A case of sclerosing odontogenic carcinoma: a rare entity

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Abstract

Sclerosing odontogenic carcinoma (SOC) is a very rare entity, first recognized in the WHO 4th edition (2017). It is a highly infiltrative intraosseous jaw tumour with small nests, strands and cords of cells showing only mild cytological atypia, surrounded by a dense fibrocollagenous stroma. The lesion frequently infiltrates adjacent tissues and bony structures and demonstrates perineural and intraneural invasion. The malignant islands of cells may be compressed by the stroma, making them difficult to identify. On immunohistochemistry, they are positive for cytokeratins (including CK5/6, CK14, CK19) and p63. Several other (more common) lesions present in a similar way and show similar histological features, and need to be excluded before establishing a diagnosis of SOC. Here, we present a case in a 37 year old male who presented with a several month history of a lump over the right mandible.

Keywords head and neck bone tumours; malignant odontogenic tumours; odontogenic and maxillofacial bone tumours; sclerosing odontogenic carcinoma; tumours of the jaw bone

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Case report

A 37 year old white male presented with a 3–4 month history of a lump slowly increasing in size over the right mandible. On examination, the lump was firm and painful when pressed. The patient additionally reported occasional numbness over the area of the inferior dental nerve.

Orthopantamogram revealed a loss of cortication at the right lower border. The lower right 5, 6, 7, 8 teeth were all vital. This led to a diagnosis of "query chronic infection". He was initially treated with antibiotics for 4 weeks, which failed to resolve the lump, so a biopsy was taken and the lesion was later excised.

The initial biopsy showed sclerotic stroma, but malignant epithelial strands were difficult to discern. Histological examination of furhter levels revealed thin cords and strands of tumour cells invading the marrow spaces and surrounding soft tissue. The stoma was notably sclerosed and desmoplastic. There was extensive bony invasion with medullary space involvement. Perineural invasion involving the inferior alveolar nerve was also observed. Immunohistochemistry showed strong positivity for CK19 and AE1/3 in the tumour cells (see Figure 1).

Discussion

Sclerosing odontogenic carcinoma (SOC) is a very rare malignant odontogenic tumour, first included in the 2017 (4th edition) of the WHO Classification of Head and Neck Tumours.[1] It has a slight female predilection and affects patients aged 30–75 years, with most cases occurring between the ages of 50–70 years old.[2] It has an unknown aetiology. However, it has been proposed to arise from odontogenic epithelial rests or the malignant transformation of odontogenic epithelial cyst lining.[2,5] The most affected site is the posterior mandible, with maxillary cases presenting more anteriorly. Most patients present with a painless swelling of several months' duration, with only a few presenting with paraesthesia, pain or tooth mobility.[2,4]

Radiologically, SOCs usually demonstrate radiolucency with poorly defined borders and destruction of the cortical bone. They frequently extend beyond the radiographic margins and display aggressive signs including invasion of surrounding soft tissue and perineural invasion.

Macroscopically, the tissue has the appearance of a dense fibrous lesion and may show infiltration of adjacent structures and tissues, including fat, muscle and bone. Microscopically, they are unencapsulated infiltrative lesions with a characteristic fibrocollagenous stroma. The tumour cells are malignant epithelial cells that form thin cords ("single file"), small nests and strands. These cells display only mild cytological atypia, infrequent mitoses and necrosis is usually absent. Occasionally, signet ring, clear cell change and glandular differentiation have been described.[4] The stroma frequently compresses the malignant cells, which can make them difficult to see on haematoxylin and eosin (H&E) stained sections and small biopsy specimens. The stroma may also include cementum-like calcifications. The lesion frequently infiltrates adjacent structures and tissues. Perineural and intraneural invasion is usually observed, however, lymphovascular invasion is not commonly reported.[2] Despite the infiltrative and malignant features, SOCs have a good prognosis, with only local recurrences reported and no distant metastases reported in the literature to date (2022).[2,3,6]

There are no defining immunohistochemical markers for SOC. The malignant epithelial component stains positively with cytokeratins CK5/6, CK14, CK19 and p63.[2] Likewise, there are

