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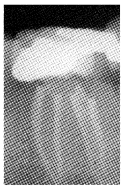

CASE REPORT

Maintaining a high level of suspicion for recurrent malignant disease: report of a case with periapical involvement

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Abstract

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Aim To report the unusual endodontic presentation and radiographic features of a subgroup of pleomorphic adenoma called carcinoma ex pleomorphic adenoma and to stress the importance of maintaining a high level of suspicion in cases where primary or recurrent neoplasia is included in the differential diagnosis.

Summary This paper describes a case in which a patient with a previous history of malignant neoplasm presented with signs and symptoms similar to a dental infection. The pathology report however confirmed recurrence of the previous tumour in a malignant fashion. The importance of maintaining a high level of suspicion in early management of such disease is highlighted.

Key learning points

- Pleomorphic adenomas, also known as benign mixed tumours, are common salivary gland tumours, which infrequently undergo malignant transformation, with potentially devastating consequences.
- Malignant salivary gland tumours can present as dental swelling, dental pain and sudden loss of vitality of teeth so both general practitioners and specialists have the responsibility to evaluate such patients with a broad vision.
- Radiographic differential diagnosis of periapical radiolucency should also include malignant salivary gland tumours.
- This case highlights the need of vigilance at all times and emphasizes the benefits of biopsy and histological examination in the diagnosis of recurrent malignant salivary gland tumours.

Keywords: carcinoma ex pleomorphic adenoma, periapical dental infection, pleomorphic adenoma, recurrent malignant disease, root canal treatment, salivary gland tumour.

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Introduction

Pleomorphic adenoma is the most common salivary gland tumour (Waldron *et al.* 1988, Yih *et al.* 2005, Pires *et al.* 2006). It is benign and consists of epithelial cells in a matrix of mucoid, myxomatous or chondroid tissue. Because of their remarkable histological diversity, these neoplasms have also been called mixed tumours (Cawson *et al.* 2001). Seventy percent of the tumours of minor salivary glands are pleomorphic adenomas, and the most common intraoral site is the palate, followed by the upper lip and buccal mucosa (Clauser *et al.* 2004). The majority (60%) of pleomorphic adenomas occur in the parotid, and less commonly in the submandibular and minor salivary glands. The term 'pleomorphic' relates to the wide variety of histological appearances. Although such tumours are benign, historically the main clinical problem with pleomorphic adenoma has been the risk of recurrence and progression to a clinical or histological based malignancy (Seifert *et al.* 1990). Recurrence is most commonly seen in the parotid gland. A carcinoma can infrequently arise in a pleomorphic adenoma, called a *carcinoma ex pleomorphic adenoma* or a malignant mixed tumour (Lewis *et al.* 2001, Ethunandan *et al.* 2006). The incidence of malignant transformation increases with time, being about 2% for tumours present <5 years and almost 10% for those of more than 15-year duration (Cotran *et al.* 1999). *Carcinoma ex pleomorphic adenomas* are amongst the most aggressive of all salivary gland malignant neoplasms and account for approximately 12% of malignant salivary gland tumours (LiVolsi & Perzin 1977, Tortoledo *et al.* 1984, Eveson & Cawson 1985, Gnepp 1993, Lewis *et al.* 2001). The cancer usually takes the form of an adenocarcinoma or undifferentiated carcinoma and when they reoccur are the most aggressive of all salivary gland malignant neoplasms (Olsen & Lewis 2001, Felix *et al.* 2002). This paper reports the unusual clinical and radiological presentation of a recurrent *carcinoma ex pleomorphic adenoma* affecting the anterior maxilla. It also highlights the role and importance of the general or specialist dental practitioner in early diagnosis and management of such patients.

Case report

Background

A 44-year-old male patient was referred by his general medical practitioner to the Department of Oral and Maxillofacial Surgery, Morriston Hospital, Swansea in 2002 regarding a palatal swelling affecting the left side of his maxilla. This was diagnosed as a pleomorphic adenoma affecting the left posterior maxilla extending into the left maxillary antrum. Atypical features were noted in the histology report (increased mitotic activity and mild nuclear atypia). At that time, partial maxillectomy and subsequent reconstruction with a radial forearm free flap was undertaken and a maxillary obturator was fitted to restore the defect. Eighteen months later, in July 2003, the patient was re-biopsied. A high rate of mitosis was noted and a diagnosis of *carcinoma ex pleomorphic adenoma* was made. The tumour was then affecting the left anterior maxilla, and was treated aggressively due to its early recurrence. This was done by surgical excision and radiotherapy. Following this, a new obturator was constructed in October 2003 to restore the defect in the left maxilla. The patient was then reviewed regularly at the Department of Restorative Dentistry.

