2. Davis JM, Campbell LA. Fatal air embolism during dental implant surgery: a report of three cases. Can J Anaesth 1990: **37**: 112–121.
3. Lazaridis N, Tilaveridis I, Venetis G, Lazaridou M. Maxillary sinus osteoplasty with vascularized pedicled bone flap. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2008: **106**: 828–832.
4. Lopatin AS, Sysolyatin SP, Sysolayatin PG, Melnikov MN. Chronic maxillary sinusitis of dental origin: is external surgical approach mandatory? Laryngoscope 2002: **112**: 1056–1059.
5. Mason ME, Triplett RG, Alfonso WF. Life-threatening hemorrhage from placement of a dental implant. J Oral Maxillofac Surg 1990: **48**: 201–204.
6. Mason ME, Triplett RG, Van Sickels JE, Parel SM. Mandibular fractures through endosseous cylinder implants: report of cases and review. J Oral Maxillofac Surg 1990: **48**: 311–317.
7. Regev E, Smith RA, Perrott DH, Pogrel MA. Maxillary sinus complications related to endosseous implants. Int J Oral Maxillofac Implants 1995: **10**: 451–461.

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Case Report
Head and Neck Oncology

Clear cell carcinoma of the major salivary glands in an HIV-infected patient

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Abstract. Clear cell carcinoma is a rare type of salivary gland carcinoma. It has a low degree of malignancy and long-term prognosis is favourable after surgical removal. The authors describe the case of a human immunodeficiency virus (HIV) infected 43-year-old woman who presented with a tumour on the floor of the mouth. After biopsy, left suprahyoid lymph node dissection and removal of the submandibular and sublingual glands was performed, followed by radiotherapy. Histologically, the tumour presented the characteristic features of hyalinizing clear cell carcinoma, defined as a variant of clear cell carcinoma by the latest World Health Organization classification. Hyalinizing clear cell carcinoma has a characteristic histological pattern and, to date, there is insufficient information to determine whether both forms behave similarly or differently. The present case illustrates a highly uncommon tumour variant occurring in a HIV-infected patient. To date, this association has not been described in the medical literature. The low grade of malignancy reported for this tumour demands a precise diagnosis and complete tumoral excision.

Keywords: clear cell carcinoma; human immunodeficiency virus; HIV; major salivary glands.

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Human immunodeficiency virus (HIV) infected patients often experience an increase in the size of the salivary glands, due to a wide range of conditions, including inflammatory processes, infections and neoplasms. In some patients, it is the first sign of disease. An understanding of the underlying salivary pathology is necessary to guarantee correct treatment[3]. HIV patients have approximately a 40% chance of developing a malignant disease, a rate that is expected to rise due to their