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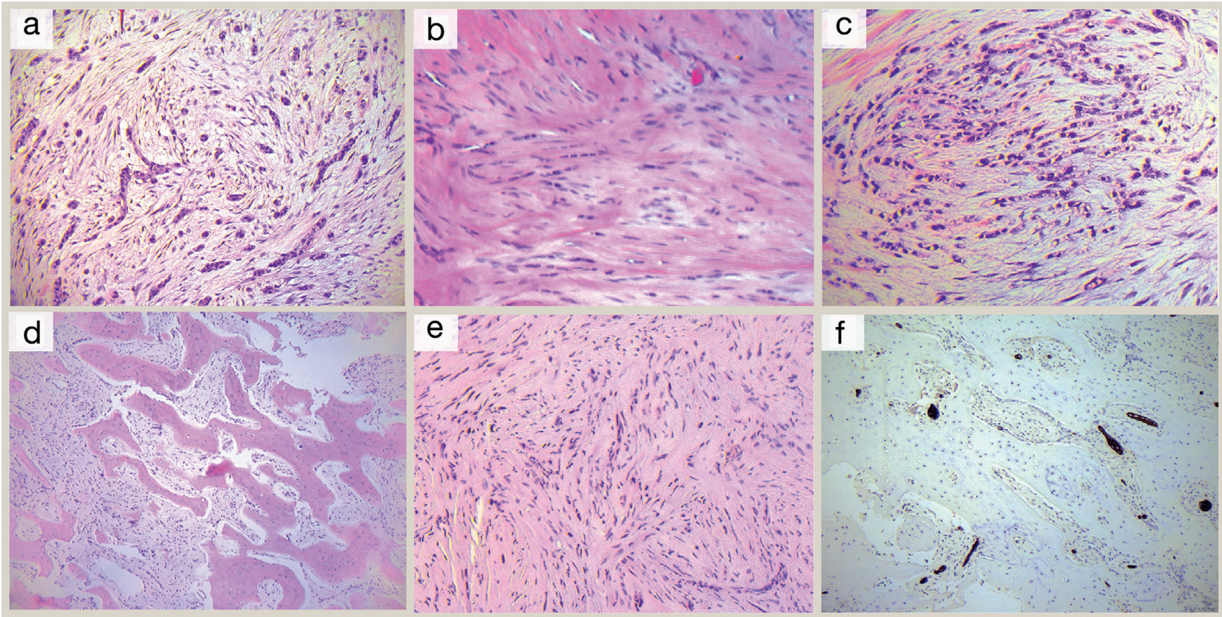

Figure 1 (**a**) Small nests and strands of epithelial cells with only mild cytological atypia within a desmoplastic stroma (H&E, x10 magnification), (**b**) Malignant epithelial cells in "single file" pattern (H&E, x20 magnification), (**c**) Occasionally, signet ring, clear cell change and glandular differentiation may be seen (H&E, x20 magnification), (**d**) The stroma may contain cementum-like bone (H&E, x5 magnification), (**e**) The dense fibrocollagenous stroma can compress the epithelial cells, making them hard to discern (H&E, x10 magnification), (**f**) Malignant epithelial cells stain positive for cytokeratins and p63 (CK19, x5 magnification).

Summary of the features of entities that appear histologically most similar to sclerosing odontogenic carcinomas.

Entity	Location	Radiology	Distinct histologic features	IHC and SS	Molecular
Central Odontogenic Fibroma	Tooth bearing jaw, maxilla > mandible	Well defined lesion	Bland fibrous tissue with occasional odontogenic epithelial nests and cords	Epithelium positive for AE1/3, CK14, CK19	Nil
Conventional Ameloblastoma, desmoplastic subtype	Posterior molar region of the mandible	Multilocular radiolucency with "soap bubble" appearance	Densely collagenous stroma with spiky islands of epithelial cells that usually show reverse polarity and peripheral palisading.	Epithelium positive for CK5, CK14, CK19, CD56, calretinin, p63, p40 Epithelium negative for SOX10	BRAFV600E
Calcifying Epithelial Odontogenic Tumour	Tooth bearing jaw, mandible > maxilla	Multilocular lesion with mixed radiolucency; may be associated with unerupted teeth.	Sheets, cords or nests of polyhedral cells with intercellular bridges and nuclear pleomorphism. Can infiltrate adjacent medullary spaces. Produces amyloid.	Amyloid stains with Congo red and shows birefringence under polarized light.	Nil
Cemento-ossifying Fibroma	Mandibular premolar and molar area	Well defined radiolucency with downward bowing of the inferior border.	Thin fibrous capsule and well delineated from adjacent normal bone. Fibroblastic stroma with woven bone, dentinoid or cementoid. The stroma may be hyper cellular, but doesn't contain epithelioid cells.	Nil specific	*HRPT2* in syndromic forms
Primary Intraosseous Carcinoma	Inferior body and ramus of mandible.	Poorly defined osteolytic area, tooth resorption and cortical erosion.	Atypical squamous cells in nests and islands with intercellular bridges, but keratinization is minimal. Metastasis from outside the jaw must be ruled out.	Epithelial cells are positive for CK19	Nil

IHC, immunohistochemistry; SS, special stains.

