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CASE REPORT

Primary small cell carcinoma of the nasal cavity with an unusual oral manifestation

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Small cell carcinoma (SCC) is a malignancy that mainly occurs in the lung, with primary lesions in the head and neck being very rare. This neoplasm has an aggressive growth pattern, high recurrence rate, and tendency to metastasize to other sites via the lymphatics and bloodstream. The prognosis of patients with SCC is poor, as the 5-year survival is only 13%. Treatment options include surgical excision, multiple-agent chemotherapy, and radiation therapy. We report a rare case of primary SCC of the nasal cavity presenting as a lesion of the hard palate and describe its clinical, histologic, and immunohistochemical features.
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Case report

A 68-year-old Caucasian woman was referred to the Unit of Oral Medicine and Pathology of the University of Milan in October 2004 with a 3-week history of an annoying mass of the hard palate that prevented her from wearing her superior denture. Her medical history included a hysterectomy, cholecystectomy, appendectomy, and tonsillectomy, and she was seropositive for hepatitis C virus (HCV). She had never smoked or abused alcohol.

Physical examination showed a tender, 5 × 3 cm mass in the hard palate fixed to the underlying tissues, which showed increased consistency, with irregular margins and an ulcerated surface (Fig. 1a). No clinical evidence of lymphadenopathy was present.

Computed tomography (CT) and magnetic resonance imaging (MRI) revealed an ill-defined mass in the main left nasal cavity (Fig. 1b) with bone destruction in the palate for 3 cm laterally.

An incisional biopsy of the oral mass was performed, and microscopic examination showed an infiltrative tumor characterized by a diffuse, solid growth pattern, in the deepest part of the chorion. Hematoxylin and eosin (H&E) stained sections showed small, monotonous, round neoplastic cells with scant cytoplasm and hyperchromatic nuclei (Fig. 2a). Immunohistochemical staining was positive for cytokeratin (CK) (AE1/AE3) (punctuated perinuclear positivity) (Fig. 2c), synaptophysin (SY38) (Fig. 2d), neuron-specific enolase (NSE), and epithelial membrane antigen (EMA) (E29) (Fig. 2b); CD 45 Ro, CD20, CD3, and CD138 were negative. The diagnosis of small cell undifferentiated carcinoma was determined.

To differentiate primary SCC from a metastatic lung SCC, a plain chest X-ray and high-resolution chest CT were performed, which revealed no lesions. In addition, abdominal CT was negative for malignancies.

Given the extent of the neoplasm, the patient was judged inoperable and a monthly chemotherapy schedule of three cycles with a platinum-based regimen (cisplatin and etoposide) was completed between November 2004 and January 2005. Subsequently, she underwent radiotherapy (60 Gy in 30 fractions). After chemo/radiotherapy, complete remission of the tumor was achieved (Fig. 1c,d). The patient was free from tumor until July 2005, when signs of recurrence in the neck lymph nodes were detected during a follow-up visit. One month later, the patient died from bone marrow aplasia, possibly a consequence of chemotherapy. No autopsy was performed.

Comments

Small cell carcinoma (SCC) is a malignancy that mainly affects the lung and accounts for about 20% of all lung carcinomas. Primary extrapulmonary lesions are very uncommon, and very few cases of SCC of the head and neck are described in the literature (1). In this region, the most common sites are the larynx, oral cavity, pharynx, nose, and paranasal sinuses (1). Primary SCC of the nasal cavity and paranasal sinuses is extremely uncommon (2).

The prognosis of patients with SCC is poor, as the 5-year survival is only 13% with a median survival from diagnosis of only 14.5 months (3). In SCC of the head and neck, the prognosis seems to differ with localization: tracheal SCC has the worst prognosis, laryngeal, and hypopharyngeal SCC have intermediate survival, while