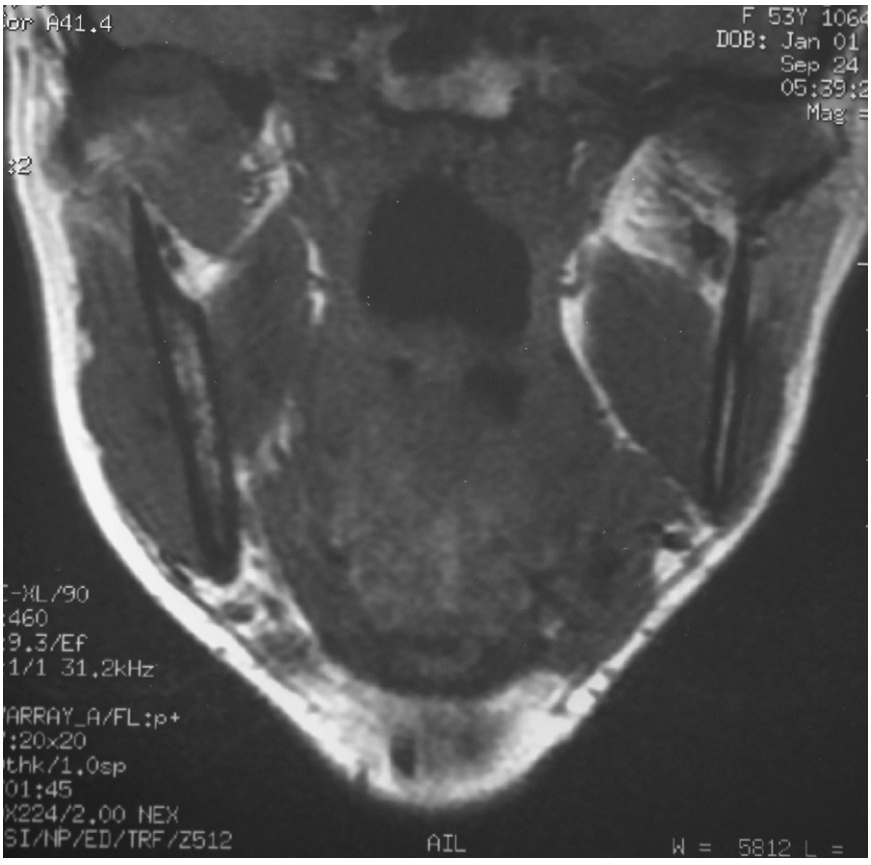

Fig. 1. MRI showing a tumour on the left side of the floor of the mouth.

increased survival[4]. The most frequent head and neck tumours in HIV-infected patients are Kaposi's sarcoma (over 15%) and non-Hodgkin's lymphoma (3–10%)[4,7]. During the last few years, the risk of developing oral squamous cell carcinoma has increased[4].

Clear cell carcinoma (CCC) is a rare salivary gland tumour that shows a low grade of malignancy[1,2]. It has a certain potential for recurrence and metastasis, but long-term prognosis is favourable after removal, with or without radiotherapy[1]. It most often affects minor salivary glands[5] and occurs predominantly in women as a painless, submucosal mass[1,9]. The latest WHO classification has defined it as a malignant epithelial neoplasm composed of a population of monomorphic cells having clear cytoplasm[5]. Many types of salivary gland neoplasms may contain a component of clear cells, but CCC is distinguished by the absence of the typical characteristics of other neoplasms and its monomorphic population of clear cells[5].

Hyalinizing CCC (HCCC) is considered a variant of CCC, distinguished by a densely hyalinized stroma. Both tumours have similar clinical characteristics[5].

The authors describe the case of a HIV-positive female patient who developed HCCC in a sublingual location. It is interesting not only because of the relation between HIV infection and the tumour but also because it concerns a rare morphological variant and a major salivary gland.

Case report

A 43-year-old woman was referred by her dentist for the evaluation of a painless tumour on the floor of the mouth. In 1995, during a laboratory analysis she was diagnosed HIV-positive, and since then she has been receiving antiretroviral therapy (didanosine, lamivudine and efavirenz). She has been asymptomatic with no AIDS-related disorders. The tumour was detected 1 month before surgery. Laboratory analysis confirmed the HIV positivity and showed a normal CD4 count. Complementary studies included orthopantomography, which ruled out bone involvement, and MRI, which showed a tumour on the left side of the floor of the mouth (Fig. 1). No local or regional adenopathies were present. A diagnostic biopsy was carried out and a diagnosis of CCC of salivary gland was obtained. It was decided to perform a left suprahyoid lymph node dissection and to remove the submandibular and sublingual glands. The surgical sample had two nodular areas (of 3.5 and 3.9 cm) attached by a thin fibrous band (Fig. 2). The smallest had a firm, irregular, solid aspect with intermixed adipose tissue whilst the largest one corresponded to the submandibular salivary gland.

