

Case Report

Primary intra-osseous squamous cell carcinoma arising from an odontogenic cyst: a case report

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Abstract Primary intra-osseous squamous cell carcinoma (PIO SCC) is a rare tumour which occurs centrally within the jaws. It is believed to arise from odontogenic epithelial remnants or from pre-existing odontogenic cysts/tumours. A case of PIO SCC arising from an odontogenic cyst in a 57-year-old female is discussed. Initial clinical and radiographic examination was suggestive of an odontogenic cyst / cystic tumour. The lesion was enucleated and sent for diagnostic histopathology which revealed the presence of an invasive carcinoma arising from the walls of the odontogenic cyst. The patient then underwent right mandibular resection and reconstruction as well as right supra-omohyoid neck dissection. Long standing odontogenic cysts have the potential to undergo malignant transformation though this may not always be the case. Relying only on radiographic findings for the management of cyst-like lesions without obtaining histopathological diagnosis is extremely ill-advised.

Keywords: odontogenic cyst; odontogenic tumour; squamous cell carcinoma.

Introduction

Primary intra-osseous squamous cell carcinoma (PIO SCC) also known as primary intra-alveolar epidermoid carcinoma, is an uncommon tumour which occurs centrally within the jaws (Barnes *et al.*, 2005). It is believed to arise from either odontogenic epithelial remnants or from pre-existing odontogenic cysts/tumours. PIO SCC has been classified by the World Health Organization (WHO) into three subtypes (Barnes *et al.*, 2005): (1) solid tumour, (2) PIO SCC in association with benign odontogenic tumours, (3) PIO SCC arising from an odontogenic cyst.

Diagnosis of PIO SCC is at times complicated as it needs to be differentiated from carcinomas that have invaded bone from the surface epithelium, metastatic carcinomas, odontogenic carcinomas, intra-osseous mucoepidermoid carcinoma and

also maxillary sinus tumours (Suei *et al.*, 1994; Barnes *et al.*, 2005), more so when the tumour has perforated through the cortex and appears to have merged with the overlying mucosa. The histopathologic features of PIO SCC are often indistinguishable from mucosal squamous cell carcinoma (SCC). As such, diagnosis based on histopathologic findings alone is unadvisable, and correlation with clinical and radiographic findings is mandatory.

In cases where PIO SCC is believed to arise from the lining of an odontogenic cyst, the pathologist would need to identify the transition of benign cyst epithelium to invasive squamous cell carcinoma (Barnes *et al.*, 2005; Gardner, 1975). A study had previously suggested that the prognosis for patients is relatively poor with high recurrence and mortality rates; however, the number of cases for the study was very low (39 patients) (Huang *et al.*, 2009). As such, due to the

relatively small number of reported cases with outcome data, prognosis for patients with PIO SCC is still indeterminate (Barnes *et al.*, 2005). Here we would like to present a case of PIO SCC arising from an odontogenic cyst.

Case report

This study has been registered with the National Medical Research Registry and was given ethical approval by the relevant Medical Research Ethics Committee (Ref. no: NMRR-15-268-25292). Patient consent was obtained accordingly.

A 57-year-old Malaysian-Indian female with a complaint of pain and swelling over the posterior part of the right side of the mandible was seen at a district oral and maxillofacial surgery clinic. The swelling had progressively increased over the period of two months. She previously had tooth extractions over that region a few months back. She had a history of anaemia and was allergic to non-steroidal anti-inflammatory drugs as well as seafood. Upon clinical examination, an obvious swelling was present over the right mandibular region measuring around 2 cm x 2 cm. The swelling was bony hard in consistency with no obvious change in the overlying skin or mucosa. There was no paraesthesia noted. No palpable submandibular/cervical lymph nodes were detected. On panoramic radiography, there was a large radiolucency over the right side of the mandible suggestive of an odontogenic cyst / cystic tumour (Fig. 1).

A working diagnosis of an inflamed odontogenic cyst was made and surgical enucleation of the lesion was performed and the specimen was sent for histopathological examination. The surgical specimen consisted of multiple fragments of formalin-fixed tissue measuring 40 mm in aggregate diameter. Microscopically, an invasive carcinoma arising from the walls of the odontogenic cyst was observed (Fig. 2 and 3). After discussion with the surgeon involved, further imaging was done of the head & neck region as well as thorax to rule out the possibility of the mandibular lesion being a metastatic deposit. Imaging showed no obvious abnormalities.

