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# Primary intraosseous carcinoma arising in dentigerous cyst: Case report

Alix Marchal\*, Éric Gérard, Rémi Curien, Geoffrey Bourgeois

Department of Oral Surgery, Regional Hospital Center of Metz-Thionville, Mercy Hospital, France

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## ABSTRACT

**INTRODUCTION:** Carcinomas arising in odontogenic cysts are uncommon. Malignant transformation of a dentigerous cyst is a rare observation. A primary intraosseous carcinoma from a dentigerous cyst in a 69 years old female is presented in this case report.

**PRESENTATION OF CASE:** The patient initially consulted for pain in the mandibular left molar region. Primary investigations firstly showed a probably benign lesion but immunochemistry analysis finally revealed a squamous cell carcinoma arising in a dentigerous cyst. An extension assessment was performed and no evidence of lymph node extension or distant metastasis were found. A non-interrupting mandibular bone resection without neck dissection was realized. The patient made a good recovery after surgery without postoperative complication. No clinical symptoms or sign of local recurrence or metastasis was detected after 17 months follow-up.

**DISCUSSION:** PIOC arising in a dentigerous cyst is a rare observation. PIOC from odontogenic cysts have an incident rate of 0,3 to 2% and only 16%–51% of them are PIOC from dentigerous cyst. There are no clinical or radiological pathognomonic characteristics. They often look like benign lesion and the diagnosis is often made fortuitously. A surgical excision with clear margin is the cornerstone of treatment. Clinical and radiological follow-up of the patient is recommended.

**CONCLUSION:** This case underlines the importance of a systematic and careful microscopic analysis of any lesion, even benign at first sight. Surgeons and pathologists should be aware of the malignant potential of odontogenic cysts. This can modify the surgical management and the follow-up of the patient.

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## 1. Introduction

Dentigerous cysts are the second most common odontogenic cysts of the jaws and the most common developmental cysts. They develop around the crown of an impacted or partially erupted tooth by expansion of its follicle with accumulation of fluid between the reduced enamel epithelium and the crown of the tooth at the cemento-enamel junction. Permanent third molars and maxillary canines are the most frequently associated teeth. Radiographic appearance is not unique or specific but frequently presents as well-circumscribed, spheroid, corticated, unilocular radiolucency centered on the crown of a retained tooth [1].

Without treatment, evolution of the cyst is exclusively local, with expansion and destruction of the peripheric structures. Malignant degeneration is extremely rare. We present here the case of a primary intraosseous carcinoma (PIOC) arising in a dentigerous cyst.

## 2. Presentation of case

A 69 years old female consulted for pain in the mandibular left molar region. No extraoral swelling was observed. Clinical examination of the left lower third molar region revealed no inflammatory signs on the underlying mucosa. A panoramic radiograph disclosed an impacted mandibular left third molar with an unilocular radiolucency around the crown (Fig. 1). A Cone Beam Computed Tomography (CBCT) confirmed the presence of a unilocular lesion surrounding the crown of the mandibular left third molar. The lesion expands into vestibular and lingual cortical bones. It extends downwards thereby entering into contact with the left inferior alveolar nerve (Fig. 2). However the patient showed no clinical signs of associated neuropathy. All these informations pointed to, firstly a dentigerous cyst, secondly an odontogenic keratocyst, and thirdly an ameloblastoma. Surgical treatment performed under locoregional anesthesia included the avulsion of the mandibular left impacted third molar and enucleation of the cyst. Histological analysis using HES (hematoxylin-eosin-safran) revealed a cyst with squamous epithelium compatible with a dentigerous cyst. The cyst's wall was infiltrated by squamous cells with moderately large nucleus and abnormal mitotic activity. On

\* Corresponding author at: 6 rue Drouin 54000 Nancy, France.  
E-mail address: [a.marchal@chr-metz-thionville.fr](mailto:a.marchal@chr-metz-thionville.fr) (A. Marchal).

