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CASE REPORT

A possible ovarian carcinoma metastatic in the mandible: diagnostic perspectives

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Abstract

A very rare case of metastatic carcinoma to the left mandible of an elderly female is reported. The primary growth had caused no symptoms apart from the mandibular lesion. Histopathological examination in conjunction with step-by-step use of immunohistochemistry suggested an ovarian origin, and the diagnostic process is discussed. The suggested origin was subsequently supported by computerised tomography scan. The case highlights problems in the diagnosis of oral metastatic disease.

Reviews of the literature on jaw metastases have been published and provide useful information on gender, age, site of metastasis in jaw and site of the primary tumour[1,2]. Despite advances in imaging and diagnostic immunohistochemistry[3], individual cases can be a diagnostic challenge, particularly when the jaw lesion is the sole presenting manifestation of disease. The authors had recently the opportunity of meeting such a challenge that was considered of interest and is reported herein.

Case report

A 61-year-old female was referred by her dentist to the Oral Surgery Department at Liverpool University Dental Hospital. The patient had attended the dentist's surgery complaining of a tender swelling in the edentulous 36 area. The dentist took a periapical radiograph that showed an ill-defined radiolucency between 35 and 37. At the Oral Surgery Consultation, the patient reported that she had been aware of the swelling for approximately 2 months and felt that it was increasing in size and was occasionally painful. The medical history indicated hypoactive thyroid, arthritis and anxiety. Regular medication included propanolol, thyroxine, carbimazole, felodipine, diazepam, vitamins and senna tablets. The patient did not consume alcohol but had smoked 16 handrolled cigarettes daily for the last 40 years. She had recently had a chest X-ray that was normal and had no symptoms in any other part of the body.

On clinical examination, there was facial asymmetry caused by a tender, hard-fixed swelling of approximately 2 × 3 cm, which was present in the area of the left body of the mandible (Fig. 1A). There was no evidence of regional lymph node enlargement. Intraorally, all teeth present were vital, and none were tender to percussion or mobile. There was a palpable expansion in the left buccal sulcus extending from 37 to 35 (Fig. 1B). Cranial nerve examination demonstrated significant paraesthesia of the left inferior dental nerve.

Radiographic examination included panoramic and lower 90° occlusal, radiographic views. The appearances of the former are seen in Figure 1C; the occlusal view showed buccal and lingual bony expansion.

The poorly defined radiographic appearance of the plain films together with the significant paraesthesia and lack of obvious dental aetiology caused serious concern. Computerised tomography (CT) scanning of