Due to the relative rarity of such a case, it was discussed at a consensus meeting and as metastatic disease was ruled out and no obvious communication with the oral cavity was present at the time of enucleation, a final diagnosis of PIO SCC arising in a pre-existing odontogenic cyst was made. The patient was then referred to a tertiary institute specialising in oncology. After further assessment, the patient was given the option for further surgical intervention and the patient agreed to undergo right mandibular resection and reconstruction as well as right supra-omohyoid neck dissection under general anaesthesia. The resection specimen's surgical margins were clear of tumour tissue. No metastatic deposits were seen in the supra-omohyoid neck dissection as well. At the last follow-up, 36 months after the resection and reconstruction, the patient was fit and well with no recurrence or complications.

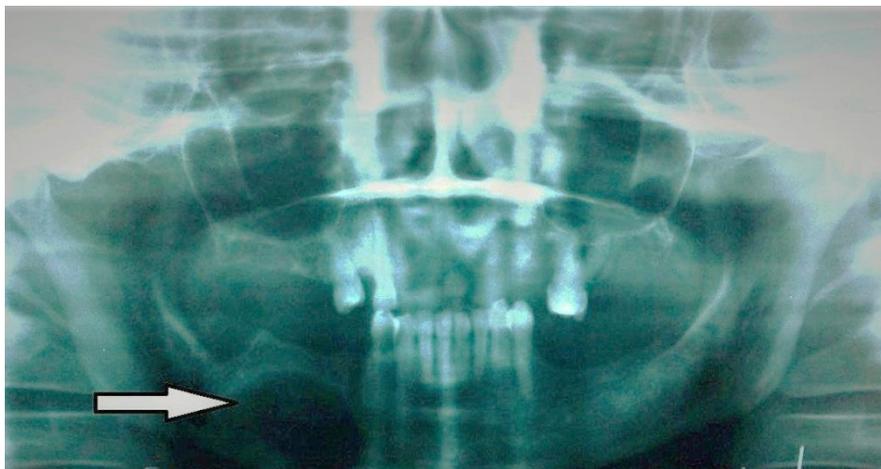


Fig. 1 Pre-operative orthopantomogram showing a cyst-like lesion in the right side of the mandible (arrow).

