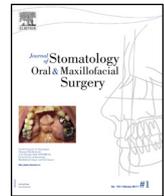




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Case Report

Mandible extensive intra osseous destructive lesion, a diagnostic challenge

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ARTICLE INFO

Historique de l'article :

Received 10 July 2019

Accepted 3 October 2019

Keywords:

Intraosseous verrucous carcinoma

Squamous cell carcinoma

Osteomyelitis

Mandible

ABSTRACT

Intraosseous verrucous carcinoma of the mandible is a rare situation often confused with chronic osteomyelitis. Despite the low aggressiveness of the tumor, prognosis is poor because of delayed diagnosis. We report 3 cases, from three different hospitals, initially diagnosed with a chronic osteomyelitis of the mandible after wisdom extraction. Imaging, bacteriological and histological samples supported each time this interpretation. The 3 patients worsened with intraosseous extension of the lesions and outflow of whitish and purulent debris. Only extensive resection with mandibulectomy allow the pathologists to identify the tumor. Adjuvant radiotherapy or radiochemiotherapy followed the surgery. One patient is in clinical remission. In front of mandible lesion resistant to antibiotic therapy and sequestrum resection, atypical squamous cell carcinoma must be evoked. MRI and CT-scan are not able to distinguish osteomyelitis and intraosseous verrucous carcinoma. Presence of whitish lysed and debris of keratin must draw the attention. Firm evidence must be provided to the pathologist but samples should be wide and thick.

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1. Introduction

Oral verrucous carcinoma (OVC) accounts for 2 to 12% of oral carcinomas. It is mainly located in the inner face of the cheek, gingiva and larynx and preferentially affects men aged from 60 to 70 years. Risk factors are tobacco, alcohol and poor oral hygiene. It can occur as a result of deterioration of premalignant lesions, including oral verrucous leukoplakia, oral lichen planus, oral submucous fibrosis and odontogenic keratocyst [1]. We reported three cases of intraosseous oral verrucous carcinoma from

3 different hospitals and expose the difficulties experienced to achieve diagnosis and patient's management.

2. Case Reports

A 67-year-old male, with no history of tobacco or alcohol consumption or head and neck tumour, was referred to hospital for several episodes of swelling, redness, induration around the mandibular angle, persistent pain, trismus, asthenia and weight loss 3 months after mandibular wisdom teeth extraction. Oral examination showed osseous exposure and signs of chronic infection. Cervico-facial CT-scan revealed a cyst and MRI inflammation of the temporal, masseter and pterygoid muscles, and an abscess near the mandibular canal extending to the left coronoid process with osteolysis. The patient underwent several general anaesthesia to drain the collections, remove sequestrum and perform anatomicopathological and bacteriological swabs. Probabilistic antibiotic therapy was initiated. Each time, no inflammatory syndrome was found on biological examination; bacteriological

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<https://doi.org/10.1016/j.jormas.2019.10.002>

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analysis indicated classical polymicrobial oropharyngeal infection and histologic analysis a nonspecific acute and chronic inflammation of the mucosa with chronic osteomyelitis but without dysplasia. After 3 more months, the patient's condition worsened. A left temporal cutaneous fistula appeared with extrusion of whitish debris (Fig. 1), and paraesthesia in the territory of the inferior alveolar nerve. Dental panoramic showed extensive osteolysis (Fig. 2). MRI and CT-scan showed multiple collections surrounding the mandible, extending to the temporal muscle, tragus and infratemporal fossa, and lysis of the ramus and zygomatic arch (Figs. 3 and 4).