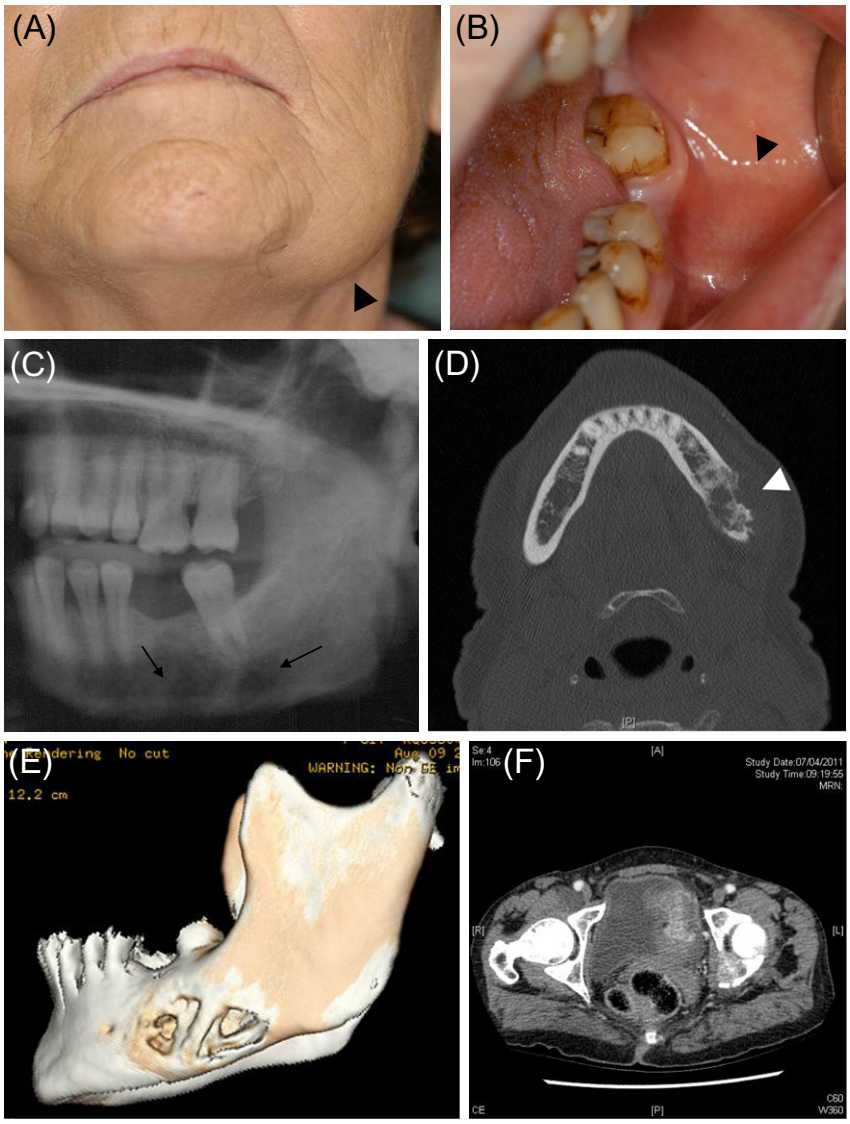

Figure 1 (A) Extraoral swelling (arrowhead). (B) Intraoral appearances. Shallow vestibule (arrowhead) attributable to expanded non-alveolar bone. (C) Panoramic radiograph showing a poorly defined radiolucency (arrows) centred on the left body of the mandible. (D) Conventional computerised tomography (CT) scanning shows variable destruction of cortical bone in the posterior, left mandible (arrowhead). (E) The destruction of the buccal cortical bone as appreciated on three-dimensional CT scanning. The alveolar process is not affected. (F) The abdominal CT scan image showing the ovarian mass.

the area was arranged and showed a permeative lesion affecting the left mandible and variably breaching the cortices at the level of the lower molar teeth but not related to any roots. The lesion measured approximately 3.2 cm in length × 1.7 cm combined with a component of soft tissue swelling adjoining the area (Fig. 1D and E).

An open incisional biopsy was performed under local anaesthesia. A full-thickness mucoperiosteal flap, extending from the 35 to 37, was raised and revealed obvious destruction of the buccal cortical bone. Pieces of soft tissue and bone were removed, fixed in 10% neutral buffered formalin and sent to the Oral Pathology laboratory for examination. The patient had minimal problems post-operatively, although the healing was slow.

The fixed material was routinely processed for histology. Obtained sections showed trabecular bone with foci of neo-ossification, which was variously invaded/destroyed by a non-enacapsulated tumour. The tumour showed epithelial cords and non-rigid tubules set in variously cellular/fibrous stroma. The tubules showed variable microcystic change, intraluminal tufts/micropapillary projections and occasionally contained amorphous eosinophilic material. The tumour cells were cuboidal or polygonal with indistinct boundaries, eosinophilic cytoplasm and densely or lightly staining nuclei. Production of mucin was not obvious. There was moderate cellular pleomorphism/atypia; mitotic activity was inconspicuous, and necrosis was not seen (Fig. 2A and B).