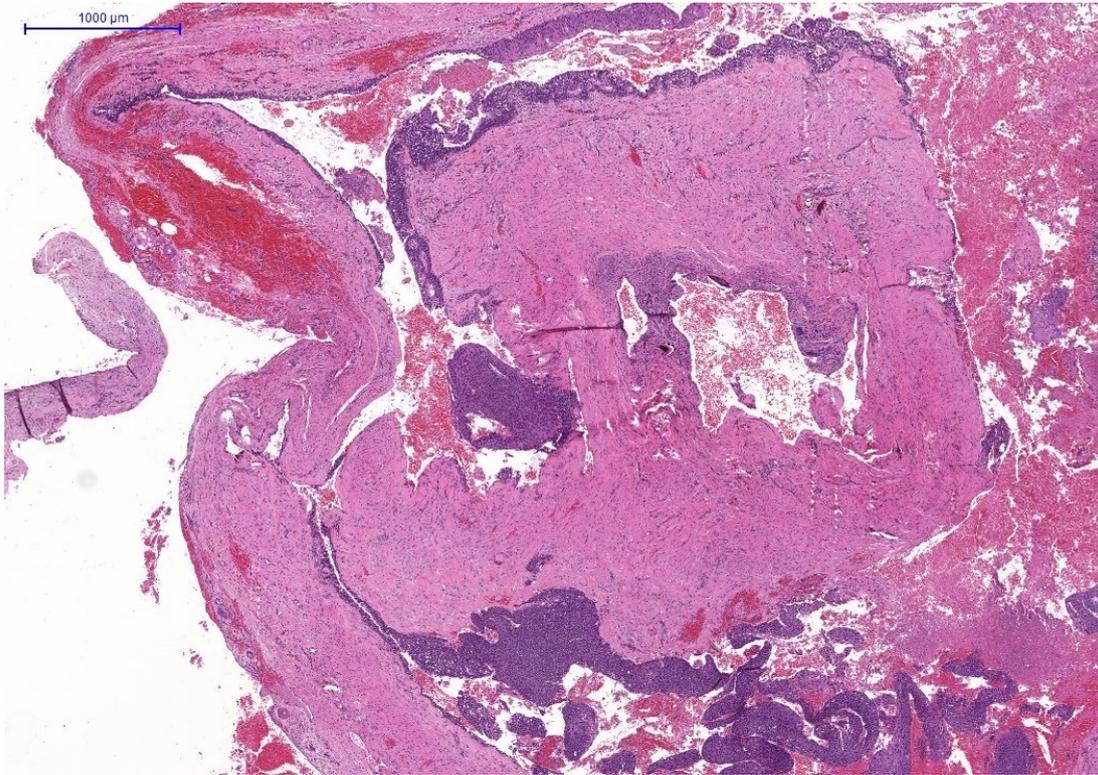


Fig. 2 Hematoxylin and eosin stained section showing PIO SCC arising from the epithelial lining of an odontogenic cyst (scale in upper left corner).

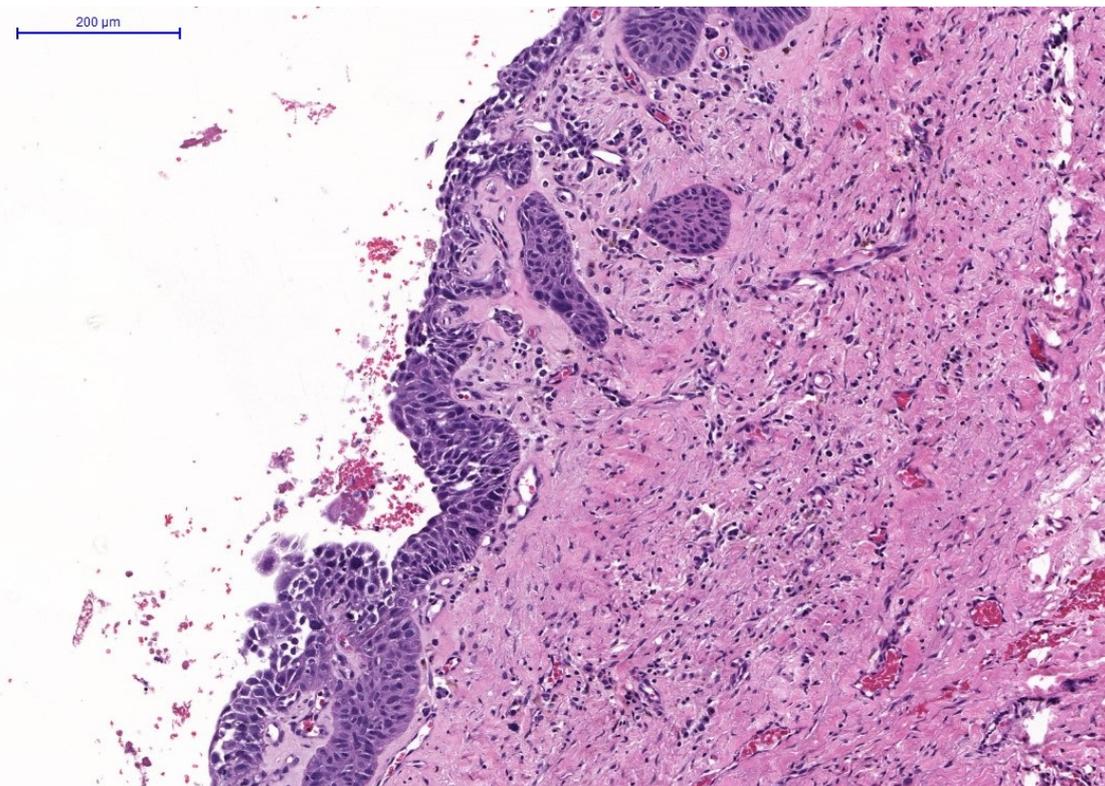


Fig. 3 Hematoxylin and eosin stained section showing the dysplastic epithelial lining and tumour islands (scale in upper left corner).

Discussion

Although PIO SCC is not commonly encountered, it is an entity that is well-recognized with a relatively poor prognosis. Long standing odontogenic cysts have the potential to undergo malignant transformation; however, this is very rare (Bodner *et al.*, 2011). PIO SCC arising from odontogenic cysts is thought to occur more frequently in males and in the 6th and 7th decades of life (Barnes *et al.*, 2005; Bodner *et al.*, 2011; Gardner 1975). Nevertheless, this subtype of PIO SCC has been shown to occur in a wide range of ages and the male predominance may simply reflect the higher occurrence of odontogenic cysts in adult males (Bodner *et al.*, 2011; Bodner and Manor 2010).

