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CASE REPORT

Low-grade ovarian serous carcinoma metastasis to the maxilla

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Abstract

The maxillofacial region is an uncommon site for metastases from distant primary tumours, representing only 1–2% of malignancies at this site. Such metastases usually present in the mandible rather than the maxilla. The most common sites of primary tumour are the breast, lung and kidney. We describe the clinical, radiological and histologic features of the first-known case of a low-grade serous carcinoma of the ovary metastasising to the posterior maxilla. Low-grade serous carcinoma of the ovary is an uncommon entity and is biologically distinct from high-grade serous carcinoma. Extra-abdominal spread is uncommon and bony metastases are rare. Intraosseous metastases are often associated with disseminated disease and confer a poor prognosis.

Research Highlights

- Metastases to the maxillary bone are rare
- Metastases of low-grade ovarian carcinoma to the maxilla have not previously been described
- High index of suspicion is required when assessing oral lesions in patients with history of malignancy
- Atypical metastatic pattern is associated with poor patient prognosis
- Diagnosis of craniofacial metastases may be associated with initial diagnosis of cancer or diagnosis of metastatic malignancy in patients. This can have significant implications to their health

Introduction

Intraosseous lesions of the maxilla and mandible are commonly encountered. Lesions may be related to teeth or their developmental remnants (odontogenic in origin) or they may be unrelated (non-odontogenic). Squamous cell carcinoma is by far the most common malignant neoplasm in the maxillofacial region[1]. Metastatic deposits are uncommon and represent 1–2% of all malignancies in this area[2]. The majority of these occur in the mandible[3] and present as asymptomatic incidental lesions. Advanced lesions may present with pain, tooth mobility or dysaesthesia. Radiological examination may also show expansion or erosion of overlying cortical bone[3].

Metastases in the maxillofacial tissues are associated with discovery of disseminated metastatic disease in up to 25% cases, or may be the initial presentation in 23%[4]. Metastases of ovarian tumours to the oral and maxillofacial region are rare. Ovarian malignancies usually disseminate intraperitoneally. Extra-abdominal spread is uncommon, with bony metastases rarely described.

A high index of clinical suspicion and pathological examination are required to differentiate a primary

neoplasm from metastatic disease. In this case report, we describe the first-known reported case of an intraosseous metastasis to the maxilla from a low-grade ovarian serous carcinoma.

Case Report

A 59-year-old woman was referred to an Oral and Maxillofacial Surgeon (OMFS) by her local dentist with a persistent periapical mixed radiopaque and radiolucent lesion in the left posterior maxilla (Figs 1 and 2). On clinical examination, there was no obvious lesion or swelling.

A radiographic abnormality was initially noted in 2013 (3 years prior to referral) as a radiolucency on orthopantomogram (OPG) and cone beam computerised tomogram (CBCT) (Fig. 1) and was thought to be due to a periapical dental infection of the teeth 25, 26 and 27. The lesion measured roughly 15 × 12 × 8 mm, and the teeth were not noted to be mobile. The 25 and 27 were extracted by her dentist, and endodontic treatment was completed on the 26. The extraction socket sites were noted to heal without issue. The patient was subsequently lost to follow-up until 2016, when the dentist noted progression of the lesion (Fig. 2) and arranged OMFS referral. On presentation to the surgeon, the patient was asymptomatic but a biopsy of the lesion was arranged.

The histopathology sections showed multiple fragments of trabecular bone and new woven bone. The marrow spaces were expanded by metastatic low-grade serous carcinoma. The tumour was composed of micropapillae with surrounding artefactual clefting. The cells showed mild pleomorphism with hyperchromatic ovoid nuclei and indistinct nucleoli. Abundant psammoma bodies were present. Immunohistochemical staining showed positivity for cytokeratin AE1/AE3, PAX-8, ER (oestrogen receptor), WT-1 and p53 (wild type).