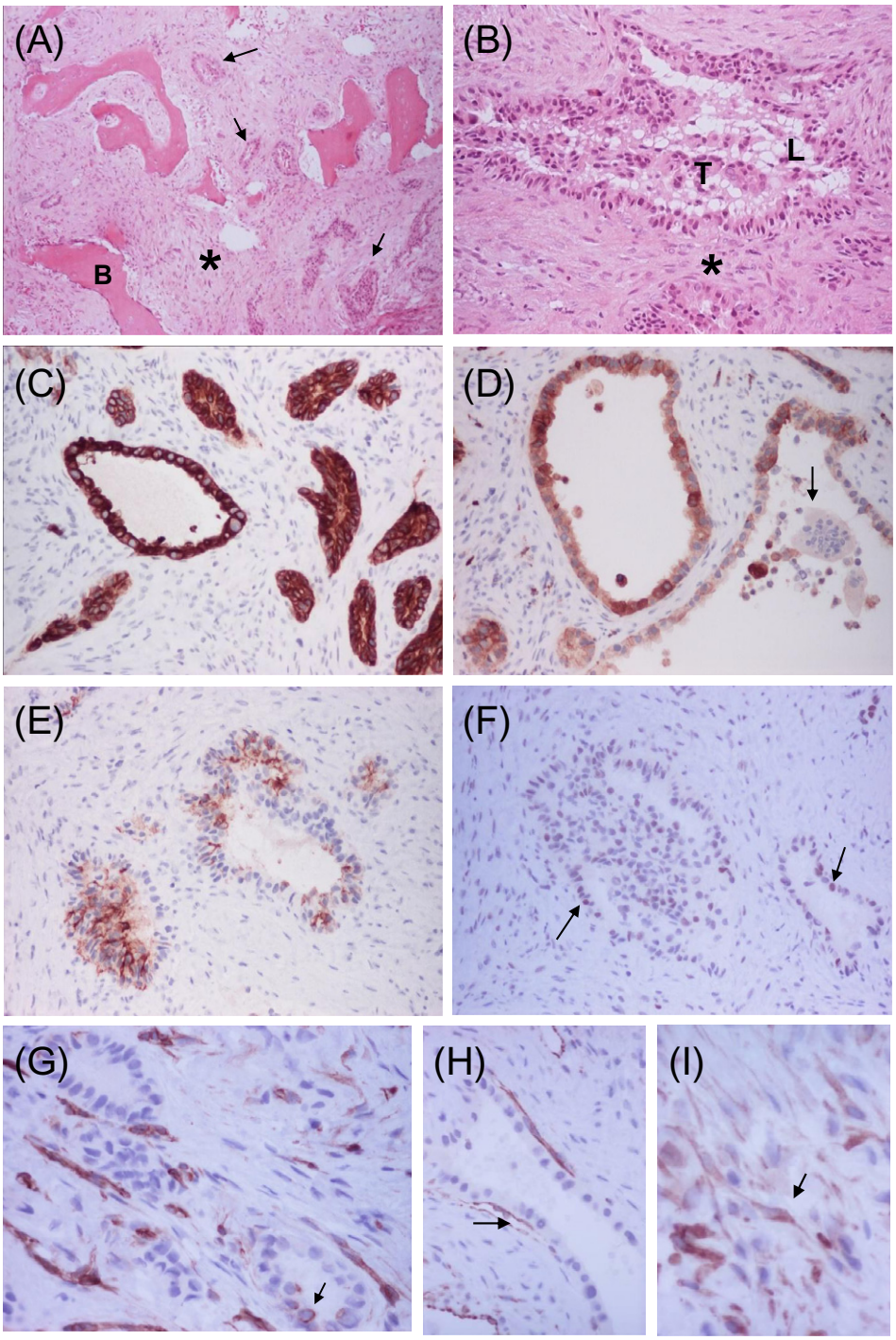

Figure 2 (A) Variously compressed tubular structures (arrows) in stroma (asterisk). B, bone trabeculae (haematoxylin and eosin; objective magnification ×4). (B) Tufted tumour cells (T) are projecting into a microcystic lumen (L). Note hyperchromatic nuclei and variable cellularity of stroma (asterisk) (haematoxylin and eosin, objective magnification ×10). (C) cytokeratin 7 is strongly expressed in the cytoplasm of the tumour cells (objective magnification ×10). (D) Variable cytoplasmic, carcinoembryonic antigen immunoreactivity of tumour cells. The arrow indicates a multinuclear histiocyte in a lumen (objective magnification ×10). (E) Varying numbers of tumour cells expressing cancer antigen 125 are present in the lining of tubules (objective magnification ×10). (F) p53 immunoreactivity. The arrowed cells show strong nuclear staining (objective magnification ×10). (G) Wilms' tumour (WT-1) expression is seen in stromal elements and in the cytoplasm of a tumour cell (arrow) in the lining of a tubule (objective magnification ×20). (H) WT-1 immunoreactive, spindled cells, one of which is arrowed, are subadjacent to the lining of a tubule; the adluminal tumour cells are unstained (objective magnification ×40). (I) Cytoplasmic WT-1 immunoreactivity of a stromal, spindled cell (arrow) (objective magnification ×40).

Table 1 Description of antibodies

Antibody clone	Specificity	Pretreatment	Dilution	Source
1D5	Oestrogen receptor α	Heat-induced epitope retrieval, high pH, EDTA buffer at pH 9.0	1:200	Dako†
PgR 636	Progesterone receptor	»	1:200	Dako
LL002	Cytokeratin (CK) 14	»	1:100	Leica‡
OV-TL 12/30	CK7	»	1:500	Dako
Ks20.8	CK20	»	1:100	Dako
Polyclonal	Carcinoembryonic antigen	»	1:5000	Dako
8G7G3/1	Thyroid transcription factor 1)	»	1:100	Dako
M11	CA-125	»	1:100	Dako
DO-7	p53	»	1:200	Dako