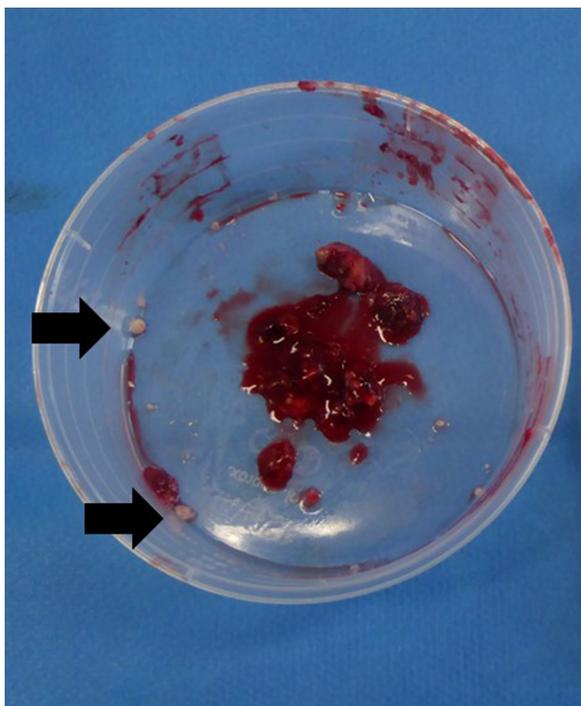


Fig. 1. Whitish lysed debris. Purulent secretion with whitish lysed and debris tissue removed from the mandible angle (black arrow).

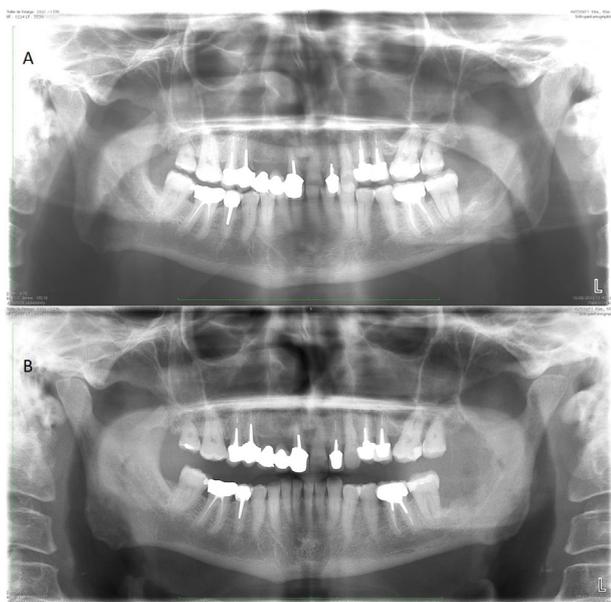


Fig. 2. A. Initial dental panoramic showing only the cavity of tooth 38 extraction. B. After 5 months, dental panoramic showing extensive mandible osteolysis of the left angle and of the whole ramus.

Finally, given the aggressive nature an atypical tumour was suspected. Left hemi-mandibulectomy and neck dissection allowed histopathological analysis led to the diagnosis of a well-differentiated squamous cell carcinoma compatible with a P16 negative verrucous carcinoma. As no mucosal lesion was identified, a diagnosis of intraosseous verrucous carcinoma was established (Fig. 5). Complementary treatment including radiotherapy was decided followed by palliative chemotherapy with Erbitux and Carboplatin because of recurrence.

Summary of the two other patients is reported in Table 1.

3. Discussion

In our case series we reported 3 situations with a similar medical history and without information from the imaging, bacteriology or histology analysis evoking a malignant proliferation.

The differential diagnoses of chronic swelling, trismus, pain and osseous exposure after a third molar extraction, with the presence of non-neoplastic tissue on histologic analysis can be divided into two groups: chronic osteomyelitis (grouping actinomycotic chronic osteomyelitis, diffuse sclerosing osteomyelitis, chronic suppurative osteomyelitis and osteoradio- or osteochemionecrosis) and atypical malignant process (grouping primary intraosseous carcinoma, cuniculatum carcinoma and verrucous carcinoma).

If chronic suppurative osteomyelitis is suspected, microbiological sampling is important for diagnosis and appropriate treatment. However, results are often disappointing owing to salivary contamination [2]. Dental panoramic radiographs show subperiosteal bone formation, CT-scan periosteum reaction, mixed density area, cortical erosion, sequestrum which is the pathognomonic sign and air bubbles in soft tissue, and MRI a mixed sclerotic and lytic pattern in the cortex with T1 and T2 hypo signal, T2 hyper signal of near soft tissue. Diagnosis can also be established with PET-Scan [3]. In case of chronic actinomycotic osteomyelitis, diagnosis is delayed and more often established from histopathological analysis than from bacteriological sampling. Treatment consists of mandible decortication, periosteal disruption and sequestrum removal in combination with long-term targeted antibiotic therapy [4]. Our patients' symptoms were close to those above but the treatment performed did not improve the situation and no bacteria were isolated in spite of the numerous bacteriological and anatomicopathological swabs performed.