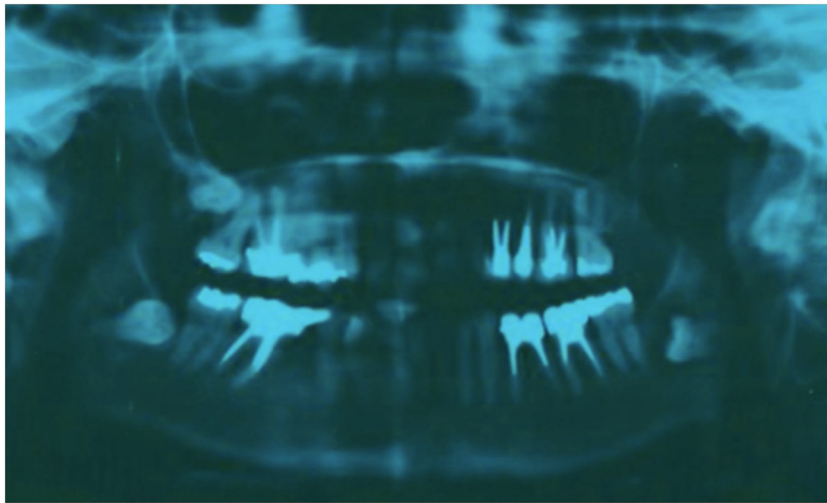


Fig. 1. Panoramic radiograph revealing an impacted mandibular left third molar with a well-defined, round, unilocular radiolucent lesion surrounding the crown.

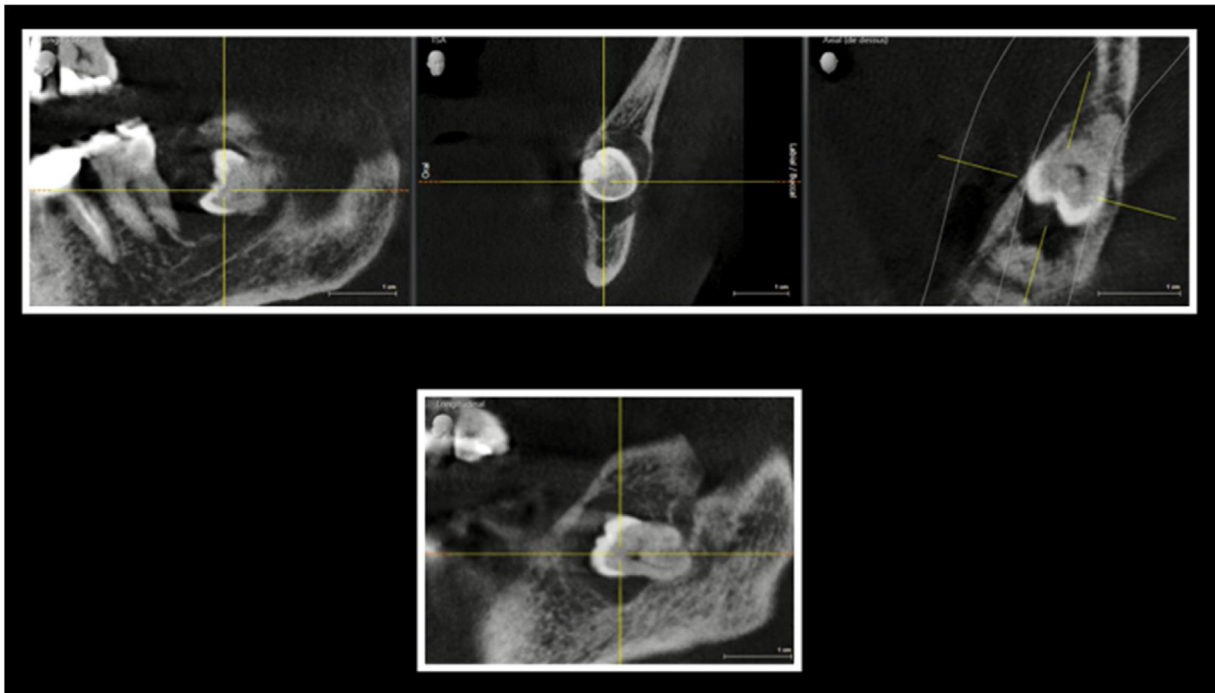


Fig. 2. CBCT showing the presence of an unilocular lesion surrounding the crown of the mandibular left third molar. The lesion expands into vestibular and lingual cortical bones. It extends downwards thereby entering into contact with the left inferior alveolar nerve.

immunochemistry analysis, tumoral cell proliferation expressed P40 marker and Ki67 rated at 20% (Fig. 3). A second immunochemistry analysis has been performed. P53 was intensely expressed in the infiltrating part of the tumour. This expression was limited to the deep layers. In accordance with cellular atypia, abnormal mitoses and P53 expression, the second analysis demonstrated the presence of a squamous cell carcinoma arising in a dentigerous cyst.

Postoperatively, a cervico-facial MRI and cervico-thoracic CT with contrast were performed and revealed no metastases in the cervical lymph nodes.

