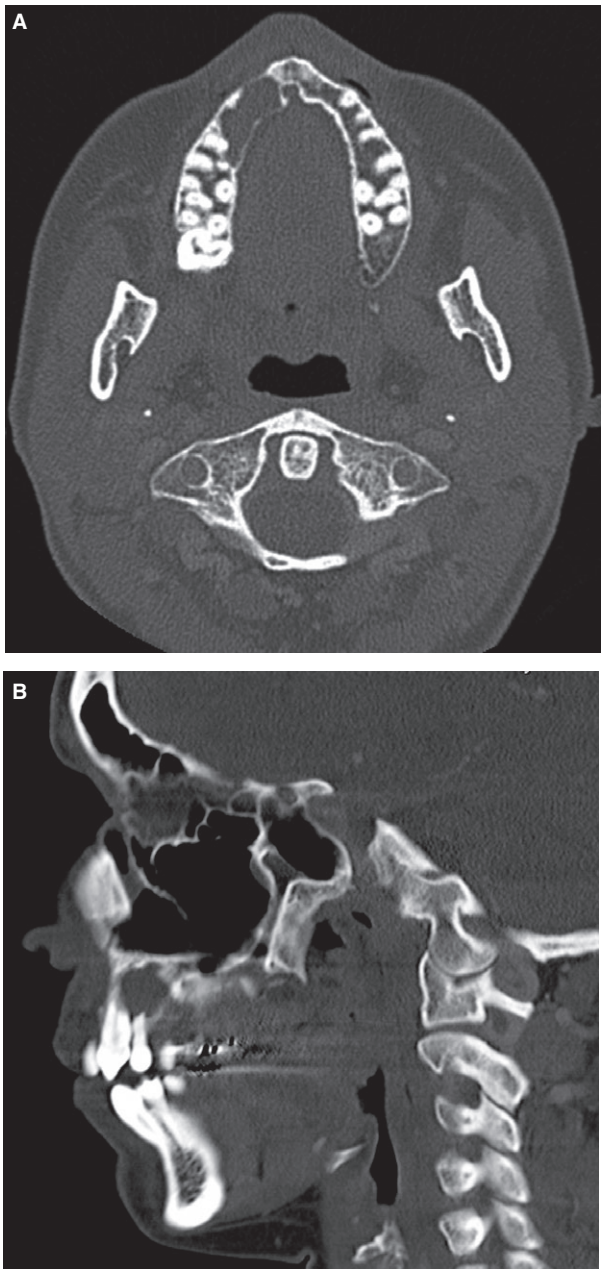

Figure 2 (A) Axial computerised tomography (CT) scan demonstrating a radiolucent lesion occupying the right anterior maxilla with cortical thinning and erosion. (B) Sagittal CT showing the lesion extending into the floor of the nose, invading the palatal soft tissue and eroding the roots of involved teeth.

Since there was no convincing evidence of malignancy, a conservative enucleation of the entire lesion was undertaken as a second procedure.

Intraoperatively, the lesion was found to have obliterated the root of the lateral incisor, was adherent to the canine and first premolar and had created a full thickness (buccal to palatal) defect of the maxillary alveolar bone (Fig. 3). The lesion was removed piecemeal and the resultant cavity curetted to remove any macroscopic tumour remnants.

Histopathology and immunohistochemistry

The excised tissue was evaluated by the local pathologist initially, but due to the unusual features a further specialist opinion from the regional oral and maxillofacial pathology department was sought. The tumour comprised islands of epithelium set within fibrous connective tissue that was myxoid in places but with more collagenous and sclerosed areas (Fig. 4A). These epithelial islands contained small, mildly pleomorphic cells with oval, predominantly vesicular nuclei and moderate amounts of eosinophilic cytoplasm, resembling odontogenic rest cells and with no evidence of mitoses. There were also small areas (<10%) of glycogen-rich clear cells confirmed using Periodic Acid Schiff (PAS) stain with and without diastase digestion. Evidence of perineural invasion was also seen with bland epithelial islands within and around nerve fibres.