If malignant process is suspected, intraosseous cuniculatum carcinoma and verrucous carcinoma should be evoked. Oral carcinoma cuniculatum is a low-grade variant of squamous cell carcinoma. It has a papillomatous keratinized surface with a propensity for local invasion, especially into bone. Clinical presentation is indolent and mimics osteomyelitis or a dental abscess. Imaging shows bone destruction with a moth-eaten pattern [5]. The tumour is composed of well-differentiated epithelial cells that lack cytological atypia and have a blunt papillary/pebbly surface and keratin-filled crypts extending deep into the connective tissue. Pathologic diagnosis is very difficult, especially with small sample because the “cuniculatus” (rabbit burrow) cannot be identified in non-solid tissue or superficial biopsies, highlighting the need for wide and thick biopsies. The difference between the two entities still is under debate in the literature. Some authors considered both as the same entity whereas other described that cuniculatum carcinoma harboured an exophytic as well as an endophytic growth, as opposed to the exclusively exophytic form of verrucous carcinoma. Interestingly, it has already been described similar case reports of intraosseous cuniculatum carcinoma with initial negative biopsies [6].

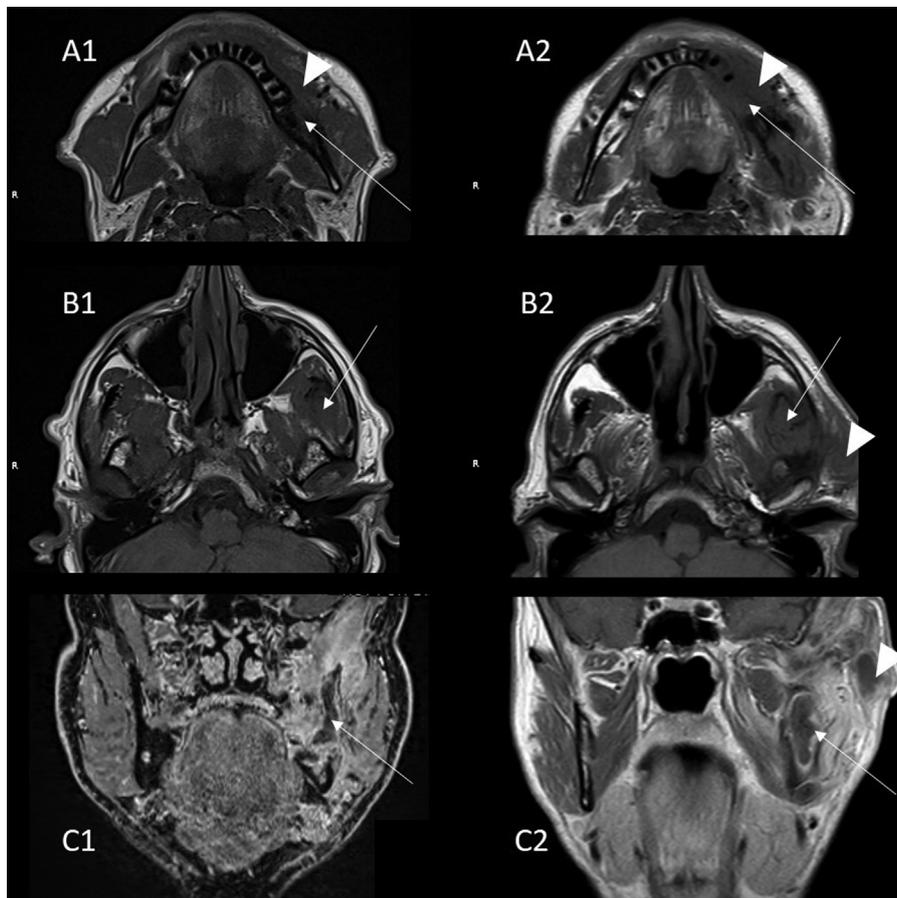


Fig. 3. Left column shows the first MRI, right column shows the second MRI 6 months later. First row (A1 and A2) shows the infiltration of the mandible as a decrease of the T1 signal (thin arrow), more expanded on the second MRI (A2); soft tissue infiltration (arrowhead) is also more pronounced on the 2nd MRI. Second row shows the infiltration of the temporal muscle (thin arrow), and appearance on the 2nd MRI of a temporal subcutaneous mass (arrowhead). Last row (C1 coronal T1 after injection and Fat saturation, C2 coronal T1 after injection) shows the necrotic mass in the coronoid process (thin arrow) and appearance on the 2nd MRI of a temporal subcutaneous mass (arrowhead). MRI performed at 6 months. The coronal view, weighted in T2 shows spread of the abscess to the temporal fossa, lysis and signs of inflammation in the jaw muscles and mandibular bone marrow with large collections involving the temporal fossa (black arrows).

