J Oral Pathol Med (2006) 35: 579–81

www.blackwellmunksgaard.com/jopm

CASE REPORT

Mixed testicular germ cell tumor presenting as metastatic pure choriocarcinoma involving the maxillary gingiva

P. Scolozzi[1], N. Marret[1], H. Bouzourene[2], F. Luthi[3], J. Bauer[3], B. Jaques[1], T. Lombardi[4]

[1]*Division of Oral and Maxillofacial Surgery, University Hospital CHUV, Lausanne;* [2]*Institute of Pathology, University Hospital CHUV, Lausanne;* [3]*Multidisciplinary Oncology Center, University Hospital CHUV, Lausanne;* [4]*Laboratory of Oral & Maxillofacial Histopathology, Division of Stomatology, Geneva, Switzerland*

Gingival metastases are infrequent and invariably associated with a widespread disease and a poor prognosis. Because of their unremarkable clinical appearance, they can be difficult to distinguish from more common gingival hyperplastic or reactive lesions, such as pyogenic granuloma, peripheral giant cell granuloma, and peripheral ossifying granuloma. We are reporting here an unusual case of a 36-year-old man with a mixed testicular germ cell tumor presenting as a metastatic pure choriocarcinoma involving the maxillary gingiva, extending from the first left premolar to the left second maxillary molar, mimicking a 'benign looking' gingival mass. Gingival metastases may be the first manifestation of a widespread metastatic disease and therefore particular attention must be paid to gingival lesions associated with atypical clinical symptoms and/or signs.
J Oral Pathol Med (2006) **35:** 579–81

Keywords: choriocarcinoma; germ cell tumors; gingival metastasis; humans; male

A 36-year-old man was admitted to the Emergency Room of the Centre Hospitalier, Universitaire Vaudois, Lausanne, Switzerland in December 2004 complaining of a rapidly progressive dyspnea of 1-week duration. For several weeks, he had complained of chronic fatigue, episodic cough, vomiting, and melena preceded by the appearance of a rapidly growing gingival mass in the upper left maxilla. He also noticed an enlarged right testicular mass that was not painful. A diagnostic work-up was therefore initiated. The chest X-ray showed multiple 'cannonball' lesions in both lungs consistent with the diagnosis of metastases. Thorax and abdomen computed tomography (CT) scans revealed extensive lymphadenopathy including anterior mediastinum, prevascular, left periaortic, and right iliac lymph nodes. A duodenal and a right testicular mass and three subcutaneous nodules were also detected. Brain CT scan disclosed a 1-cm lesion within the posterior limb of the right internal capsule homogeneously enhanced following intravenous contrast administration. Head CT scan revealed a broad-based gingival mass on the upper left premolar and molar area. Ultrasonography showed a 6.5×4 cm heterogeneous mass of the right testicle. Serum tumor markers showed an elevation of both beta human chorionic gonadotropin (βHCG) at 100 000 U/l (normal: <5 U/l) and α-fetoprotein (AFP) at 41 kU/l (normal: <5 kU/l). Two days after the admission, he developed a spontaneous left pneumothorax drained by tube thoracostomy as well as a pericardial effusion with tamponade drained by pericardiocentesis. Cytologic analysis of the pericardial fluid did not reveal any tumor cells. The gingival lesion was approximately $4 \times 3 \times 3.5$ cm in size and appeared as a purple, exophytic, and lobulated mass extending from the first left premolar to the left second maxillary molar (Fig. 1a). A biopsy was performed, and the histopathologic examination (hematoxylin–eosin, original magnification ×100) showed the presence of an ulcerated tumor composed of large multinucleated syncytiotrophoblastic cells and medium-sized cytotrophoblastic cells lying in a hemorrhagic and necrotic stroma (Fig. 2a). The tumor cells were positive for βHCG immunostaining and negative for AFP (Fig. 2b). The diagnosis was consistent with a metastatic pure choriocarcinoma. The patient also underwent an upper gastrointestinal endoscopy revealing a protrusive 1.5-cm bleeding lesion of the first part of the duodenum, which was injected with 10 ml of 1/1000 adrenalin and biopsied. Microscopic examination also revealed a pure choriocarcinoma. The tumor was a stage III according to the simplified AJCC staging classification with poor prognostic factor according to the International Germ Cell Cancer Collaborative Group (1).