Immunohistochemistry confirmed the epithelial nature of the lesion. The tumour cells showed diffuse staining for pancytokeratins (AE 1/3) and cytokeratin 5, 14 and 19 but were negative for cytokeratin 7. Ki-67 showed a proliferation index <1%. An odontogenic fibroma was ruled out due to the infiltrative pattern of the epithelial islands, although the epithelial pattern, hyalinisation and immunohistochemistry (CK7 negative, CK19 positive) were consistent with an odontogenic aetiology (Fig. 4B).

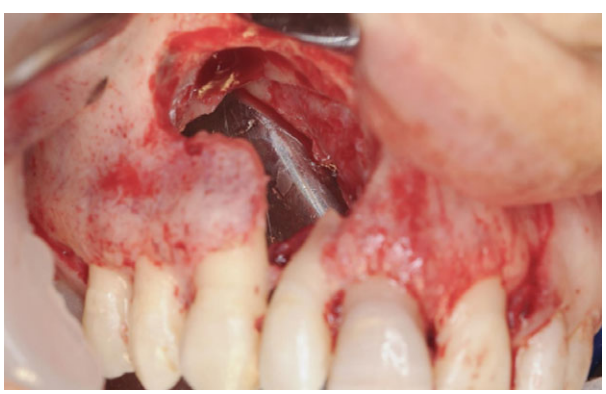

Figure 3 Intraoperative photograph during enucleation highlighting the through and through maxillary defect created by the lesion.

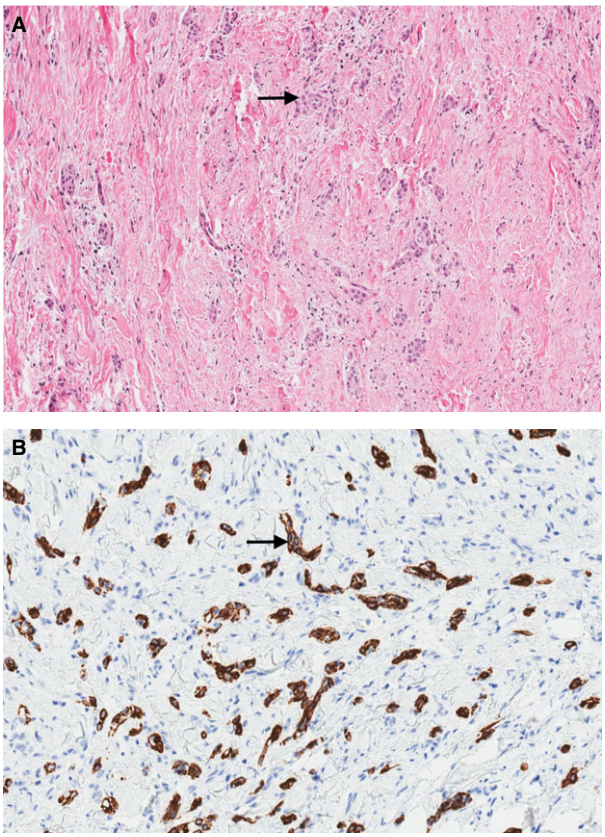

Figure 4 (A) Representative photomicrograph showing variably sized islands of infiltrative but bland epithelium (arrow) in a sclerotic and dense fibrous stroma. (B) Immunohistochemistry for CK19 highlighting the infiltrative epithelial islands (arrow) (×200 magnification).

The possibility of a clear cell odontogenic carcinoma (CCOC) was considered due to the presence of scattered clear cells, however, fluorescent in situ hybridisation for Ewing's sarcoma breakpoint 1 (*EWSR1*) gene rearrangement, was negative ruling out a CCOC. Furthermore, it was not an odontogenic fibroma as it lacked calcifications and showed perineural invasion.

