Odontoma-like Tumours of Squirrel Elodont Incisors—Elodontomas

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Summary

Since 2003, nine squirrels were presented at a South African veterinary dental practice with lesions in the maxilla consistent with the clinical, radiological and histological features of odontomas as described in prairie dogs, rats and mice. These odontoma-like masses have not previously been described in squirrels. This report describes the clinico-pathological features and possible pathogenesis of the lesions and proposes the term "elodontoma" for these hamartomatous odontogenic lesions in the jaws of animals with continuously erupting (elodont) teeth.

Tree squirrels, which belong to the order Rodentia, family Sciuridae are becoming increasingly popular as pets in South Africa and, accordingly, their health, including oral health, is attracting increasing interest. Squirrels have a dental formula of I 1/1, C 0/0, P 1-2/1 M 3/3 (Legendre, 2003) with elodont incisor teeth (Sainsbury *et al*., 2004) and brachyodont premolars and molars (Legendre, 2003). Elodont teeth are defined as continually growing, aradicular teeth (Kertesz, 1993). Oral disease in captive and free-living squirrels, which is similar to that encountered in other rodent species (Legendre, 2003), includes malocclusion (especially affecting the incisors), variations in the number, size and shape of teeth, presence of supernumerary teeth, periodontal disease, dento-alveolar abscesses (sometimes with osteomyelitis), caries, traumatic lesions of the oral soft tissue and attrition (mainly of cheek teeth) (Miles, 1990; Wiggs and Lobprise, 1997; Sainsbury *et al*., 2004).

Black-tailed Prairie dogs (*Cynomys ludovicianus)* are large ground-dwelling squirrels in which space-occupying masses in the maxillae have been described, such lesions being termed "odontomas" (Wagner, 1999; Phalen *et al*., 2000; Capello, 2002). They are usually associated with the apex of the incisor teeth and, due to the obligatory nasal breathing of these animals, result in upper respiratory symptoms which may be severe enough to cause death. Since 2003 we have examined nine tree squirrels (*Paraxerus cepapi*) with maxillary lesions consistent with the so-called "odontomas" of prairie dogs. Because this abnormality has not previously been reported in the Sciuridae, the present study was undertaken (1) to evaluate the clinico-pathological features, (2) to throw light on the pathogenesis, and (3) to examine the applicability of the term "odontoma".

The study was based on two control tree squirrels (nos 1 and 2), humanely killed for medical reasons unrelated to the present study, and nine abnormal pet tree squirrels (nos 3–11), referred to a veterinary dental clinic since 2003. Details of the animals are given in Table 1. Squirrels 3, 4, 7, 9 and 11 had various degrees of dyspnoea; squirrel 8 and 10 had deformed maxillary incisors, resulting in malocclusion and inappetence; squirrel 7, in addition to dyspnoea, had a maxillary mass ventro-lateral to the right eye; and squirrel 5 was found on X-ray to have a mass periapical to the right maxillary incisor (Fig. 1). After clinico-radiological examination, a provisional diagnosis of odontoma was made in all nine abnormal squirrels.

Table 1.