6F-H2	Wilms' tumour 1 Protein	»	1:50	Dako

†Dako UK Ltd, Cambridgeshire, UK.
‡Leica Microsystems (UK) Ltd, Buckinghamshire, UK.
CA, cancer antigen; EDTA, ethylenediaminetetraacetatic acid.

Table 2 Immunoreactivities of tumour cells

Marker	Tumour cells
Oestrogen receptor	–
Progesterone receptor	–
CK14	–
CK7	+
CK20	–
CEA	+/–
TTF-1	–
CA-125	+/–
p53	<20%
WT-1	–/+

+/– The tumour cells are often but not always positive.
–/+ The tumour cells are occasionally/focally positive.
CA, cancer antigen; CEA, carcinoembryonic antigen; CK, cytokeratin; TTF, thyroid transcription factor; WT, Wilms' tumour.

The histological appearances indicated metastatic papillary carcinoma. A step-by-step immunohistochemical investigation (Table 1) was undertaken in an attempt to establish the site of the primary. The results summarised in Table 2 and illustrated in Figures 2C-2I suggested a diagnosis of metastatic ovarian carcinoma.

Following the histological diagnosis, the patient was referred for a CT scan that was reported as follows: 'There is omental caking anteriorly in the abdomen as well as enhancement of the peritoneum and moderate ascites in the upper abdomen. In the left side of the pelvis there is enhancing soft tissue anterior to the uterus which measures 4 × 4 cm in cross section (image 106). I think this is likely to represent a gynae malignancy and is probably the site of the primary tumour. With the ascites and omental caking I think this is likely to be an ovarian primary'. Image 106 is shown in Figure 1F. A subsequent positron emission tomography scan showed possible additional metastases in the mediastinum, left lobe of the liver and left kidney. On these grounds, it was concluded that the patient had stage IV ovarian carcinoma according to the International Federation of Gynaecology and Obstetrics staging system[4]. The patient was referred for palliative care.

