Primary intraosseous carcinoma, NOS arising from a dentigerous cyst: A case report

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Abstract

Introduction: Primary intraosseous carcinoma, NOS (PIOC), is a rare malignancy which has been described in the maxilla and mandible often arising from odontogenic cysts. The authors describe a case of PIOC arising from a dentigerous cyst associated with a lower right third molar in 78-year-old male.

Aims: To demonstrate that seemingly innocuous pathology may represent a malignant process. In the presence of 'red-flag' symptoms, one must consider alternative diagnoses and action them accordingly.

Findings and Discussion: The initial clinical and radiographic features suggested a common innocuous presentation, although other features which presented later were suggestive of malignancy. PIOC is treated conventionally by radical surgery to achieve a disease-free margin with adjuvant neck dissection. In the case described, the patient underwent hemi-mandibulectomy with neck dissection and fibula free flap reconstruction.

Conclusion: Pathology associated with third molars is extremely common, very occasionally malignancy can mimic these more common conditions. As such, careful clinical examination of the affected site and neighbouring structures (including the lymph nodes of the head and neck) should be routinely performed in all patients. Even in the presence of typical features clinical and radiographic features, tissue samples should be sent for histopathological analysis of what may appear to be harmless follicular or early cystic tissue.

KEYWORDS
mandibular third molar, NOS, Pericoronitis, primary intraosseous carcinoma

Clinical Relevance

BACKGROUND

Pathology involving impacted wisdom teeth is common, including pericoronitis, resorption, cystic change and periodontal disease and caries affecting the disto-cervical region of the adjacent second molar teeth.

PRINCIPLE FINDINGS

The case we present initially suggested a provisional diagnosis of pericoronitis around a partially erupted lower third molar tooth; however, the persistence of pain following...
INTRODUCTION

Primary intraosseous carcinoma, NOS (PIOC), is a rare, malignancy which has been previously described in the literature. The authors describe a case of PIOC arising from a dentigerous cyst in a medically fit and well patient. The initial clinical and radiographic features suggested a common innocuous presentation, although other features which presented later were highly suggestive of a malignant process.

Case presentation

A 78-year old male was referred by his general dental practitioner (GDP) to the Department of Oral and Maxillofacial Surgery at the Royal London Hospital regarding a partially erupted lower right third molar.

The patient complained of a dull ache which had been present for several months but never progressed to an acute infection or swelling. The GDP took a panoramic radiograph (Figure 1) which demonstrated horizontal impaction of the lower right third molar, with possible cystic change around the crown. The patient was subsequently referred to the department for assessment for possible surgical removal of the tooth.

At initial examination, the patient was fit and healthy but reported an allergy to peanuts and aspirin. He was a non-smoker who drank occasional small amounts of alcohol. The extra-oral examination was unremarkable with no evidence of lymphadenopathy in the head and neck region. Intra-oral examination revealed a partially dentate patient whose remaining teeth were heavily restored. There was generalised recession compatible with the patient’s age. His oral hygiene was good, and there were no areas of visible calculus.

The LR8 was partially erupted with 3–4 mm of the crown showing. The overlying mucosa had a small sinus present. A panoramic radiograph supplied by the GDP on initial referral showed that there was a high likelihood of an intimate relationship with the inferior alveolar canal (IAC) along the mesial aspect of the crown and the possibility of early cystic change around the tooth.

The initial treatment plan was to monitor LR8, whilst a cone beam-computed tomography (CBCT) scan was obtained to further investigate the relationship between the LR8 and the IAC (Figure 2).

At the next appointment approximately 6 months after initial assessment, the patient reported no significant change in his symptoms. The CBCT demonstrated narrowing of the IAC and loss of cortication between the tooth and canal. The LR8 was also lingually placed with dehiscence of the lingual plate.

The position of the tooth and the possibility of damage to the inferior dental nerve during surgical removal of the tooth was explained and discussed in detail with the patient. Due to the manageable nature of the symptoms, the patient chose to monitor the tooth rather than have any surgical removal and pre-operative neurosensory changes of the inferior alveolar nerve suggested more than a benign entity.

IMPLICATIONS

Always consider alternative diagnoses, particularly in the presence of ‘red flag’ features and repeat attendances for the same problem.

FIGURE 1 The panoramic radiograph provided by the GDP showed high probability of an intimate relationship between the lower right third molar and inferior alveolar canal.
treatment. A further factor in his choice was his active participation in a choir and the risk of altered sensation in his lip affecting his singing ability. Instructions on oral hygiene and use of chlorhexidine gel were given and a review appointment was made. At the next appointment 6 months later, the patient again reported no further deterioration in the symptoms and again opted for monitoring the tooth rather than any surgical intervention.

At a 2-year review appointment, the patient reported that although considerable effort had been made to keep the area clean with good oral hygiene measures, the overlying gingiva had remained chronically inflamed and was now increasingly painful. A panoramic radiograph also confirmed an increase in the size of the radiolucent area surrounding the tooth. At this stage, it was decided after considerable deliberation and discussion with the patient to surgically remove the tooth under local anaesthetic.

Shortly before the scheduled surgery, the patient reported to the unit urgently with a purulent discharge in the lower right wisdom tooth region and associated loss of sensation along the division of the right inferior alveolar nerve (IAN). Following assessment, he was prescribed a course of amoxicillin 500 mg three times per day for 5 days and metronidazole 400 mg, three times per day for 5 days. This offered partial resolution of pain, although the altered sensation persisted in the division of the right IAN. The tooth was surgically removed 12 days after the end of the antibiotic course. The socket was curetted, and there was soft tissue present within the socket consistent with granulation tissue resulting from chronic infection. This was sent for histopathological analysis.