Current report

The patient attended as an emergency to the Department of Restorative Dentistry in September 2006 and reported that he noted abrupt swelling associated with the apices of

teeth 11, 12 and 13. The swelling was of 1-day duration and there was no obvious pain, discomfort or symptoms other than some looseness of the tooth 11. On clinical examination, there was periapical swelling in relation to teeth 11, 12 and 13 which was firm on palpation. The teeth were not tender to percussion and periodontal examination of teeth 11, 12 and 13 revealed normal probing depths in the range of 2–3 mm. Tooth 11 was grade I mobile. Teeth 11, 12 and 13 did not respond to sensitivity testing with an Electronic Pulp Tester (Analytic Endodontics, Redmond, WA, USA) and ethyl chloride (Dr Georg Friedrich Henning Chemische Fabrik Walldorf GmbH, Walldorf, Germany). Radiographic examination included a standardized intraoral periapical film (Kodak K, E.K.C, Rochester, NY, USA) exposed with a holder (Rinn Corporation, Elgin, IL, USA) (Figs 1–3) and dental panoramic tomogram (DPT) (Instrumentarium Corporation, Helsinki, Finland) (Fig. 4). The intraoral radiographs showed a large periradicular radiolucency associated

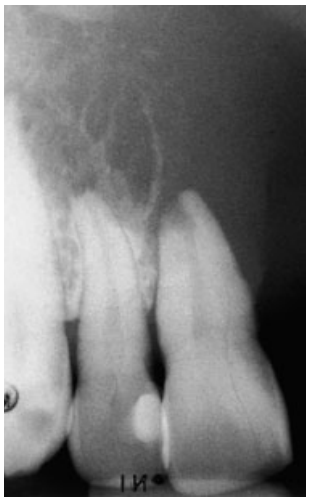

Figure 1 Periapical view of teeth 11 and 12 showing area of radiolucency and apical resorption of the tooth 11.

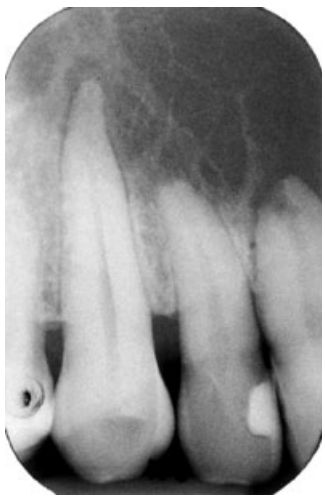

Figure 2 Periapical view of the tooth 13 showing well circumscribed area of radiolucency.

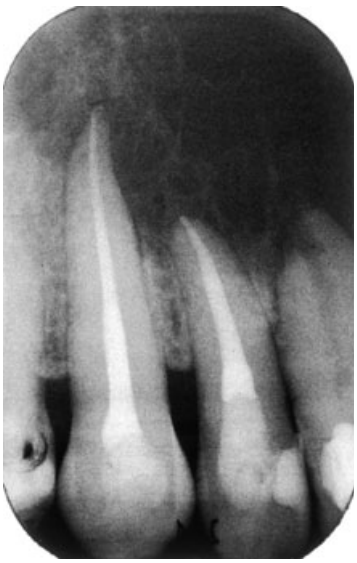

Figure 3 Post-obturation periapical view of teeth 12 and 13.

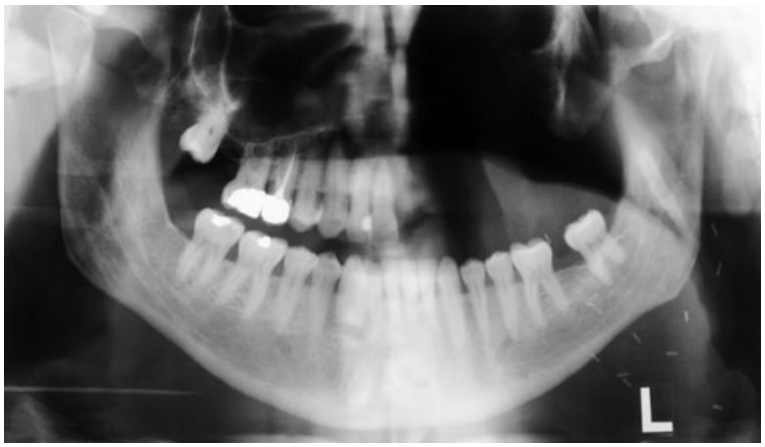

Figure 4 DPT showing previous maxillectomy of the left side and periradicular changes associated with teeth 11, 12 and 13.

with the apices of teeth 11, 12 and 13. The radiolucency was diffuse in nature with an irregular outline. There was also more localized, well-circumscribed apical widening of the periodontal ligament space around the roots of 12 and 13 and some apical resorption of tooth 11. This gave a mixed and slightly confusing radiographic picture.