The tumour morphology, coupled with the immunohistochemical phenotype, was consistent with metastatic low-grade serous carcinoma of the ovary (Figs. 3,4).

The patient was known to have had a low-grade serous carcinoma of the ovary diagnosed in 2012. The metastatic lesion in the maxilla showed the same microscopic morphology and immunohistochemical prolife to the original ovarian tumour (Fig. 5).

The primary tumour was diagnosed in 2012 as a FIGO (International Federation of Gynaecology and Obstetrics) stage IV low-grade serous carcinoma of the ovary, with metastases to uterus, omentum, peritoneum, bowel and lung. On initial PET, no abnormal FDG avidity was noted in the maxilla. The primary tumour was treated with neo-adjuvant chemotherapy (three cycles of carboplatin and paclitaxel), followed by interval debulking surgery with a radical hysterectomy, bilateral salpingo-oophorectomy, supra-colic omentectomy, and rectosigmoid resection with primary anastomosis. Post-operatively the patient completed a further three cycles of carboplatin and paclitaxel.

The patient was followed up for 12 months (2013); an increase in serum CA-125 (cancer antigen 125) triggered restaging computerised tomography (CT) and positive emission tomography (PET) which

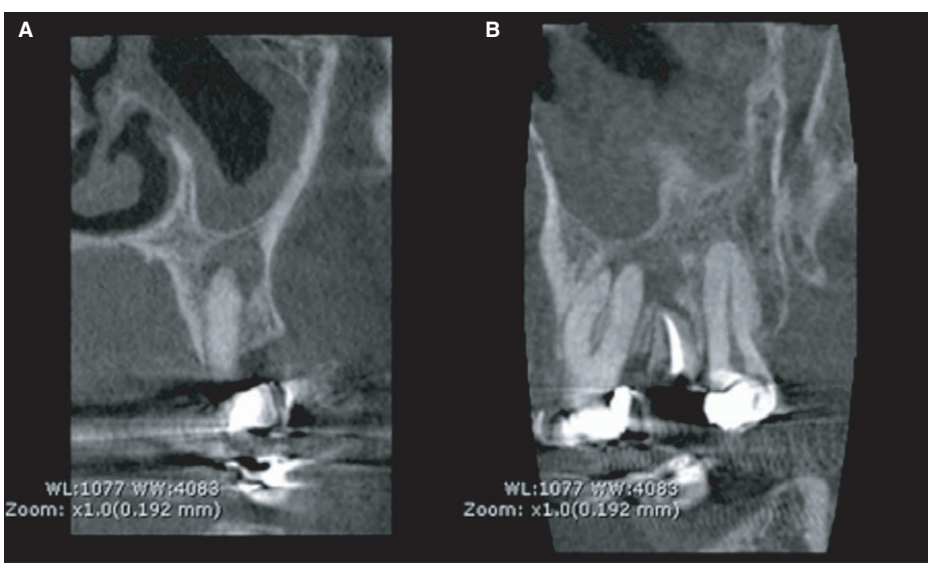

Figure 1 Initial CBCT showing radiolucency associated with 26 and 27 roots. Date of exposure: 27 July 2013. (A) coronal view; (B) sagittal view.