Microscopically, the tumoral nodule showed salivary gland parenchyma (sublingual) extensively infiltrated by a neo-

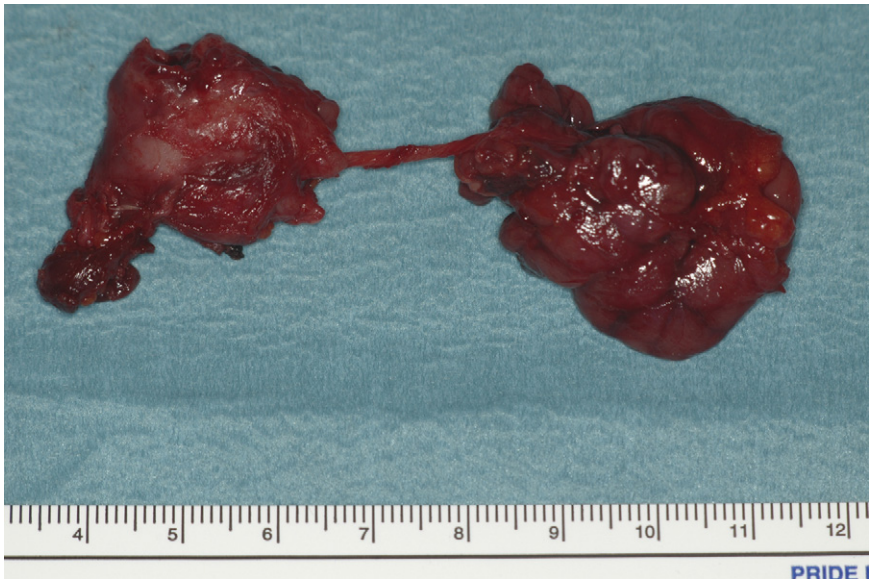

Fig. 2. The surgical sample had two nodular areas (3.5 cm × 3.4 cm × 1.5 cm and 3.9 cm × 3.1 cm × 2 cm) attached by a thin fibrous band.

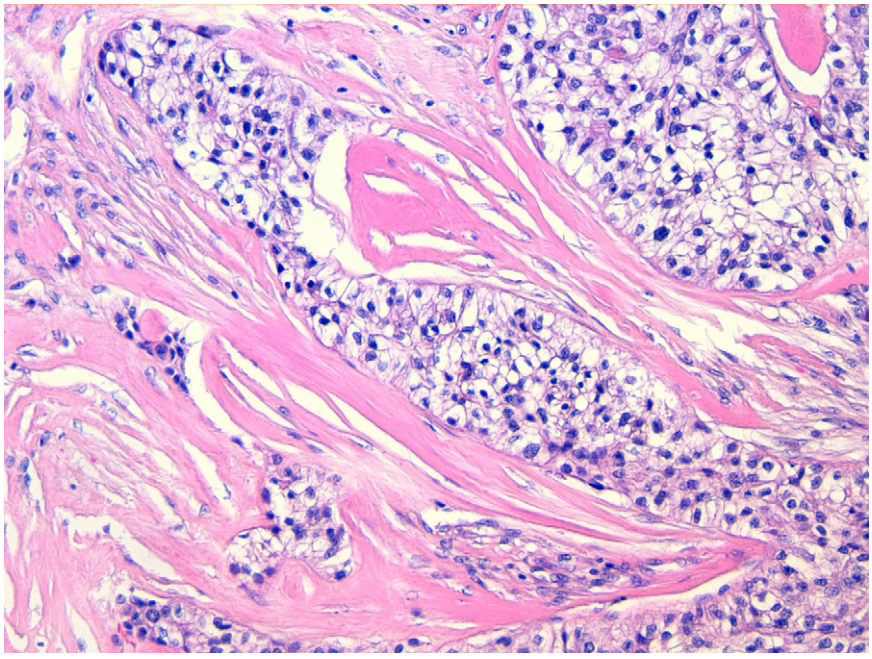

Fig. 3. Variably sized solid nests of clear neoplastic cells are seen in a dense, fibrous stroma consisting of wide areas of hyalinizing connective fibrous tissue (haematoxylin–eosin, 20×).