Few documented cases of intraosseous verrucous carcinoma involving the mandible [7] or the maxilla [8,9] are reported in the literature. One case of mandibular verrucous carcinoma with temporal and infra temporal extension is reported [10]. It can occur as a result of deterioration of premalignant lesions but no risk factors or mucosal premalignant lesions were identified. The tumor seemed to proliferate from the bone but it could not be ascertained whether this was due to malignant transformation of an odontogenic keratocyst or secondary to chronic inflammation caused by osteomyelitis. No visible lesion was observed in the oral cavity of our patients but they experienced gradually ascending destruction of the mandibular bone, temporal and infra temporal extensions with secretion of whitish keratosis tissue surrounding bone exposure which are features of the infiltrative form. Verrucous carcinoma is divided into three types: exogenic, cystoid and infiltrative. The first is characterized by local and slow exophytic growth and cauliflower-like warty lesions surrounded by whitish (leukoplakic) mucosa. In contrast, the other two types grow rapidly, forming bean dreg-like white dry keratosis. Histologically, verrucous carcinoma is a low grade, very well-differentiated hyperplastic epithelial lesion, characterized by exophytic growth, with a densely keratinized surface and increased numbers of inflammatory cells. The basement membrane remains intact. Sometimes, however, large sub epidermal extensions with a tumour mass filled with keratin and basement

membrane disruption are observed. The histopathological aspect appears benign with poor mitotic activity and normal maturation. In about 20% of cases, verrucous carcinoma is hybrid with aggressive and invasive squamous cell carcinoma, which destroys the basal membrane. Biopsy sampling often destroys the architecture of the tumor and in our observation, histological diagnosis was established from the excised tumor. Imaging are also confounding, The MRI appearance (low T1 signal of the mandible, extension to the surrounding tissue as a non-enhanced mass with peripheral enhancement only) as well as the CT-scan appearance of the bone (type 2 Lodwick lytic lesion) can be seen in both neoplastic or infectious conditions. Firm evidence of suspicion of verrucous carcinoma must be provided to the pathologist and samples should be wide and thick to help guide diagnosis.

First intention management of VC is tumour resection with a histological margin of a least 5 mm, to avoid the risk of recurrence [11] however complete resection is rarely possible. Neck dissection is controversial but not recommended in the absence of node extension [12]. Hypertrophic nodes seen on CT-scan are mostly an inflammatory reaction [13]. Radiotherapy can cause anaplastic transformation with early recurrence. However, it can be indicated after surgery if margins are involved or in case of recurrence and in patients contraindicated for surgery. Complementary surgery is to be preferred if margins are involved. Survival rate is higher after surgery alone than in combination with adjuvant radiotherapy [13].

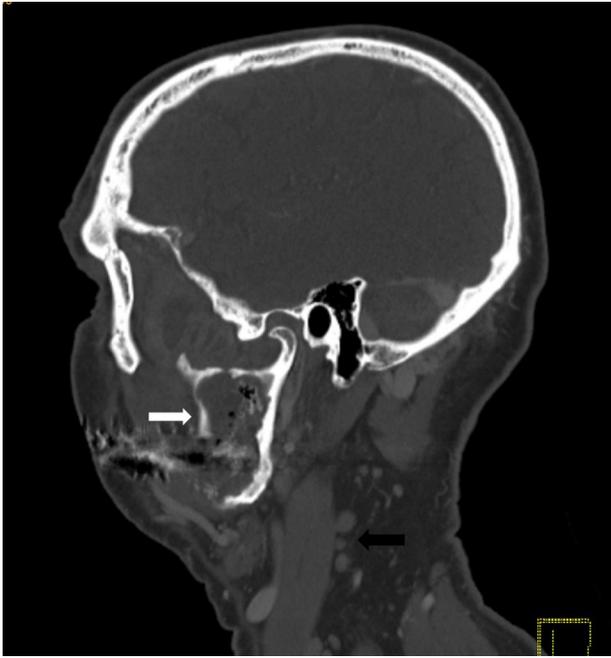


Fig. 4. Injected Cervico-facial CT-scan at 6 months. The sagittal view shows osteonecrosis of the two third posterior parts of the corpus and of the whole ramus except the condyle with sequestrum, cortical interruptions and loss of spongiosa trabeculation (white arrow). Several nodes along the left jugular and carotid axis are also observed (black arrow).