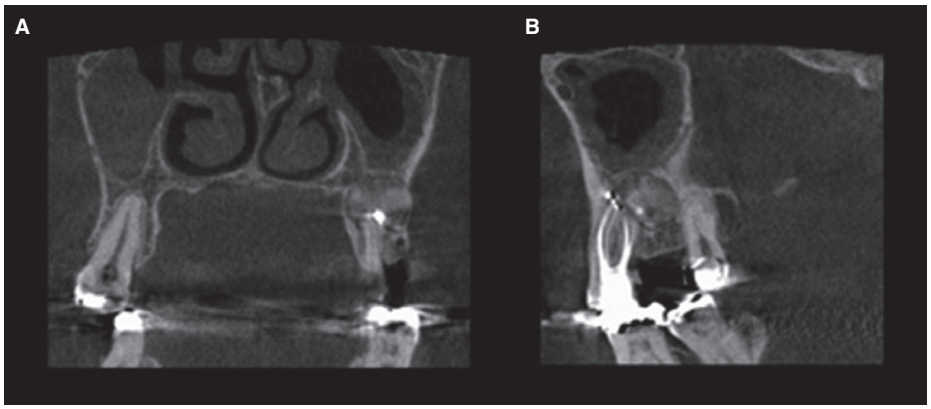

Figure 2 Subsequent CBCT of lesion showing progression in size, and development of radiopaque characteristic of lesion. Date of exposure: 24 October 2016. (A) coronal view; (B) sagittal view.

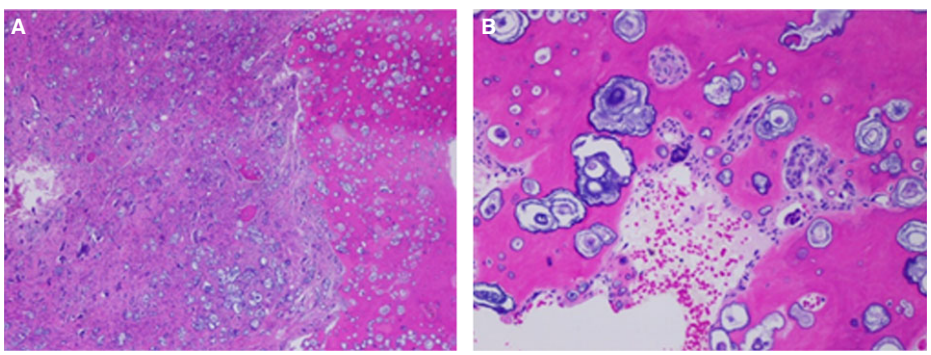

Figure 3 Histopathology from metastatic deposit in left posterior maxillary bone. (A) Bone and intervening fibrous tissue invaded by epithelial structures and psammoma bodies, x4 magnification. Haematoxylin and eosin; (B) Psammoma bodies and micropapillary structures in bone, x20 magnification. Haematoxylin and eosin.

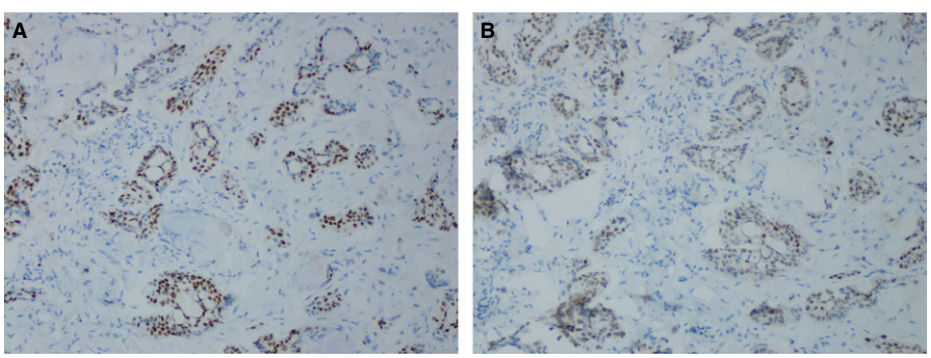

Figure 4 Immunohistochemistry from metastatic deposit in left posterior maxillary bone. (A) ER-positive stain at 20x magnification; (B) PAX-8-positive stain at 20x magnification.

showed slow progression of her pelvic and abdominal disease. At the time of PET, a moderate level of FDG avidity was noted in the left posterior maxilla (Fig. 6), but this was assumed to be physiological (standardised uptake value, SUV, of less than 2.0) and not investigated further.