After multidisciplinary concertation, surgical retreatment with non-interrupting mandibular bone resection in macroscopically healthy area without neck dissection was decided. The sacrifice of the left mandibular second molar was necessary. The lower alveo-

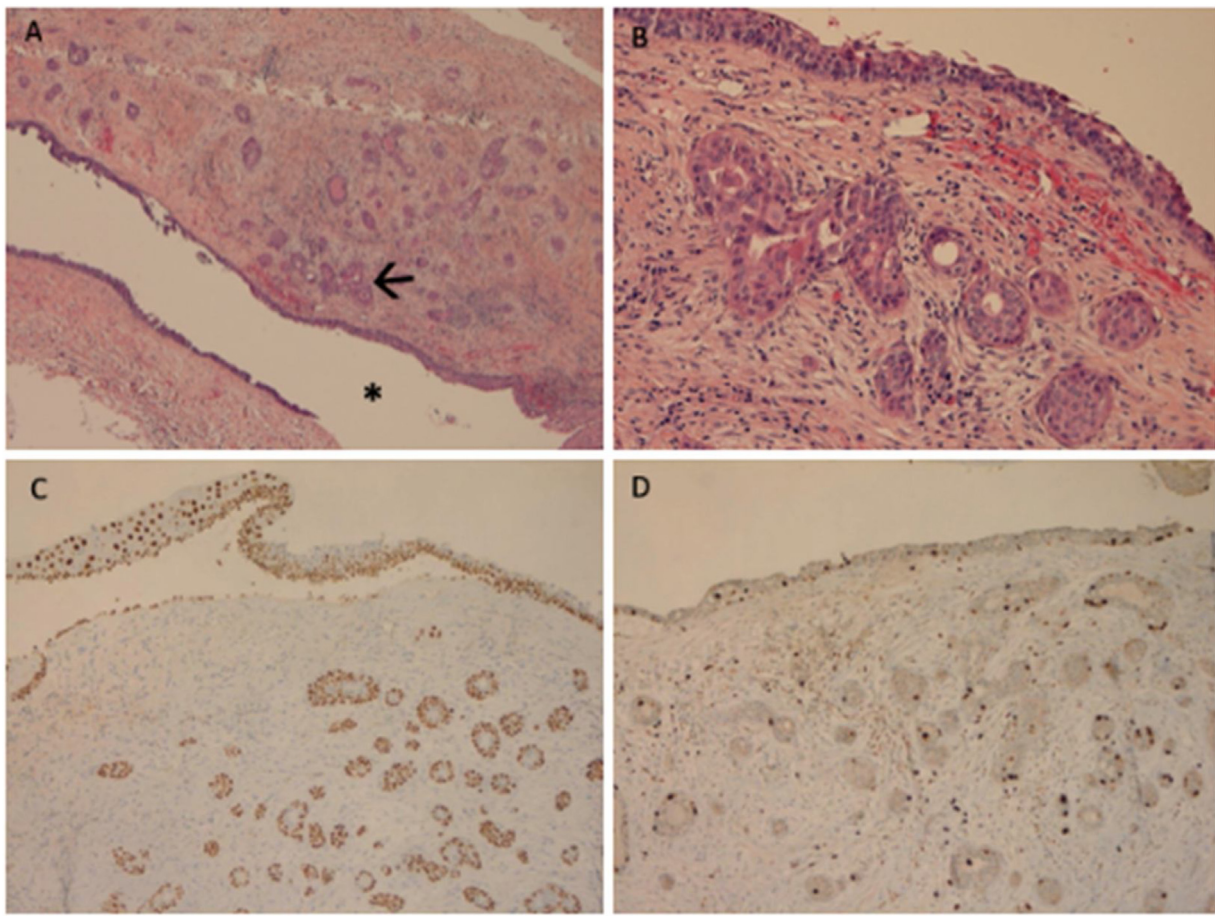
lar nerve has been preserved. The microscopic examination of the postoperative sample did not find any tumour residue. Therefore, no additional treatment was decided but quarterly clinical combined with CT monitoring was planned.

The operative suites has been simple. We observed a complete healing of the operative area, without aesthetic damage. The patient did not feel any sign of dysesthesia.

No clinical symptoms or sign of local recurrence or metastasis was detected after 17 months follow-up.

### 3. Discussion

PIOC arising in dentigerous cyst is extremely rare. After cross-checking the last 3 reviews on the subject, only 35 cases have been reported from 1958 to 2015 [2–4]. In addition two other



**Fig. 3.** **A** Cystic light (\*). Cystic wall with islets which represent carcinological infiltration (←) (HES x25). **B** Centered section of the cystic wall infiltrated by the carcinoma (HES x100). **C** Immunohistochemistry : nuclear expression of p40 by tumor cells infiltrating the cyst wall (x100). **D** Immunohistochemistry : Ki67 staining at 20% in hot spot (x100).

cases were published in 2017 and 2020 in English literature [5,6].