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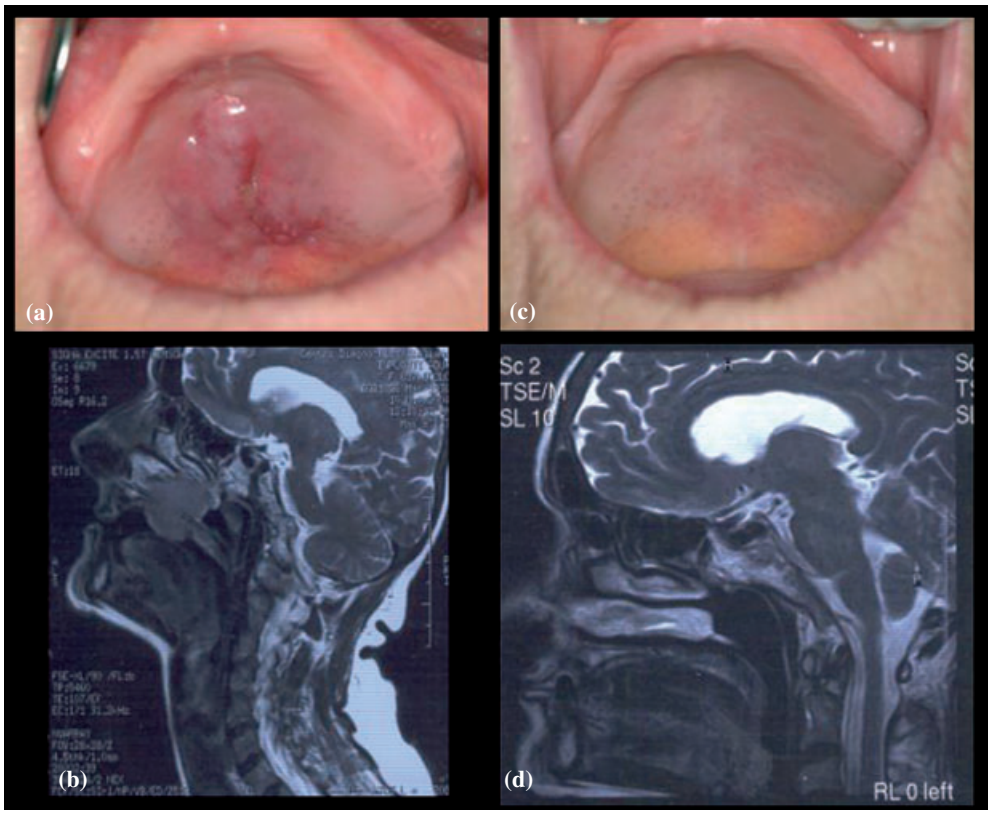

Figure 1 (a) Intraoral appearance of patient at the time of initial presentation. (b) Magnetic resonance image showing the paranasal sinus filled with tumor mass destroying the palatal bone. (c, d) Clinical and radiographic remission of the tumor by chemotherapy.

SCC of the nose, paranasal sinuses, and parotid gland have the best prognosis (4). The lungs, liver, and bone are the most frequent sites for distant metastases from head and neck SCC (4).

The presentation of SCC depends on the site of origin. Salivary gland lesions produce symptoms of a mass lesion in the affected gland. Nasal and paranasal tumors cause recurrent epistaxis, rhinorrhea, and nasal congestion, and oral lesions produce a painful mass and tenderness. In our case, MRI showed a mass involving the entire left nasal cavity and part of the right, together with a small mass in the oral cavity. It was impossible to determine whether this case was a primary SCC of the nasal mucosa with extension to the hard palate or an SCC that arose from the palate (mucosa or minor salivary glands) and spread to the nasal cavity.

The diagnosis of SCC was made from tumor tissue obtained by biopsy. Conventional microscopy is generally insufficient for the diagnosis of SCC, as it shares histological features with other neoplasms, such as lymphomas, sinonasal undifferentiated carcinoma, and olfactory neuroblastoma. An immunohistochemical analysis and electron microscopy are helpful in the differential diagnosis, which includes adenoid cystic carcinoma, lymphoepithelioma, poorly differentiated adenocarcinoma, epidermoid carcinoma, lymphoma, and malignant melanoma (1).

The histopathological aspects of SCC include round to spindle-shaped small cells with hyperchromatic nuclei, inconspicuous nucleoli, and sparse cytoplasm with a high nucleus-to-cytoplasmic ratio. Mitosis and local invasion, including skeletal muscle, vascular, and perineural invasion, are reported frequently. The ultrastructural analysis of the neoplastic cells shows a screwed condensation of chromatin along the nuclear margin with numerous ribosomes and mitochondria in the cytoplasm. Characteristic electron-dense core granules 80–250 nm in diameter are present (4). The immunohistochemical analysis confirms the diagnosis of SCC in the presence of a 'neuroendocrine' phenotype. The battery of immunohistochemical stains includes antibodies to EMA, CK, synaptophysin (SY38), and NSE. Moreover, to differentiate SCC from malignant lymphoma, the presence of the $CD56^{+}/CD45^{-}$ phenotype can be helpful. Our patient exhibited the typical histopathological changes of SCC and was positive for CK, SY, and EMA, and negative for CD45. Furthermore, we differentiated this case from sinonasal undifferentiated carcinoma because the tissue was positive for SY (5), while the fibrillar neurophil and Flexner–Wintersteiner rosettes of olfactory neuroblastoma were absent (6).

As all SCCs have a propensity to metastasize to other tissues, it is important to diagnose any extrapulmonary SCC as a primary site and not a metastasis from another primary SCC (5). To distinguish metastatic pulmonary SCCs, a normal chest radiograph and CT of the chest, or negative bronchoscopy are required (1). In our patient,