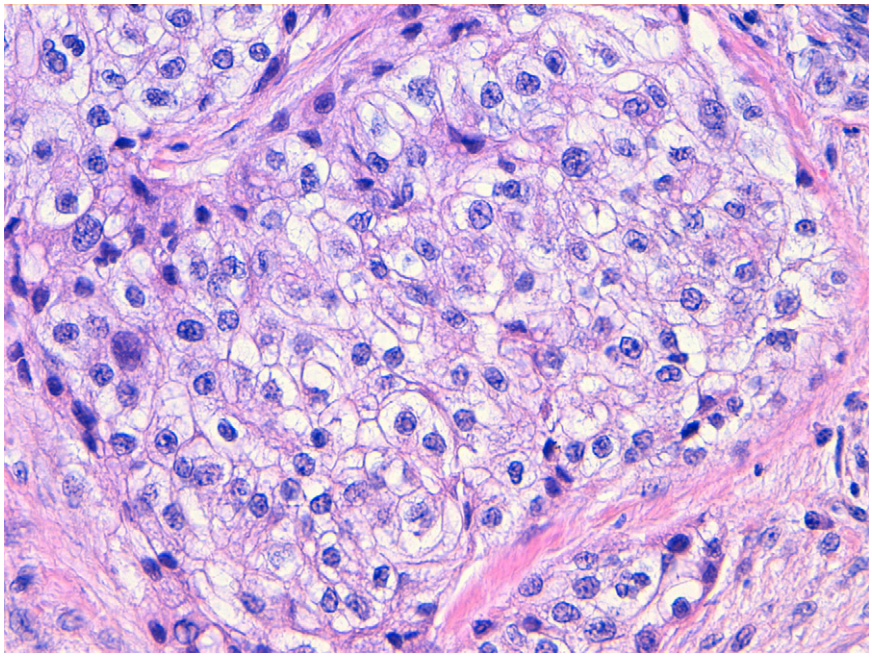

Fig. 4. Tumoral cells were large, polygonal and the majority showed a clear, empty cytoplasm with well defined cytoplasmic membranes (haematoxylin–eosin, 40×).

plastic epithelial growth. It showed a greatest dimension of 2.7 cm. Tumoral cells formed variably sized solid nests and irregular cords. Characteristically, the stroma was dense and fibrous consisting of wide areas of hyalinizing connective fibrous tissue with few fibroblasts and lymphocytes (Fig. 3). The tumoral cells were large, polygonal and the majority showed clear, empty cytoplasm with well defined cytoplasmic membranes (Fig. 4). The cells were moderately pleomorphic with occasional nucleoli and mitotic figures. In addition to clear cells, a few nests showed a population of peripherically distributed, smaller cells with slightly eosinophilic cytoplasm. No squamous, acinar or mucinous differentiation was seen. There was no necrosis, vascular or neural invasion. The neoplasia was not encapsulated and showed an infiltrative growth pattern with focal, microscopic involvement of the surgical limits. The submandibular gland showed no abnormalities. The surgical specimen included two small periglandular lymph nodes that showed no metastases. Tumoral cells showed a positive reaction with PAS staining and immunohistochemical expression of cytokeratins (AE1/AE3). There was no expression of S-100 protein, smooth muscle actin, muscle-specific actin, carcinoembrionic antigen or calponin. Isolated cells expressed epithelial membrane antigen. Histology and immunohistochemistry were characteristic of HCCC involving the sublingual gland. After surgery, the patient received radiotherapy with an external radiation cycle over 6 weeks. She was given 5040 cGY in 28 fractions to the submandibular, cervical and supraclavicular lymph nodes, bilaterally, and 6120 cGY in 34 fractions to the floor of the mouth. There has been no recurrence or metastasis in the 24 months since the first operation.

Discussion

CCC is a rare form of adenocarcinoma of the salivary glands. Based on the experience of the Army Forces Institute of Pathology, CCC accounts for 0.7% of all salivary gland tumours (2% of the malignant)[5]. In an English series, 14 of 608 salivary gland tumours (2%) were composed predominantly of clear cells, causing great difficulties in diagnosis[5].