Following examination, a differential diagnosis of periapical abscess, periradicualr cyst, periradicular granuloma and tumour or tumour like lesion, e.g. recurrence of previous malignancy was made. A provisional diagnosis of apical periodontitis in relation to the teeth 11, 12 and 13 was made and the immediate plan included:

1. Access and drainage of 11, 12, 13. Mechanical and chemical disinfection with rotary Ni–Ti Endodontic files (Endo Sybron, Glendora, CA, USA) and sodium hypochlorite (Tesco value bleach, Tesco, Cheshunt, UK).

2. Incision and drainage of labial swelling to relieve pus.

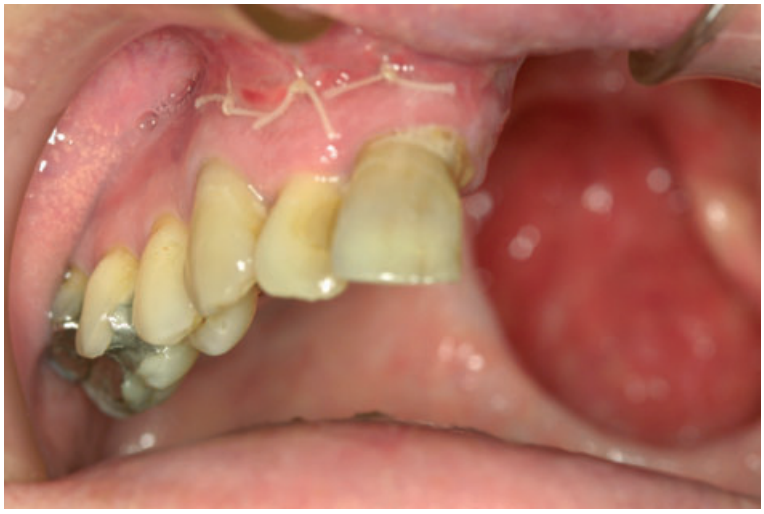

Figure 5 Photograph taken after the biopsy, showing persistent swelling in relation to teeth 11, 12 and 13 following incision and drainage.

3. Systemic course of oral amoxicillin, 250 mg thrice daily for 5 days, as a precautionary measure to prevent further acute flare-up.
4. Review 1 week later on a restorative consultant clinic.
5. Referral to Oral and Maxillofacial department for biopsy to rule out recurrence of adenoma or cystic pathology.

Necrotic pulp tissue was found on access to teeth 11, 12 and 13. The teeth were prepared and cleaned and calcium hydroxide (Cefn Coed Hospital Formula, Huddersfield Royal Infirmary Pharmacy Manufacturer Unit, Huddersfield, UK) intermediate root canal medication was placed following debridement and disinfection. Incision of the labial swelling revealed no pus, and the labial swelling did not reduce in size. At the next appointment 1 week later, the patient reported 'dental pain' in relation to the apical swelling. On examination, there was no change in the swelling size or consistency. However, the tooth 11 had increased mobility to grade II. Teeth 12 and 13 were not tender to percussion and the canals were dry and clean. Therefore, a decision was taken to obturate the teeth 12 and 13 with gutta-percha and sealer using a combination of System B (Analytic; Sybron Dental Specialities, Glendora, CA, USA) and Obtura (Sybron Dental Specialities). Obturation of tooth 11 was deferred due to the presence of increasing mobility with respect to initial presentation. A post-obturation intraoral radiograph (Fig. 4) showed the periapical radiolucency to have a more irregular and diffuse outline. Additionally, in view of the patients previous history and increasing concern over the nature of the signs and symptoms, it was decided to refer the patient urgently to the Department of Oral and Maxillofacial Surgery, Morriston Hospital, Swansea. The patient was seen the following day at the Head & Neck Multi-disciplinary Team clinic and it was decided to biopsy the swelling. An incisional biopsy was taken from the site of the swelling (Fig. 5). The biopsy confirmed the diagnosis of a '*recurrent carcinoma ex pleomorphic adenoma*'. The patient underwent radical surgical excision of the right maxilla following which a new obturator was fitted to restore the whole maxilla.