According to the latest WHO Classification of Tumours made in 2017, the term « Primary intraosseous carcinoma » was defined as a central jaw carcinoma that cannot be categorized as any other type of carcinoma. It is assumed to arise from odontogenic epithelium. Some cases arise in odontogenic cysts or other benign precursors. Primary intraosseous squamous cell carcinoma, primary intra-alveolar epidermoid carcinoma and primary odontogenic carcinoma are synonyms of PIOC [7].

PIOC arising in an odontogenic cyst is a rare observation with an incident rate of 0,3 to 2% [3]. Only a hundred cases have been published [8]. Therefore, the appearance of a PIOC arising in a dentigerous cyst in particular is even more rare : approximately 16% of PIOC arising in odontogenic cyst according to Bodner et al. [8] and up to 51% for other authors [9]. The pathogenesis of PIOC is not yet fully understood, however, it is commonly accepted that a period of chronic inflammation can be a predisposing factor for the malignant transformation of odontogenic cysts [8].

Dentigerous cysts occur within the age range of 20–30 years and squamous cell carcinoma arising in dentigerous cysts are often diagnosed in age range of 50–60 years with a mean age of 57 years [3]. Therefore, we can suggest that PIOC have a relatively slow mode of development, as is observed in the case discussed here.

The male to female ratio of 2,3:1 shows men are more involved than women. This observation reflects the prevalence of dentigerous cysts between men and women.

The mandible is more frequently affected (86.7%) [4] with a predilection for the lower 3rd molar [3] as occurred in this case. Clinically, PIOC arising in the epithelium of a dentigerous cyst are mostly painless. When clinical signs do appear, swelling is the most common sign (43.4%) followed by pain (13.3%) and nerve impairment (10.0%) [4].

Radiological characteristics are often non specific and do not suggest a malignant transformation in first place. Indeed, it frequently appears as a well-circumscribed unilocular radiolucent lesion variable in size and shape. These images mainly suggest benign lesions such as dentigerous cyst, unicystic odontogenic keratocyst or ameloblastoma [1,4]. The diagnosis of squamous cell carcinoma is often made fortuitously during a systematic microscopical examination, as it is presented in this case.

The extent of the carcinoma should always determine the therapeutic approach. When carcinoma is in situ, further surgery may be postponed albeit with regular clinical and radiological follow-ups [3,8]. When carcinoma is infiltrating, a surgical revision is indicated. Depending on the extent of the tumour, surgical resection with wide margins is performed. It often involves radical excision with mandibulectomy or maxillectomy which is sometimes associated with neck dissection. Indeed, a cystic enucleation without any additional radical treatment increases the risk of local recurrence [10].

After resection with positive margins or with carcinoma in the surrounding bone, surgical management can be completed by radiotherapy or chemotherapy [4,8].

In this case an additional assessment using cervico-thoracic CT with contrast and cervico-facial MRI were performed. No secondary metastatic location was found. In view of the invasive nature of the carcinoma it was decided therefore to carry out a radical surgical revision with non-interrupting large alveolar resection without dissection of the neck as there was no lymph node involvement. Actually, cervical metastases stemming from PIOC arising in odontogenic cysts are very rare at the time of diagnosis [4,8,10]. The examination of the resection specimen did not find any residual carcinoma, therefore no other complementary treatment was carried out. It was decided a quarterly follow-up plan with lymph node examination and CT. Although real prognosis of these malignant tumours is not easy to evaluate due to the heterogeneity of cases, studies and follow-up periods. Nevertheless, there is an overall survival rate of patients with PIOC arising in the wall of a dentigerous cyst of 64.7% at 2 years and 28.6% at 5 years according to Gay-Escoda et al. [4], and 40% at 5 years according to Odell and al [7]. This case is reported in line with the SCARE guideline [11].

#### 4. Conclusion

The diagnosis of PIOC arising in dentigerous cyst is extremely rare. Surgeons have to be aware about the malignant potential of odontogenic cysts. Therefore, even in the absence of clinical or radiological pathognomonic characteristics, systematic microscopic examination of a cystic enucleation piece should be undertaken. It is important for the pathologist to recognize this type of malignant transformation in order to conduct a careful microscopic study. A malignant transformation can modify the surgical management and the follow-up of the patient.

#### Conflicts of interest

All authors have nothing to disclose.

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#### Ethical approval

There were no ethics approval required for this case report.

#### Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

#### Author contribution

Alix Marchal: Study design, data collection, data interpretation, writing the paper.

Eric Gérard: Data interpretation, reviewing the paper.

Rémi Curien: Data interpretation, reviewing the paper.

Geoffrey Bourgeois: Data collection, data interpretation, reviewing the paper.

#### Registration of research studies

Not applicable.

#### Guarantor

Geoffrey Bourgeois.

#### Provenance and peer review

Not commissioned, externally peer-reviewed.

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