Details of squirrels included in this study

| Squirrel no.	Age (years)	Sex	Clinical presentation	Treatment
1	1	M	Normal jaws	Euthanasia
2	1	F	Normal jaws	Euthanasia
3	5	M	Bilateral masses with dyspnoea	Euthanasia
4	4	M	Bilateral masses with dyspnoea	Euthanasia
5	3	M	Unilateral mass with dyspnoea	Extraction then euthanasia
	2	M	Bilateral masses with periapical distortion	Extraction
7		M	Unilateral mass ventral eye, with dyspnoea	Biopsy of mass
8	1	F	Bilateral apical distortion and malocclusion	Died under anaesthesia
9	5	F	Bilateral masses with dyspnoea	Euthanasia
10	Unknown	F	Bilateral masses with tooth deformity	Extraction
11	3	F	Bilateral masses with dyspnoea	Rhinotomy
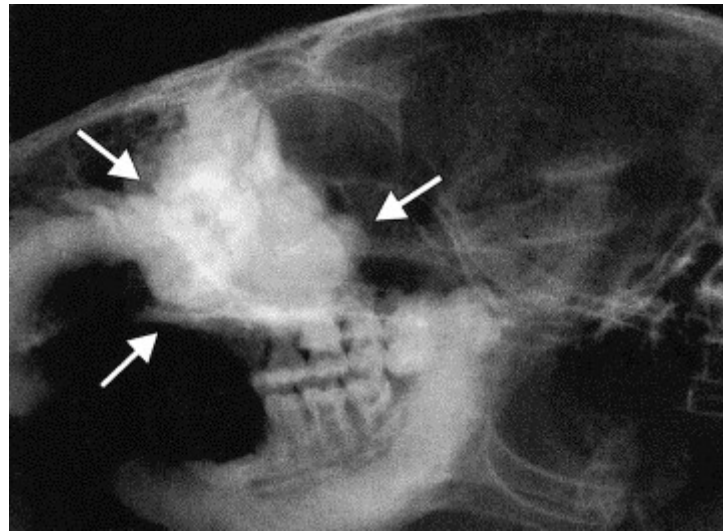
Fig. 1. Lateral radiograph showing a large radiopaque mass in the rostral maxilla (arrows).

The specimens from which material was examined histopathologically included: five heads (squirrels 1 and 2 [controls], and 3, 4 and 5); three incisor teeth, extracted because of peri-apical masses (squirrels 5, 6 and 8); and a biopsy sample from a peri-apical mass (squirrel 7). Squirrels 9, 10 and 11 were not examined histopathologically.

The five squirrel heads were prepared for examination by removal of the skin, followed by fixation in 10% buffered formalin for 48 h, after which they were cut perpendicularly to the palatal surface with a water-cooled, low speed, Buehler diamond precision cut-off wheel (Micromet Scientific, Midrand, South Africa). Five to seven coronal slices were then cut between the nose and the posterior margin of the jaw bones. The slices were demineralized with a solution consisting of HCl 37% and HNO_3 63%, embedded in paraffin wax, sectioned at 5 μm and stained with haematoxylin-eosin (HE). The three extracted teeth and biopsy sample were demineralized as described above. Two of the teeth were sectioned longitudinally and one transversely, through the apical mass. These also were embedded in paraffin wax, sectioned at 5 μm and stained with HE.

Macroscopical examination revealed features that varied from normal patent respiratory tracts with or without periapical lesions of the maxillary incisors to large bilateral tumour-like masses in the maxillae, resulting in occlusion of the respiratory tracts at different anatomical levels (Fig. 2).
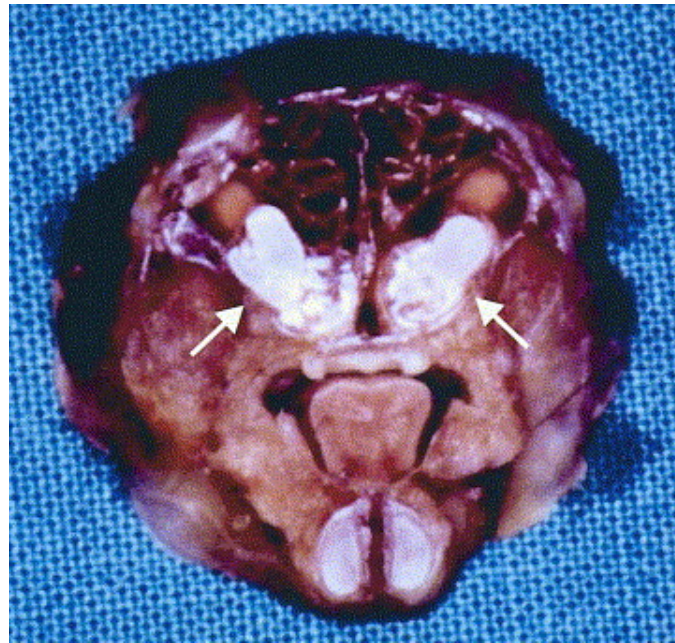
Fig. 2. Coronal slice though the caudal maxilla clearly showing bilateral masses in the apical area of the maxillary incisors, with occlusion of nasal passages (arrows).