Discussion

Intraoral mixed tumours, especially those noted within the palate often lack a well-defined capsule. Lesions of the palate frequently involve periosteum or bone. Approximately 25%

of benign mixed tumours undergo malignant transformation (Clauser *et al.* 2004). Malignant change in a pleomorphic adenoma has been associated with the long-term presence of the tumour, recurrent tumour, radiotherapy, increasing age of patient and tumour size (LiVolsi & Perzin 1977, Spiro 1986, Gnepp 1993). An exceptionally late recurrence of pleomorphic adenoma of the palate is reported in the literature (Turner & Smith 2006) where a latency of about 35-year duration between initial excision and recurrence was noted. Here, a case is presented of pleomorphic adenoma of the palate with the second malignant recurrence 4 years after the initial presentation. This recurrent tumour was intraosseous in nature, affecting the right anterior maxilla and presented with symptoms consistent with that of endodontic pathosis. The tendency to progress to malignancy has traditionally been based on the diagnostic criteria for *carcinoma ex pleomorphic adenoma* (a mixed tumour in which a second epithelial tumour develops) (LiVolsi & Perzin 1977, Lewis *et al.* 2001, Ethunandan *et al.* 2006).

A high index of suspicion for malignant recurrence was suggested by the following:

1. The patient had a history of recurrence 18 months after it was diagnosed for the first time.

2. One-day sudden onset of swelling in relation to the anterior teeth with no previous history of dental pain.

3. The pathology was close to the previous area of resection.

4. The clinical examination revealed a swelling which was firm on palpation with no fluctuation.

5. Pulps of three teeth becoming nonvital with no obvious reason or cause.

6. Sudden onset of mobility of tooth 11 with good periodontal health.

7. The teeth involved were not tender on percussion, which is usually the case in acute dental infection.

8. On incision and drainage, there was a lack of pus and no change in the size of swelling was noted.

9. The patient reported severe 'dental pain' at the second appointment after the necrosed pulp was extirpated and the canals instrumented under local anaesthesia.

10. Post-obturation radiograph of teeth 12 and 13 revealed an area of apical radiolucency with irregular outline.

Although the patient was initially managed for a dental infection of teeth 11, 12 and 13, it was prudent to consider recurrence of pleomorphic adenoma as the other likely cause of the swelling. This was particularly so in view of the previous history and as atypical features were noted on the first excision when a diagnosis of *carcinoma ex pleomorphic adenoma* was provided on histopathological examination of the first recurrence.

Differential diagnosis of radiolucent lesions affecting the jaws are broadly classified into cysts and tumours of odontogenic or nonodontogenic origin, giant cell lesions and fibro-cemento-osseous lesions (Kramer *et al.* 1992). Salivary gland neoplasms affecting the jaw bone appear to be uncommon with most cases being mucoepidermoid carcinomas (Brookstone & Huvos 1992). Primary intraosseous salivary gland tumours are rare, however they can manifest as an endodontic lesion and there are two cases reported in the literature when central adenoid cystic carcinoma of the mandible mimicked a periapical pathosis (Favia *et al.* 2000, Chen *et al.* 2004). Malignant squamous carcinoma (Thompson *et al.* 1992, Levi *et al.* 2005) and fibro-osseous lesions such as focal cemento-osseous dysplasia involving mandibular lateral incisor (Galgano *et al.* 2003) can also manifest as endodontic lesions. An unusual case of sickle cell crisis developing a unilateral infarct of mandible, leading to pulpal necrosis of premolar and molar teeth has been reported in the literature (Bishop *et al.* 1995).

This case is unique as no such dental and radiological manifestations are mentioned in the literature regarding *carcinoma ex pleomorphic adenoma*. Recurrent malignant salivary

gland tumours can register as periapical pathology on first presentation. This can vary from being an abrupt swelling in relation to the apices of tooth/teeth or dental pain. The present case represents intraosseous presentation of *recurrent carcinoma ex pleomorphic adenoma* masquerading as a lesion of apical dental infection emphasizing the importance of considering various radiological differential diagnoses of radiolucent lesions of the jaws as the cause of the pathology.

Carcinoma ex pleomorphic adenoma is an aggressive tumour (Altini *et al.* 1997), Auclair & Ellis (1996) and is a poorly understood salivary gland malignancy. Misdiagnosis is common, because the residual mixed tumour component might be small, and various carcinoma subtypes are possible (Olsen & Lewis 2001). Although occurrence of salivary gland tumours in intraosseous locations is rare, it is important to maintain a high degree of suspicion in patients with previous history of malignancy.

Conclusion

The main objective in reporting this case is to draw attention to the fact that malignant salivary gland tumours such as *carcinoma ex pleomorphic adenoma* can manifest as a periapical lesion both clinically and radiologically. Maintaining a high level of vigilance at all times in patients with previous history of malignancy is an important factor in early diagnosis and management of its recurrence. A differential diagnosis of radiolucent lesions of jaw bones should always be considered in diagnosis and treatment planning of such patients.

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Disclaimer

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