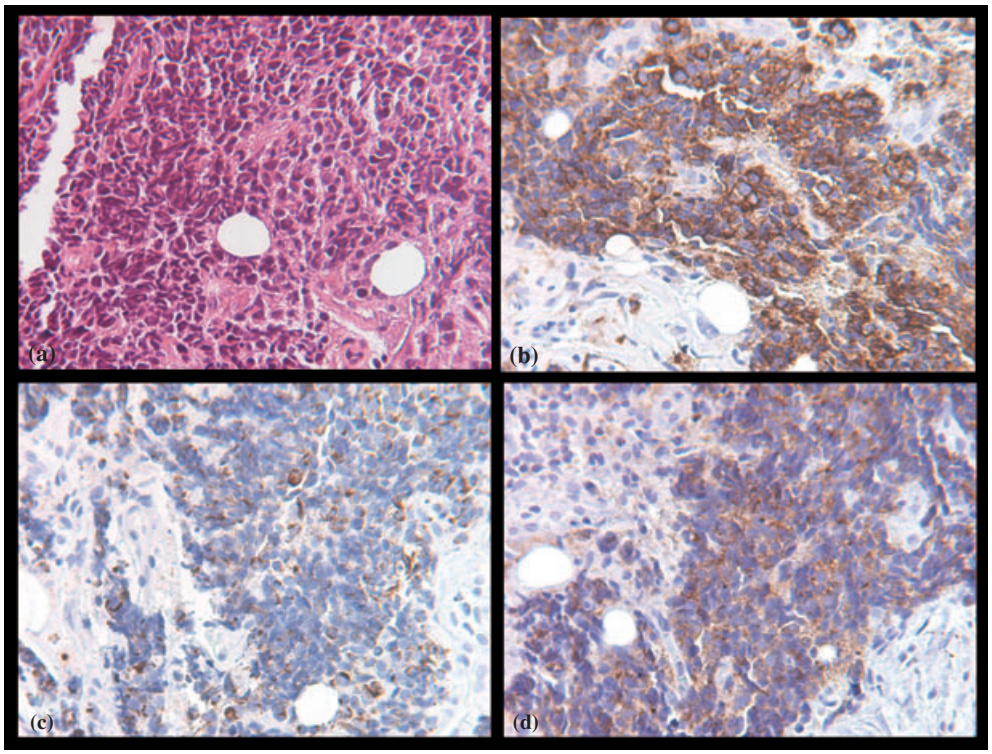

Figure 2 (a) Photomicrograph of the tumor showing neoplastic cells with a high nucleo/cytoplasmic ratio and hyperchromatic nuclei arranged in solid sheet structure (hematoxylin and eosin stain, ×250). (b, c and d) Immunohistochemistry reveals positive reactivity for EMA, cytokeratin (AE1/AE3), and synaptophysin (SY38) (original magnification ×250).

as the chest radiograph and CT of chest and abdomen were negative, the lesion involving the nose and hard palate must be considered a primary neoplasm.

Small cell carcinoma can produce ectopic hormones. In the past, some authors considered this neoplasm an endocrine tumor in the amine precursor uptake decarboxylase (APUD) series. However, other studies have reported that ectopic hormone production is infrequent for SCC, and occurs less frequently in SCC of the head and neck than in pulmonary SCC (1). Moreover, the hormone production by SCC was recently attributed to ectopic secretion or tumor dedifferentiation, and SCC is not considered as an endocrine tumor (4). The ultrastructural granules present in SCC probably reflect the fine structural direction of differentiation in the tumor cells, rather than its origin or possible function (2). In our patient, the hormone secretion was normal.

Although the treatment of this tumor has not been defined clearly, it can require surgical excision of localized disease, radiation therapy to the primary site, multiple-drug chemotherapy, or a combination of these modalities (1). In our case, surgery was considered inappropriate given the dimensions of the mass and its aggressive nature, with the potential for rapid growth and distant metastasis. Combination chemotherapy is considered more effective than the use of a single agent because of additive and synergistic effects. The response rate (a reduction in tumor size exceeding 50%) to chemotherapy is 80% in limited disease and 67% in extensive disease (1). Our patient received chemotherapy (cisplatin and etoposide) and radiotherapy with a temporary complete remission of the tumor. Subsequently, signs of recurrence were observed in the neck lymph nodes, reflecting the poor prognosis of SCC. The reported median survival from diagnosis is only of 14.5 months, and our patient died 9 months after the initial diagnosis.

References

1. Kim SG, Jang HS. Small cell carcinoma of the oral cavity: report of a case. *J Oral Maxillofac Surg* 2001; **59**: 680–4.
2. Perez-Ordonez B, Caruana SM, Huvos AG, Shah JP. Small cell neuroendocrine carcinoma of the nasal cavity and paranasal sinuses. *Hum Pathol* 1998; **29**: 826–32.
3. Weiss MD, Defries HO, Taxy JB, Braine H. Primary small cell carcinoma of the paranasal sinuses. *Arch Otolaryngol* 1983; **109**: 341–3.
4. Baugh RF, Wolf GT, Mcclatchey KD. Small cell carcinoma of the head and neck. *Head Neck Surg* 1986; **8**: 343–54.
5. Mendenhall WM, Mendenhall CM, Riggs CE, Villaret DB, Mendenhall NP. Sinonasal Undifferentiated carcinoma. *Am J Clin Oncol* 2006; **29**: 27–31.
6. Mahooti S, Wakely PE. Cytopathologic feature of olfactory neuroblastoma. *Cancer* 2006; **108**: 86–92.

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