The diagnosis of the maxillary metastatic deposit of ovarian carcinoma led to restaging by her oncology team. This demonstrated progression of her metastatic disease, with pulmonary, hepatic, peritoneal and new bone involvement. Bony metastases were identified radiologically in the thoracic

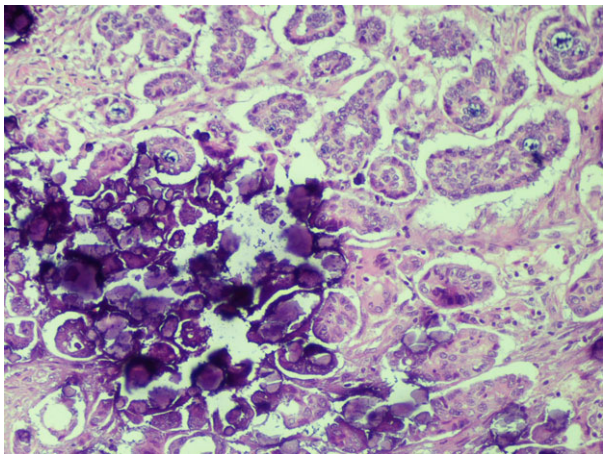

Figure 5 Histopathology from original primary ovarian tumour. Haematoxylin and eosin, 20x magnification.

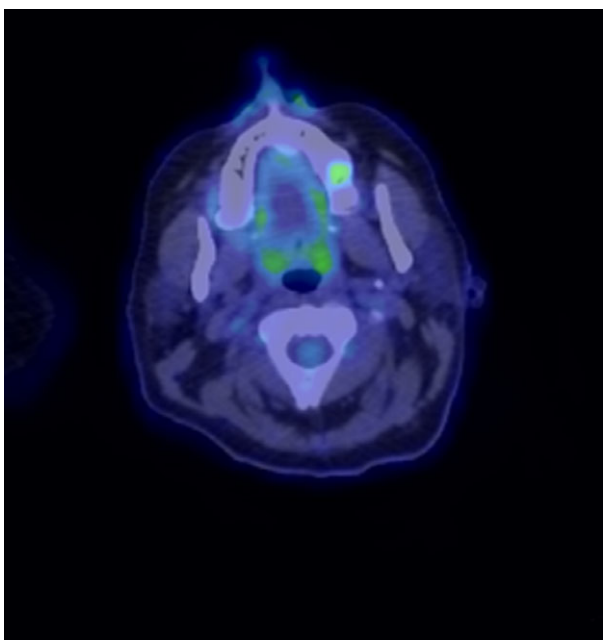

Figure 6 Positive emission tomography fused with computerised tomography to demonstrate moderate FDG uptake in left posterior maxilla in 4 years prior to presentation. Date of exposure: 19 September 2013.

vertebra, sacrum, acetabulum and femoral neck. Her chemotherapy was adjusted accordingly.

Discussion

The mechanism of metastasis to the oral and maxillofacial region is likely to be haematogenous, via the paravertebral venous plexus (Batson Plexus)[3]. Oral metastatic deposits are most commonly seen in patients aged 40–60 years[5]. The average interval from diagnosis of the primary neoplasm to development of maxillary or mandibular metastases is 40 months, similar to the case presented[2].

Osseous metastases to the craniofacial structures predominantly occur in the posterior mandible (80–85%) and usually represent metastatic adenocarcinoma[2]. The primary site is most commonly the breast, lung or kidney[3,6].

Of the osseous metastases to the maxillofacial region, 10% occur in the maxilla and 5% occur in both the maxilla and the mandible[2]. In the maxilla, lesions occur mostly (55%) in the premolar regions. The presence of maxillary metastatic deposits was closely associated with the presence of teeth (93%)[2]. A metastatic deposit within an extraction socket has previously been described[7]. It may be related to increased blood supply and inflammatory milieu.

Radiographically, bony metastases are usually poorly-defined lytic lesions. They may be associated with pain, dysaesthesia, tooth mobility or bony expansion[5] and less commonly with pathological fracture[2]. It is not clear whether the maxillary metastatic lesion seen in this case arose within a field of inflammatory change secondary to dental periapical infection, or whether the radiolucent changes observed in 2013 were already due to metastasis. It was interesting that the radiographic appearance of the lesion apical to the tooth 26 changed from lucent to opaque between 2013 and 2016.