Keeping in mind the infiltrative pattern of odontogenic epithelium with lack of a definitive edge, cellular variation, perineural invasion and the locally destructive nature seen clinically and radiologically, which is indicative of malignancy (Fig. 5A, B), a diagnosis of SOC was made. A consensus discussion within the specialist oral and maxillofacial pathology unit agreed that the clinical and histological picture of the tumour did not match that of any other odontogenic tumour, and so a diagnosis of exclusion, (which is the basis of SOC diagnosis), was possible.

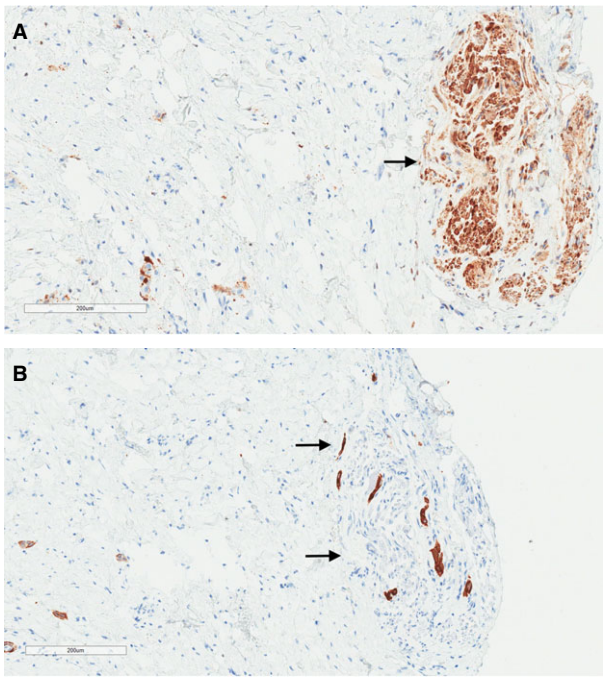

Figure 5 (A) S100 immunohistochemistry highlighting a nerve (arrow) within the specimen (×400 magnification). (B) CK19 positive epithelial islands (arrows) within that nerve confirming perineural invasion (×200 magnification).

Definitive treatment

Once a malignant diagnosis was confirmed, the patient underwent staging CT scans which showed no local or regional metastatic disease (staging T4a, N0; M0). In line with the recommendations of the head and neck cancer multidisciplinary team (MDT), further resection of the bone surrounding the tumour cavity with a conservative margin of 5 mm was taken (Brown classification IIb)[9], as a third procedure and the defect obturated but a neck dissection was not undertaken. No residual tumour was identified in this specimen and the patient did not receive adjuvant chemoradiotherapy. There has been no clinical evidence of tumour recurrence 12 months post-operatively.

Discussion

Malignant odontogenic tumours are uncommon and the subsequent histological subtypes are rare, particularly SOC given its recent description and paucity of cases[1,6]. It is therefore difficult to be certain of the natural history of these lesions and how best to treat them. In the present case, the patient was asymptomatic and the tumour was likely to have been present for many years, which suggests that it was not aggressive. Nonetheless, it was a confirmed malignancy as evidenced by the infiltrative pattern and perineural invasion requiring more radical treatment than that of a benign odontogenic lesion. The decision to proceed to a partial maxillectomy for definitive management was guided by the head and neck MDT using the few previous published cases as evidence (Table 1).

Koutlas *et al.* in their original description reported three cases of SOC all of which had 'extensive surgical procedures' with resection margins extending beyond the limits of the tumour,[1] whereas Saxena *et al.* and Hanisch *et al.* carried out a hemimandibulectomy[4,10]. These approaches achieved disease control in all patients from 10 months to 12 years post-operatively but the details of the surgical procedure undertaken in the series published by Koutlas *et al.* were not mentioned. Although wide excision with a 10 mm (or more) margin akin to that planned in the treatment of oral squamous cell carcinoma (OSCC) would ensure complete tumour removal, the morbidity of such a resection in a young female patient for a low-grade malignant tumour with a symptom-free history was deemed inappropriate by the MDT. Review of the literature showed that of the two patients with SOC treated with curettage or enucleation of the lesion alone, the tumour recurred in one, requiring a mandibular resection, whereas the other refused further surgery but was disease free after a year[3,5]. On this basis, the MDT elected to offer a partial maxillectomy with a conservative 5 mm margin to ensure complete tumour removal; an approach which was also employed successfully in treating maxillary SOC by Hussain *et al.* and Wood *et al.*[2,11]