The histopathology demonstrated fragmented fibro-myxoid connective tissue extensively infiltrated by well to moderately differentiated squamous cell carcinoma (SCC) arising from a dysplastic dentigerous cyst. The patient was urgently referred to a head and neck oncology unit where he subsequently underwent a right hemi-mandibulectomy and right level 1 neck dissection with fibular free flap reconstruction. A panoramic radiograph was taken at the point of referral (Figure 3).

Eighteen months following surgery, the patient remains well with no evidence of recurrence although does experience xerostomia and reduced mouth opening as a result of his treatment.

**DISCUSSION**

Primary intraosseous carcinoma was first described by Loos in 1913 as a central epidermoid carcinoma. It then underwent several reclassifications before finally being renamed...
as Primary Intraosseous SCC in 2005, in the World Health Organisation (WHO) classification of tumours, having kept its entity in the updated 2017 WHO Classification of Head and Neck Tumours. The differential diagnoses for this tumour include alveolar carcinomas jaw metastasis from other locations, odontogenic tumours and tumours of the maxillary sinus.

PIOC is a rare malignancy which develops as an intraosseous tumour in the jaws. It is thought to develop from either embryological remains such as the cell rests of Malassez or from an odontogenic tumour or cyst, in particular dentigerous cysts, residual peri-apical cysts and odontogenic keratocysts. In an analysis of 161 cases of PIOC arising from odontogenic cysts, Bodner et al. described the mandible as the most affected jaw (79% of cases). Furthermore, they also described PIOC most commonly arising from radicular/residual cysts (60% of the 161 cases), whilst Morita et al. more recently described the odontogenic keratocyst as the more common precursor lesion for PIOC to develop from.

It is more common for odontogenic cysts to undergo dysplastic change which results in benign tumours, but the malignant transformation of these cysts is well described, notably to mucoepidermoid carcinoma and SCC. Current statistics for the likelihood of malignant change of odontogenic cysts is between 0.13% and 2.0% with the majority of these occurring in the mandible.

The process of how benign cysts and tumours undergo malignant transformation is yet to be fully understood, yet it is hypothesised that chronic inflammation-induced carcinogenesis is responsible. The histopathology findings in the case we present also corroborate the inflammatory-type reaction, although it is uncertain whether this was attributable to co-existing periodontal disease.

In addition to histopathological confirmation of SCC, the diagnosis of PIOC is dependent on fulfilling certain criteria, which includes no communication with the oral mucosa or overlying ulceration, and the absence of metastasis from any other primary malignancies.

In the case presented here, no other primary tumours have been discovered hitherto, in an otherwise healthy patient which supports a diagnosis of PIOC.

The clinical and radiographic characteristics of PIOC can be similar to that of benign odontogenic cysts and tumours. In this case, the patient had a buccal sinus present for 2 years. Apart from this symptom, the patient remained relatively comfortable for 2 years until he presented with pain, swelling and paraesthesia. The most reported clinical features in the literature have been that of pain, swelling, sinus tract formation and lymphadenopathy. Radiographically, PIOC is likely to present above the inferior dental canal, whereas metastasis is likely to declare itself below the inferior dental canal. Clinical red flag signs that clinicians must consider include an enlarging swelling, increasingly mobile teeth, cranial nerve palsies and lymphadenopathy. Radiographic red flag signs include, a poorly defined ‘moth-eaten’/patch radiolucency which erodes rather than displaces adjacent structures, resorption of teeth, widening of periodontal ligament spaces without an obvious cause and loss of cortication of presumed cystic entities.

The majority of PIOC are either moderately or well-differentiated SCCs. In the previous WHO classification, PIOC were described as ‘primary intraosseous SCCs’, and three subtypes were described, namely:

1. a solid tumour that invades marrow spaces and induces osseous resorption,
2. squamous cancer arising from the lining of an odontogenic cyst, and
3. SCC in association with other benign epithelial odontogenic tumours.

The most recent WHO classification of Head and Neck Tumours has removed this subtyping and PIOC is now an entity with no distinct subtypes.

Early diagnosis is difficult as in the early stages as this tumour is relatively asymptomatic. A study by Thomas et al. showed that in 35 reviewed cases, most of the PIOC occurred in the posterior mandible in male patients. The age of this study group ranged from 4 to 81 years old. As such PIOC is a diagnosis of exclusion with due consideration of clinical, histological and radiological information.

Araújo et al. found that PIOC metastases can occur in up to 50% of cases and there is often perineural spread often along the respective IAN if the occurrence is in the mandible. However, another report disputed this incidence and found that although the tumour is aggressive it rarely metastasizes to the lymph nodes. Zwetyenga et al. reported nodal metastases in 28% of patients with PIOC at initial presentation.

The overall 5-year survival rate for PIOC has been cited as 38% at the most with a 60% chance of local recurrence. Whilst the delivery of adjuvant chemotherapy has been explored, the mainstay of treatment remains radical surgery to achieve disease free margins and concomitant neck dissection.

**CONCLUSION**

This case report has highlighted the importance of a complete and detailed history and examination, even in cases where the clinical and radiographic findings suggested a benign condition. History taking and examination should always incorporate questions and examination techniques which elucidate red flag signs and symptoms. The importance of routinely assessing a patient for lymphadenopathy and submitting tissue for histological assessment has been emphasised in this case report.

**CONFLICT OF INTEREST**

The authors declare they have no conflict of interest.
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