PIO SCC is more frequently found in the mandible, with the posterior mandible being the most frequently involved site (Bodner *et al.*, 2011; Suei *et al.*, 1994) and as such the site of PIO SCC in this patient is not unexpected.

The pathogenesis of malignant change in odontogenic cysts is still unclear as PIO SCC is an intra-osseous tumour and as such is not directly influenced by carcinogens such as tobacco or betel-quid. Some have suggested that long-standing chronic inflammation may play an important factor in oncogenesis as some researchers have observed that chronic inflammatory infiltrate is often seen in association with cysts that have transformed to malignancy. (Schwimmer *et al.*, 1991; Jain *et al.*, 2013). The role of chronic inflammation in oncogenesis is also an accepted phenomenon. Further evidence for this train of thought is the fact that although a variety of cysts have been implicated with PIO SCC, the cysts most commonly associated are inflammatory cysts such as residual cysts and radicular cysts (Bodner *et al.*, 2011; Woolgar *et al.*, 2013). A genetic contribution may exist as gene expression profile comparisons between odontogenic carcinomas and oral squamous cell carcinomas have several genetic events that are unique to odontogenic carcinoma (Alevizos *et al.*, 2002).

The clinical and radiographic features of PIO SCC are non-specific and are commonly seen in inflamed or infected cystic lesions of the jaw bones (Barnes *et al.*, 2005; Woolgar *et al.*, 2013; Bodner and Manor 2010). The present case clearly shows this; whereby the initial surgical treatment plan was based on the findings that were suggestive of an inflamed odontogenic cyst though it turned out otherwise. As such, although clinical and radiographic findings are extremely important for the diagnosis and management of odontogenic lesions, a pre-operative biopsy to provide histopathological information is highly advisable prior to initial treatment planning especially for large odontogenic cysts/cyst-like lesions. This would also be beneficial in reducing the number of times the patient would need to be put under general anaesthesia for surgery thus reducing morbidity, potential mortality as well as cost. However, it should be remembered that incisional biopsies at times may not truly represent the entire lesion and malignant change located in the other regions of a cyst may not be present in the biopsy specimen.

Histologically, this type of tumour is characterized by an odontogenic cyst lined by epithelium that may have varying levels of dysplasia in association with a squamous cell carcinoma (Barnes *et al.*, 2005). It has also been suggested that a transitional zone between the cyst epithelium and the infiltrative carcinoma should be identified before confirming the diagnosis of a PIO SCC arising in an odontogenic cyst (Suei *et al.*, 1994; Schwimmer *et al.*, 1991). In some cases, where the tumour is aggressive, a transitional zone may be difficult to determine as most of the preceding pathological entity such as a cyst may have been destroyed and replaced by tumour tissue. As such, correlation with clinical history is imperative in establishing a definitive diagnosis; to forego clinical, radiographic or histopathological information when making a diagnosis is ill-advised.

Management for PIO SCC is usually determined by the extent of the tumour and clinical staging of the tumour; however, surgery with/without radiotherapy is widely considered as the primary treatment modality (Thomas *et al.*, 2001; Bodner *et al.*, 2011; Huang *et al.*, 2009). A recent retrospective study found that patients who underwent surgery alone had better overall survival rates than those who received adjuvant chemotherapy or radiotherapy (Wenguang *et al.*, 2016). However, this may be due to the fact that those with more aggressive or loco-regionally extensive disease would be the ones receiving such adjuvant therapy (Wenguang *et al.*, 2016).

Prognosis for PIO SCC is thought to be relatively poor with most studies estimating the 5-year survival rate to be between 30-40 % (Bodner *et al.*, 2011; Huang *et al.*, 2009; Wenguang *et al.*, 2016). A retrospective analysis of prognostic factors associated with the outcome of PIO SCC found that high histological grade, positive nodal status and advanced “N” classification from the TNM (Tumour, Node, Metastasis) classification, to be predictive of poor prognosis in these patients (Wenguang *et al.*, 2016).

Relying solely on radiographic findings for the diagnosis and management of odontogenic cysts/cyst-like entities without obtaining histopathological diagnosis is extremely ill-advised. PIO SCC has to be considered in the differential diagnosis of cyst-like lesions detected on radiographs in view of the poor prognosis that is usually associated with this tumour.

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