Histopathological examination of the HE-stained sections showed normal anatomy and normal odontogenesis in the heads of squirrels 1 and 2 (controls) (Fig. 3a). Features of normal odontogenesis were also present in the incisors of unaffected teeth in the diseased squirrels. From the apical area to the incisal edge, the morphological transition was similar to that of the developing tooth germ as seen from bud to bell stage and then to the completed tooth. Microscopical examination of the HE-stained sections from the three diseased squirrels (3, 4 and 5) showed posterior maxillary masses situated at the apical level of the affected incisors; these extended forwards in two cases, causing bilateral obliteration of the nasal passages (Fig. 3b). Detailed histological examination of the maxillary masses showed odontoma-like conglomerates of haphazardly arranged odontogenic hard and soft tissue and bone (Fig. 4). Cementum and bone-like material with multiple cellular inclusions were directly associated with columnar odontogenic epithelium with prominent nuclear palisading, as well as with areas of stellate reticulum and fibrous connective tissue. A close connection between bone and dentine, which was seen in almost all affected cases, was also prominent at the junction of the obliterated incisor teeth and the odontoma-like masses.
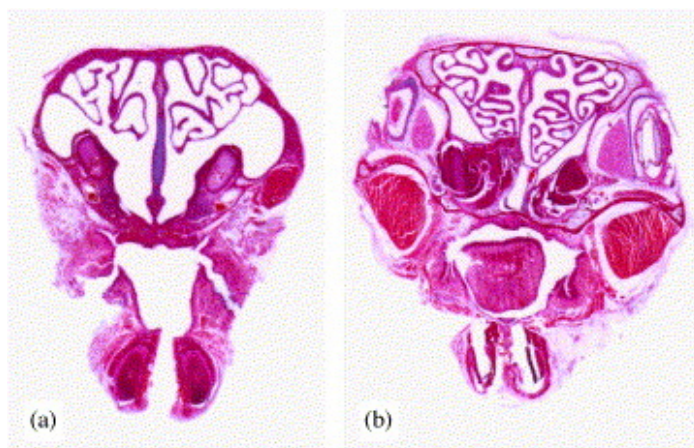

Fig. 3a, b. Low power micrographs prepared from caudal tissue slices of squirrel 4 showing (b) the extent of bilateral nasal occlusion by the mass of haphazardly arranged odontogenic tissue and bone, and (a) a similar slice from a normal animal. HE. ×8.
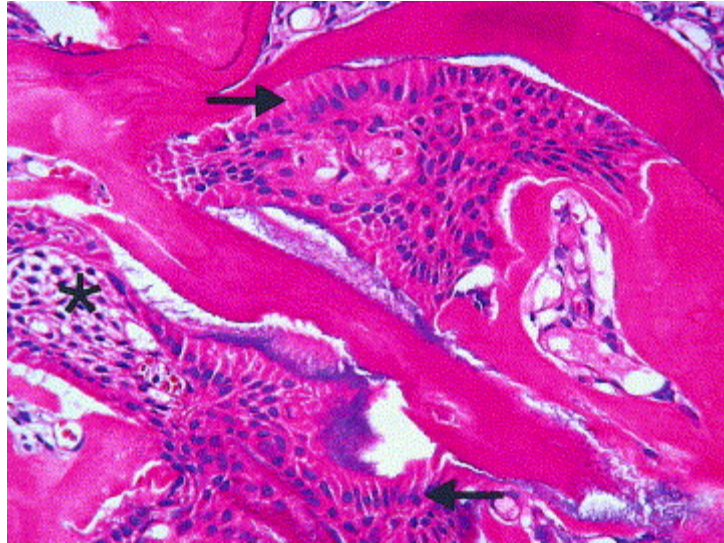
Fig. 4. High power view of Fig. 3b showing odontoma-like areas consisting of columnar odontogenic epithelium with prominent peripheral palisading (arrows) and stellate reticulum-like areas (*) in close association with dentine and cementum-like mineralized tissue. HE. ×200.