Despite no reported evidence of cervical nodal disease, three reported cases in the literature underwent ipsilateral neck dissections (two of which were radical neck dissections), none of which yielded any positive nodes[1,4,10]. Although there remains controversy over the treatment of the node-negative neck in other oropharyngeal cancers, elective neck dissection confers an overall and disease-free survival benefit in early stage OSCC. However, the characteristics and behaviour of OSCC are quite different to odontogenic carcinomas and affect different patient groups therefore the results cannot be extrapolated from one to the other. Since our patient had an N0 neck and there have been no previous reported incidences of cervical metastases in SOC, a neck dissection was not performed. Sentinel lymph node biopsy may be an alternative but this is yet to be

Table 1 Reported cases of sclerosing odontogenic carcinoma and their management

Age	Gender	Location	Symptoms	Management	Treatment of the neck	Chemoradiotherapy	Metastases	Recurrence	Follow up	Year
72	Male	Mandible	Left mandibular mass and mental nerve parasthesia	'Extensive' surgery	Ipsilateral neck dissection	No	No	No	5 years	2008[1]
46	Female	Mandible	Pain and an osteolytic right mandibular lesion	'Extensive' surgery	No treatment	No	No	No	12 years	2008[1]
73	Female	Maxilla	Right maxillary mass	'Extensive' surgery	Not stated	Radiotherapy	No	No	3.5 years	2008[1]
67	Male	Mandible	Parathesia lower left lip	Curettage followed by left segmental mandibular resection	No treatment	Chemotherapy	No	Yes after curettage (8 months)	15 months	2010[3]
54	Male	Maxilla	Sensitive upper right canine and palatal mass	Conservative excision	No treatment	No	No	No	19 months	2013[2]
42	Male	Mandible	Swelling from lower left lateral incisor to the second premolar	Excision biopsy then hemimandibulectomy	Ipsilateral radical neck dissection	Radiotherapy	No	No	10 months	2013[4]
31	Female	Mandible	Lump at site of lower right first premolar	Enucleation (patient refused further treatment)	No treatment	No	No	No	1 year	2014[5]
43	Female	Maxilla	Asymptomatic lump on the hard palate	Low level right maxillectomy	No treatment	No	No	No	17 months	2016[10]
60	Male	Mandible	Left lower third molar radiolucency and swelling	Left hemimandibulectomy	Ipsilateral radical neck dissection	No	No	No	9 months	2017[9]

established practise even in OSCC and has never been tried in odontogenic carcinomas and therefore would have been at best experimental if employed in this patient.

Two reported patients received post-operative radiotherapy to the tumour site but the indications were not detailed[1,4]. Perineural, perivascular and muscular invasion were prominent characteristics of the original description of SOC and perineural infiltration was present in all but one of the previous reports. Similar to these reports, perineural invasion and infiltration was a feature in the present case, but radiotherapy was not offered because no tumour remnants were identified in the further resected bone after the third and final procedure.

Given that the histological appearance of SOC consists of 'bland' odontogenic epithelial cells with a markedly sclerotic stroma, there was controversy over it being a unique entity or a histological variant of another carcinoma[1,12]. The differential diagnosis is wide and includes metastatic disease, desmoplastic ameloblastoma, squamous odontogenic tumour, epithelium-rich variant of central odontogenic fibroma (which was an initial diagnosis in the current patient), calcifying epithelial odontogenic tumour, CCOC and primary intraosseous odontogenic carcinoma[1,4,5]; all of which should be excluded prior to diagnosing SOC. The small number of cases reported since its first description in 2008 means a definitive set of diagnostic criteria will be difficult to achieve, therefore referral of specimens to a specialist oral and maxillofacial pathology unit with experience in characterising odontogenic tumours, as happened in this case, is recommended. Nonetheless, the broad characteristics of these tumours are those of a low-grade carcinoma with a propensity for perineural invasion but a low risk of metastatic spread, and they should be treated as such.