Discussion

While the clinical/imaging features of the present case alerted to malignancy, establishing a precise histological diagnosis was not straightforward. The routine histology corresponded to a papillary carcinoma, probably metastatic. The primary site was not obvious as characteristic features were lacking. For example, microcalcifications (psammomma bodies), a feature of ovarian carcinomas[5], were not seen. The step-by-step immunohistochemical approach applied narrowed down the possible sites. Breast, which for women heads the list of malignancies that metastasize to jaws[1,2], was first considered and excluded on the basis of absence of hormone receptors and cytokeratin (CK) 14. Second, the lack of thyroid transcription factor 1 immunoreactivity did not support a thyroid or lung primary, and the CK7 and CK20 profile (Table 2) was inconsistent with colorectal carcinoma[3]. On the other hand, the CK profile together the finding of cancer antigen 125, and carcinoembryonic antigen (CEA) expression tipped the scales towards an origin from the genital tract[3]. Further immunostaining demonstrated p53 and Wilms' tumour (WT)-1 immunoreactivities (Fig. 2F-2I), and on this basis[3,5,6], a diagnosis of metastatic ovarian serous carcinoma, possibly serous, was suggested. Serous ovarian carcinomas are regarded as usually CEA negative and diffusely WT-1 positive, which contrasts with our findings. CEA expression is a feature of mucinous ovarian and cervical carcinomas, but these entities are lacking expression of WT-1 as are gastric, pancreatic and biliary malignancies[3,6], which could have been considered from the

results of the positron emission tomography scan. Although focal, WT-1 expression appears therefore a distinctive feature of our case, supporting the suggested diagnosis of ovarian carcinoma. The diagnosis seems reinforced by the finding of WT-1 immunoreactive, spindled cells subadjacent to tumour tubules and in stroma (Fig. 2G-2I). Possibly, the finding indicates epithelial-mesenchymal transition, a feature of ovarian carcinogenesis[7]. Cytoplasmic immunolocalisation of WT1, as in the present case (Fig. 2G-2I), has been reported in a wide variety of tumours, including ovarian carcinomas[8]. Phenotypic differences between primary growth and metastases are acknowledged and, together with the tubular differentiation, could account for the finding of CEA expression in the present instance. The suggested histopathological diagnosis and the interpretation of the immunohistochemical features as discussed earlier seem consistent with the results of the CT scan.

The location of the present lesion in the molar area of the mandible corresponds to the preferential site of metastases to the jaw bones[1,2]. Such preference may reflect a microenvironment of increased vascularity attributable to healing extraction sockets, focal subclinical chronic inflammation, which may occur with increased frequency in the jaws, and areas of preserved haemopoietic marrow. It is questionable whether these speculations are applicable here. For women with jaw metastases, apart from breast, common sites of the primary growth are the adrenal glands and genital tract, followed by colon/rectum, thyroid and kidney[1,2]. When the individual organs of the female genital tract are separately considered, it becomes obvious that jaw metastases of ovarian cancer are rare. Only 17 cases of jaw metastases from the female genital tract have been reported up to 2006, ovarian carcinoma accounting for two of them[1,2]. The likelihood of skeletal metastases from ovarian carcinoma increases with advanced grade/stage of disease, which is probably reflected in the present case. Estimated incidence also depends on pro-/post-mortem data; a post-mortem figure of 6.2% has been reported, with vertebrae being the most common site[9]. A haematogenous route of spread has been postulated[1], but the significance of epithelial-mesenchymal transition events is increasingly appreciated[7].

The presented case is considered atypical because of the rarity, hidden primary growth and particular histological/immunohistochemical features. It illustrates approaches related to diagnosis and management of oral metastasis, and re-emphasises the need for collaboration between clinicians and pathologists. However, valuable histopathology alone cannot always overcome diagnostic problems. When these arise, the clinician needs to be informed of the difficulties, and the pathological features should be interpreted in conjunction with detailed personal history, clinical examination, imaging and laboratory tests.

This case highlights the need for all oral surgeons to be aware of the presentation of metastatic disease in the jaws, and the necessity for access to advanced imaging techniques and a close relationship with a pathology, or oral pathology department, to facilitate liaison in cases of diagnostic dilemmas.

Competing interests

None declared.

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Ethical approval

Not required.

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