Table 1

currently no defining molecular features and all cases tested have been negative for EWSR1 rearrangements.[2]

The lack of defining features makes SOC a diagnosis of exclusion as there are several, more common entities, that appear very similarly and must be ruled out first (see Table 1 for summary of entities and differentiating features). Beginning with central odontogenic fibromas (cOF), the main differentiating feature is that cOFs tend to be well defined lesions on radiology and the stroma appears blander than that of SOC.[2] The desmoplastic subtype of conventional ameloblastomas (AM) have a classical multilocular or "soap bubble" appearance on radiology. They also have a densely collagenous stroma. However, the islands of epithelial cells have an angular or spiky appearance and the cells usually show reverse polarity and peripheral palisading. On immunohistochemistry, the epithelial cells of the ameloblastoma show positivity for cytokeratins as well as CD56 and calretinin (which have not been demonstrated in SOCs). Most ameloblastomas also demonstrate the BRAFV600E mutation (up to 75% in the mandible), a feature not described in SOCs.[2] Calcifying epithelial odontogenic tumours (CEOT) are also multilocular on radiology. The epithelial cells appear in sheets, cords or nests but tend to be polyhedral and display intercellular bridging. Nuclear pleomorphism is more apparent than in SOCs, and CEOTs may produce amyloid, which can be stained with Congo red and shows birefringence under polarized light (this is not a feature of SOCs).[2] Cemento-ossifying fibromas are well defined radiolucent lesions with a characteristic downward bowing of the inferior border on radiology. They may have a thin fibrous capsule and tend to be well delineated from the adjacent normal bone, which contrasts to the infiltrative nature of the SOC. The stroma is fibroblastic and contains woven bone, dentinoid or cementoid, which may appear similar to the cementum-like calcification of the SOC stroma. However, the main differentiating feature of cemento-ossifying fibromas is the lack of epithelial cells within their stroma. In their syndromic form, cemento-ossifying fibromas are associated with *HRPT2* mutations.[2] SOCs must be differentiated from primary intraosseous carcinoma (PIOC), which has a poor prognosis (around 45% 5 year survival). They are poorly defined osteolytic lesions that may demonstrate tooth resorption on radiology. They comprise nests and islands of squamous cells with nuclear atypia but minimal keratinization, contrasted with SOCs which do not show keratinization and the cytological atypia is only mild.[2]

Conclusion

Here we present a case of sclerosing odontogenic carcinoma in a 37-year-old male, that presented as a persistent mandibular swelling. Sclerosing odontogenic carcinoma is a very rare entity and a diagnosis of exclusion. It has a characteristic dense fibrocollageneous/densely sclerotic stroma and thin cords or nests of mildly atypical malignant epithelial cells. The epithelial cells are positive for cytokeratins on immunohistochemistry. ◆

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Practice points

Pathological features:

- Dense fibrocollagenous/sclerotic stroma with thin cords or small nests of malignant epithelial cells with mild cytological atypia and low mitotic index.

Phenotypic features:

- Immunohistochemistry – positive for cytokeratins including CK5/6, CK14, CK19 and p63.

Molecular features:

- No defining molecular features described yet – all tested cases negative for EWSR1 rearrangements.

Multiple choice questions

1. In addition to histological examination and immunohistochemistry, sclerosing odontogenic carcinoma is diagnosed:

A) based on its characteristic fibrocollagenous stroma.
B) based on the mild cytological atypia of the malignant epithelial cells.
C) once other entities have been ruled out (i.e. diagnosis of exclusion).

Correct answer (C)

2. The malignant epithelial component of sclerosing odontogenic carcinoma shows positive immunohistochemistry for:

A) CK14, CK19 and p63
B) CK14, CK19 and S100
C) CK14, CK19 and PASD/mucicarmine

Correct answer (A)

3. Sclerosing odontogenic carcinoma is associated with mutations in which gene:

A) EWSR1 rearrangements
B) BRAFV600E
C) Wnt/beta-catenin pathway mutations
D) There are no defining molecular features at present

Correct answer (D)