Approximately two-thirds of CCC occur in the minor salivary glands, generally in the palate, tongue and floor of the mouth. More rarely they involve the parotid gland, submandibular gland or larynx[5]. Patients typically present with a painless mass, and symptoms may last from a few months to several years[5]. Despite its good prognosis, isolated cases with cervical lymph node metastasis have been reported[5,6,8]. The present case is relevant because it involved an HIV-infected patient and a major salivary gland. It is well known that HIV infection results in an increased risk of malignant disease[4]. Since no other descriptions of this precise association have been reported the authors cannot rule out a casual relation. The tumour corresponded to the unusual variant of CCC known as HCCC. This entity was first proposed in 1994 by Milchgrup et al. as a subtype of CCC[5,6,8]. It shows a low grade of malignancy and no myoepithelial phenotype. It is character-

ized by nests and narrow strings of clear cells in a densely hyalinized stroma. The predominant cell population is characterized by its polygonal shape and abundant clear cytoplasm[5]. From a histopathological point of view, the present case was similar to those described by Milchgrub et al.; the tumour cells formed solid nests and irregular strings, in a densely hyalinized stroma.

CCC and its variants are diagnoses of exclusion. Amongst the other salivary neoplasms that may present with clear cells, acinic cell carcinoma, mucoepidermoid carcinoma, myoepithelial carcinoma, squamous cell carcinoma, oncocytoma and epithelial–myoepithelial carcinoma should be considered[5,8]. The possibility of metastases from carcinomas with a clear cell component, mainly renal cell carcinoma, should also be considered[9]. Thorough histological examination of the whole tumour is mandatory before accepting a diagnosis of CCC. Immunohistochemistry is an important aid in diagnosis[2]. In this patient, the tumour showed no evidence of myoepithelial markers, or those usually expressed by renal clear cell carcinoma (vimentin and CD10). Histologically, HCCC shows characteristic features that permit a precise recognition. Tumoral stroma is abundant, dense, hyaline and desmoplastic[5,6,8]. A second population of eosinophilic cells is also commonly seen[5]. An important differential diagnosis in the present case was oral squamous cell carcinoma that may have a clear cell component and may affect HIV-infected individuals, but no histological evidence of squamous differentiation was seen.

Treatment of HCCC is surgical, aiming for complete excision. In this patient, 24 months have passed since surgery and there is no evidence of recurrence or metastasis. In conclusion, the present case illustrates a highly uncommon tumour variant occurring in a HIV-infected patient. To date, this association has not been described in the medical literature. The low grade of malignancy reported for this tumour demands a precise diagnosis and complete tumoral excision.

Competing interest

None declared.

References

1. Cardonada JL. Nuevos tumores—nuevos desafíos. Rev Med Risaralda 2002: **8**: 55–59.
2. Chen TK. Clear cell carcinoma of the salivary gland. Hum Pathol 1983: **13**: 91–93.
3. Chhieng DC, Argosino R, McKenna BJ, Cangiarella JF, Cohen JM. Utility of fine-needle aspiration in the diagnosis of salivary gland lesions in patients infected with human immunodeficiency virus. Diagn Cytopathol 1999: **21**: 260–264.
4. Epstein JB, Scully C. Neoplasic disease in the head and neck of patients with AIDS. Int J Oral Maxillofac Surg 1992: **21**: 219–226.
5. Gneep DR, Henley JD, Simpson RHW, Eveson J. Salivary and lacrimal glands. In: Gneep DR, ed: Diagnostic Surgical Pathology of the Head and Neck. Philadelphia: WB Saunders 2009: 413–562.
6. Manoharan M, Othman NH, Samsudin AR. Hyalinizing clear cell carcinoma of minor salivary gland: case report. Braz Dent J 2002: **13**: 66–69.
7. Peyrade F, Taillan B, Lebrun C, Dujardin P. Cancer chez des patients infectés par le virus de límmunodéficience humaine. Presse Med 1999: **28**: 809–814.
8. Urban SD, Keith DA, Goodman M. Hyalinizing clear cell carcinoma: report of a case. J Oral Pathol Med 1996: **25**: 562–564.
9. Wang B, Brandwein M, Gordon R, Robinson R, Urken M, Zarbo RJ. Primary salivary clear cell tumors—a diagnostic approach. Arch Pathol Lab Med 2002: **126**: 676–685.

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