In January 2005, the patient received the first cycle of a reduced dose of Platinol and Etoposide followed rapidly by a second course of chemotherapy with a

Correspondence: Dr Tommaso Lombardi, Laboratory of Oral & Maxillofacial Histopathology, Division of Stomatology, 19, Rue Barthélemy – Menn, 1205 Genève, Switzerland. Tel: +41 22382912, Fax: +41 223794082, E-mail: tommaso.lombardi@medecine.unige.ch
Accepted for publication March 21, 2006

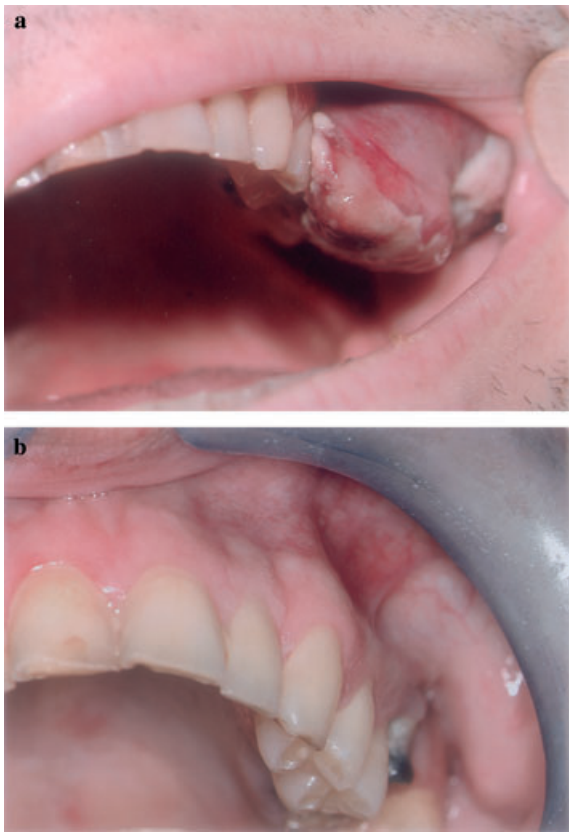

Figure 1 (a) Intra-oral view showing firm, exophytic, and lobulated gingival mass extending from the upper left premolar to the upper left second maxillary molar. (b) Intra-oral post-chemotherapy view showing the complete regression of the mass.

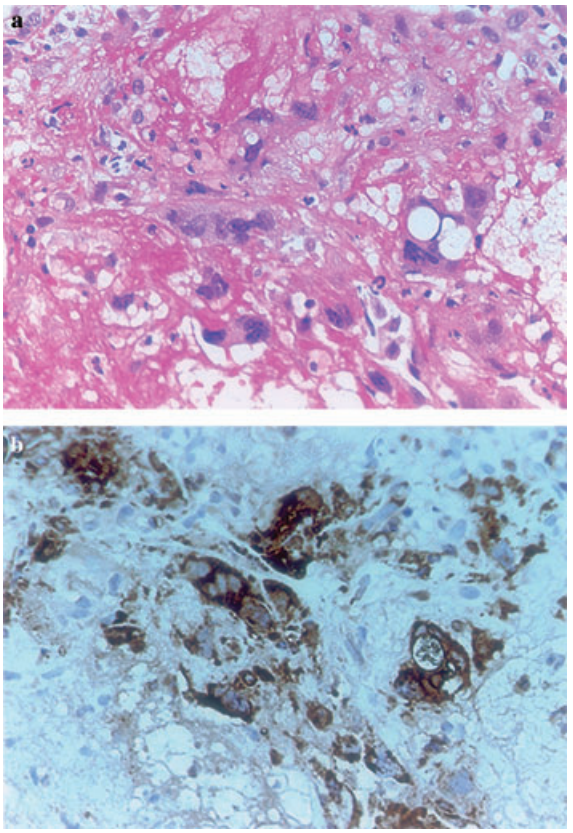

Figure 2 (a) High power view of multinucleated syncytiotrophoblastic tumor cells (hematoxylin–eosin, original magnification ×100). (b) Immunostaining of syncytiotrophoblastic tumor cells with beta human chorionic gonadotropin (βHCG; immunoperoxidase staining, original magnification ×100).

standard dose and by two cycles of Platinol, Etoposide, and Ifosfamide (PEI). After this treatment, the gingival (Fig. 1b), duodenal, and cerebral lesions completely regressed with only a partial response on the pulmonary lesions and no decline of serum βHCG. The patient received three cycles of high-dose Ifosfamide, Carboplatine, and Etoposide together with an autologous stem cell transplantation. In June 2005, the patient underwent a left orchidectomy. The histologic examination revealed an extensive necrosis and hemorrhage in the areas of choriocarcinoma together with small foci of the viable tumor, which was mainly mature teratoma. The final histologic diagnosis was that of a non-seminomatous mixed testicular germ cell tumor (GCT) with choriocarcinoma and teratoma components. In July 2005, pulmonary metastasectomy was planned but unfortunately the pre-operative cerebral magnetic resonance imaging (MRI) showed new lesions. Therefore, cerebral irradiation was initiated, but after 4 days, the patient developed a cerebral hemorrhage and died just after the hospital admission.