Conclusion

The primary aim of the treatment of oral cavity malignancies is to rid the patient of tumour with a clear margin, but unnecessary morbidity can be avoided by a more conservative resection in low-grade cancers, which may be appropriate in SOC. In the absence of a consensus on treatment, patients with SOC should be fully counselled about all of the options available.

Conflict of interest

None.

References

1. Koutlas IG, Allen CM, Warnock GR, Manivel JC. Sclerosing odontogenic carcinoma: a previously unreported variant of a locally aggressive odontogenic neoplasm without apparent metastatic potential. Am J Surg Pathol 2008;32:1613–9.
2. Hussain O, Rendon AT, Orr RL, Speight PM. Sclerosing odontogenic carcinoma in the maxilla: a rare primary intraosseous carcinoma. Oral Surg Oral Med Oral Pathol Oral Radiol 2013;116:e283–6.
3. Irié T, Ogawa I, Takata T, Toyosawa S, Saito N, Akiba M *et al.* Sclerosing odontogenic carcinoma with benign fibro-osseous lesion of the mandible: an extremely rare case report. Pathol Int 2010;60:694–700.
4. Saxena S, Kumar S, Rawat S, Arun Kumar KV. An indolent swelling of the parasymphyseal area. Oral Surg Oral Med Oral Pathol Oral Radiol 2013;116:528–33.
5. Tan SH, Yeo JF, Kheem Pang BN, Petersson F. An intraosseous sclerosing odontogenic tumor predominantly composed of epithelial cells: relation to (so-called) sclerosing odontogenic carcinoma and epithelial-rich central odontogenic fibroma. Oral Surg Oral Med Oral Pathol Oral Radiol. 2014;118:e119–25.
6. Odell E. Sclerosing odontogenic carcinoma. In: El-Naggar AK, Chan JKC, Grandis JR, Takata T, Slootweg PJ, editors: WHO Classification of Head and Neck Tumours, 4th edition. Lyon: IARC, 2017:205–60.
7. Ide F, Ito Y, Muramatsu T, Saito I. Sclerosing odontogenic carcinoma: a morphologic pattern or pathologic entity? Oral Surg Oral Med Oral Pathol Oral Radiol 2013;115:839.
8. Wright JM, Odell EW, Speight PM, Takata T. Odontogenic tumors, WHO 2005: where do we go from here? Head Neck Pathol 2014;8:373–82.
9. Brown JS, Rogers SN, McNally DN, Boyle M. A modified classification for the maxillectomy defect. Head Neck 2000;22:17–26.
10. Hanisch M, Baumhoer D, Elges S, Fröhlich LF, Kleinheinz J, Jung S. Sclerosing odontogenic carcinoma: current diagnostic and management considerations concerning a most unusual neoplasm. Int J Oral Maxillofac Surg [Internet] 2017;46:1641–9. Available at: http://linkinghub.elsevier.com/retrieve/pii/S0901502717314 87X
11. Wood A, Young F, Morrison J, Conn BI. Sclerosing odontogenic carcinoma presenting on the hard palate of a 43-year-old female: a case report. Oral SurgOral Med Oral Pathol Oral Radiol 2016;122:e204–8.
12. Woolgar J, Triantafyllou A, Ferlito A, Devaney K, Lewis JJ, Rinaldo A *et al.* Intraosseous carcinoma of the jaws: a clinicopathologic review. Part II: Odontogenic carcinomas. Head Neck 2013;35:902–5.