Ovarian tumours very rarely metastasise to soft tissue in the oral and maxillofacial region[4,8]. Ovarian metastasis to the maxillary bone has not previously been described.

The WHO (World Health Organisation) classifies serous carcinomas into low grade and high grade, reflecting their distinct biological differences[8,9]. Low-grade serous carcinoma is an uncommon entity and accounts for approximately 5% of serous carcinomas and 3.4% of all ovarian carcinomas[10].

Like other epithelial ovarian malignancies, serous carcinomas predominantly spread within the abdominal cavity and present at a late stage (75% in low-grade serous carcinoma of the ovary)[9,11]. Distant metastases usually occur during the course of the disease (22%) and are uncommon at presentation (8%)[13]. The median interval between diagnosis of ovarian carcinoma and documented extra-abdominal metastases ranged from 16 months[12] to 44 months[13].

Extra-abdominal metastases from ovarian malignancies are uncommon and spread to bone is especially rare. Two large series identified the following

metastatic sites in decreasing order of frequency. In one series, the lesions metastasised to lung, skin, pleura, brain, mediastinal lymph nodes and bone (one case)[12]; in the other series, the metastatic sites were liver, pleura, lung, central nervous system, skin, extra-abdominal lymph nodes, spleen, bone (2 patients = 1.2%) and breast[13]. The latter study also showed that metastases to certain sites tended to occur at different time periods. Metastases occurred earlier in the liver, brain, skin and later in bone and pleura[13].

A single case of low-grade serous carcinoma of the ovary metastatic to bone has been previously described; however, it involved sternum, ribs, costovertebral joint and vertebra[14].

In general, metastases of any distant primary malignancies to the oral cavity are associated with a poor prognosis, with an overall average survival of 7 months[5]. Regarding epithelial ovarian malignancies, prognosis is poor following documentation of an extra-abdominal metastasis, with a survival of 11–12 months (medial and median respectively)[12,13]. In contrast, the median survival is 32 months without distant metastases[13]. The median survival with bony metastases is 14 months[13].

Stage is a risk factor for developing extra-abdominal metastases[12,13]. Other risk factors are sensitivity of primary tumour to platinum-based chemotherapy[12], grade and lymph node involvement[13].

Prognostic factors include the presence of other sites of disease, interval time between diagnosis of ovarian carcinoma and documentation of distant metastases[13]. Although the predominant patterns of invasion in fatal cases of low-grade serous carcinoma of the ovary were micropapillary (as in our case) and/or complex papillary, cribriform or compact cell nest type, no difference in disease-free survival was demonstrated between the different patterns[11].

In general, an atypical pattern of metastasis is associated with an aggressive pattern of tumour mutation, and carries a poor prognosis.

Conclusion

Clinicians must always have a strong index of suspicion when they encounter an incidental lytic lesion in the maxillofacial structures, further heightened by a history of or risk factors for cancer. There should be a low threshold to biopsy in such lesions, and the pathologist should be alerted to any history of distant malignancy, to avoid misdiagnosis of this rare but clinically significant situation.

Diagnosis of an intraosseous metastatic deposit in the maxillofacial tissues may be the first manifestation of disseminated malignancy and in some cases may lead to diagnosis of the primary neoplasm itself. In general, development of a metastatic deposit in the oral and maxillofacial structures is associated with a poor overall prognosis. Although metastasis of ovarian carcinoma to the maxilla is exceedingly rare, this article demonstrates the importance of vigilance when approaching the diagnosis and management of incidental lesions in the maxilla that are detected on radiographs.

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Statement

This manuscript has not been submitted or published anywhere else while being considered for publication by this journal.

Informed consent

Informed consent was obtained from the individual involved in the study.

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