Comments

Choriocarcinoma is a highly malignant neoplasm, which is rare within the testis in its pure form but more often encountered as a component of mixed gonadal GCTs. In pure testicular choriocarcinoma, metastatic disease is frequently the presenting symptom as the local tumor may remain very small and non-detectable, whereas the GCTs with a choriocarcinoma component usually present as a painless testicular enlargement. This tumor has a particular propensity to metastasize early by a hematogenous route with the lung being the most common site followed by liver, intestines, and brain (2, 3).

Our case presented two remarkable and unique peculiarities. First is the presentation of a mixed testicular germinal tumor as a 'benign looking' gingival mass as the first clinical manifestation. Secondly, gingival metastasis of a testicular mixed GCT as pure choriocarcinoma. To the best of our knowledge, this clinico-pathologic scenario has not yet been reported in the literature.

Oral metastatic tumors are uncommon, accounting for approximately 1% of all malignant oral neoplasms, and they represent the first sign of metastatic disease in almost 20% of cases (4–6). Most lesions are observed in maxillary bones, especially in the posterior part of the mandible, whereas metastases in the oral mucosa are undeniably less frequent with a clear predilection for the attached mucosa in dentulous, and in the tongue and

alveolar mucosa in edentulous patients (4–6). Gingival metastases from testicular choriocarcinoma are exceedingly rare, with only two cases reported (7). Two important considerations regarding gingival metastases must be emphasized. The first concerns their clinical appearance, which can be misdiagnosed as a benign lesion (pyogenic granuloma, peripheral giant cell granuloma, and peripheral ossifying granuloma). This can delay prompt diagnosis and further treatment, even though the oral metastases usually indicate widespread disease, and treatment is often palliative. The second concerns the fact that they can represent the first manifestation of an undiagnosed tumor and for this reason, a biopsy is mandatory to rapidly obtain a correct diagnosis.

The exact mechanism by which malignant cells reach the gingiva is still poorly understood and remains speculative. Some authors have proposed that the teeth may play an important role in the preference of the metastases for attached gingiva by means of chronic gingivitis. In fact, the rich vascular network of inflamed gingival tissue may entrap tumor cells providing a fertile site for further metastatatic processes (4–6). Metastases in the oral cavity may provoke rapidly unpleasant effects, such as pain, bleeding, disturbances of mastication, and infection and for this reason, palliative treatment is indicated even in the presence of widespread metastatic disease.

In conclusion, it should be kept in mind that a 'benign looking' gingival mass might represent the 'tip of the iceberg' of widespread metastatic disease. Therefore, particular attention must be paid to gingival lesions associated with atypical clinical symptoms and/or signs.

References

1. IGCCCG. International Germ Cell Consensus classification: a prognostic factor-based staging system for metastatic germ cell cancers. *J Clin Oncol* 1997; **15**: 594–601.
2. Ulbright TM. Germ cell tumors of the gonads: a selective review emphasizing problems in differential diagnosis, newly appreciated, and controversial issues. *Mod Pathol* 2005; **18**: 61–79.
3. Gori S, Porrozzi S, Roila F, Gatta G, De Giorgi U, Marangolo M. Germ cell tumours of the testis. *Crit Rev Oncol Hematol* 2005; **53**: 141–64.
4. Ellis GL, Jensen JL, Reingold IM, Barr RJ. Malignant neoplasms metastatic to gingivae. *Oral Surg Oral Med Oral Pathol* 1977; **44**: 238–45.
5. Hirshberg A, Leibovich P, Buchner A. Metastases to the oral mucosa: analysis of 157 cases. *J Oral Pathol Med* 1993; **22**: 385–90.
6. Hirshberg A, Leibovich P, Buchner A. Metastatic tumors to the jawbones: analysis of 390 cases. *J Oral Pathol Med* 1994; **23**: 337–41.
7. Kosem M, Cankaya H, Kaya Z. Choriocarcinoma metastatic to mandibular gingiva: case report and review of metastatic gingival tumours. *J Otolaryngol* 2004; **33**: 310–4.