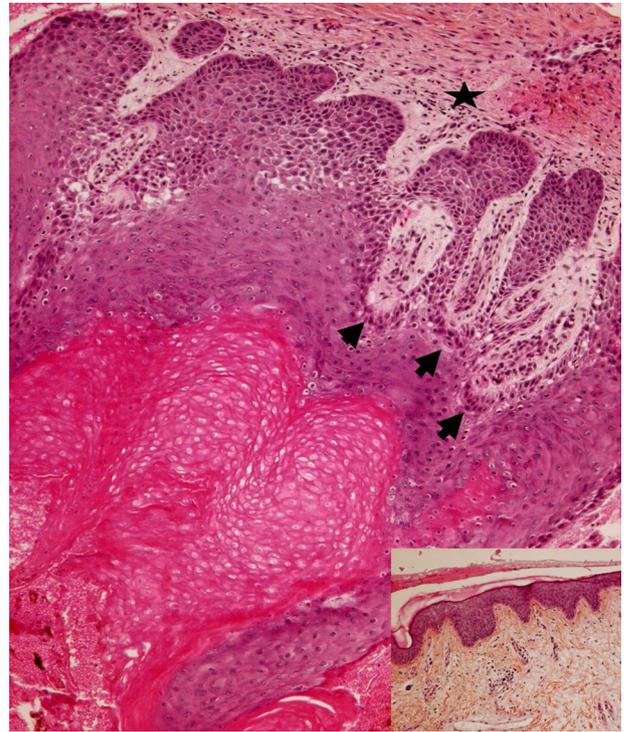


Fig. 5. Histopathological slice. Hematoxylin and eosin-stained ($\times 100$) section showing projection and invaginations of well-differentiated squamous epithelium lacking cytological atypia and mitotic activity (black arrow) with hyperkeratotic surface (black star) in the stroma. In the box below is reported a normal mucosa.

Table 1
Patients characteristics, diagnosis, treatment and evolution.

	Patient 1	Patient 2	Patient 3
Patients characteristics			
Sex	Male	Male	Male
Age (year)	67	65	60
Comorbidity			
Tabacco	No	No	No
Alcohol	No	No	No
Poor oral hygiene	No	No	No
Premalignant lesions	No	No	No
Tooth involved	38	48	48
Clinical examination			
Lesion localisation	Angle, ramus	Ramus, horizontal branch	Angle, ramus
Mucosal lesion	No	No	No
Fistula localisation	Mandible, temporal	Mandible, temporal	No
Whitish and keratotic tissue	Yes	Yes	Yes
Imaging (CT-scan and MRI)			
Localisation of abscess	Infratemporal and temporal space	Infratemporal and temporal space	Masseter and coronoid process
Localisation of osteomyelitis	Ramus Horizontal branch coronoid process	Ramus Horizontal branch	Ramus Horizontal branch coronoid process
Anatomopathological results			
After abscess drainage and sequestrectomy	No malignity		
After mandibulectomy	Accordance to chronic osteomyelitis Very well differentiated SCC compatible with intraosseous verrucous carcinoma		
Adjuvant treatment			
Radio-chemiotherapy	Yes	No	Yes
Radiotherapy	No	Yes	No
Palliative chemotherapy	Yes	Yes	No
Evolution			
Disease-free survival (months)	0 month	0 month	72 months
Overall survival (months)	16 months	32 months	78 months

4. Conclusion

Chronical “osteomyelitis” without any bacteria isolated and with secretion of whitish keratosis tissue should lead to think about intraosseous verrucous carcinoma. Firm evidence must be provided to the pathologist but samples should be wide and thick. The best treatment seems to be complete surgical resection.

Disclosure of interest

The authors declare that they have no competing interest.

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