The affected maxillary incisors showed a range of anatomical abnormalities. Disruption of the surrounding alveolar bone and impingement of proliferating bone on the dental follicle with severe disturbance of normal odontogenesis were present in some cases. Interestingly, the incisors of squirrel 8 and one of the incisors of squirrel 7 showed only abnormal, corrugated enamel on the labial surfaces with distortion of the apex, without odontoma-like masses (Fig. 5). Most affected teeth had obliterated pulp chambers extending from the apical area to the incisal edge. Some also showed prominent replacement of the posterior pulp tissue with hard tissue representing bone and cementum-like material. No microscopical lesions were encountered in any of the mandibular incisors of squirrels 3, 4 and 5.
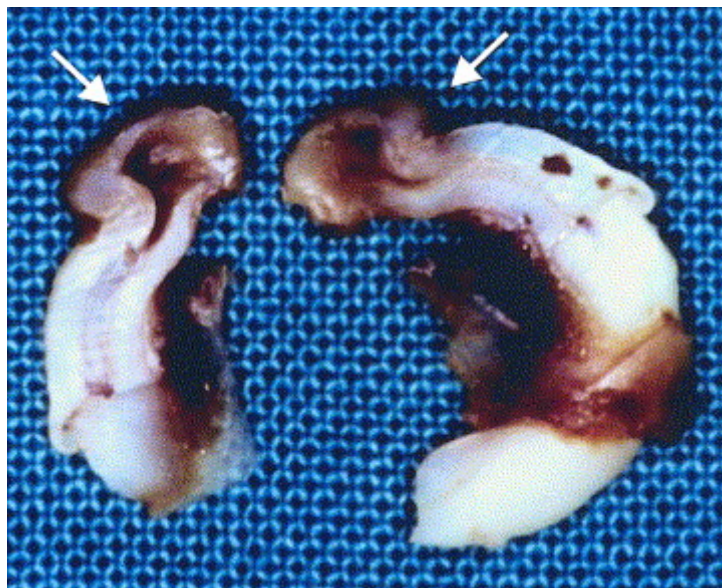

Fig. 5. Longitudinal section through an affected maxillary incisor shows apical distortion (arrows) with abnormal labial surface enamel but without an apical mass.

During the bell stage of odontogenesis, the roots of normal brachyodont teeth develop through elongation of the Hertwig epithelial root sheath, which is a continuity of the inner and outer enamel epithelium. Through epithelium–mesenchymal interaction, the pulp mesenchyme is induced to form odontoblasts, (the dentine-forming cells) and the follicle mesenchyme is induced to form cementoblasts, which will form the cementum covering the root of the tooth (Nanci, 2003). An important aspect of root formation under these circumstances, however, is the epithelial diaphragm; this results in the formation of a closed root apex, through which the neurovascular bundles penetrate the root canals (Nanci, 2003). Eventually the completed root consists of dentine covered by cementum, with no sign of enamel, and with no ability to develop further.

The elodont incisors of rodents differ from brachyodont teeth in having enamel only on the full length of their labial surfaces, extending from the apical area to the incisal edge, and no anatomical roots as described earlier. Opposing aspects have only a dentine and cementum covering (Kertesz, 1993); as a result these teeth wear to a chisel-shaped cutting edge due to the rostral-caudal gliding movement of the jaw (Crossley, 1995) during normal feeding. Elodont-type teeth grow on their pulpal axis throughout the life of the animal; the apical foramina of such teeth never close, resulting in a so-called open-rooted system (Kertesz, 1993). Due to the continuously developing nature of these teeth, all stages of odontogenesis can be evaluated at any given time from sections prepared from the apical end to the incisal edge (Ohshima *et al.*, 2005). Molecular biological studies have confirmed the existence of a "niche" for the self-renewal of adult stem cells in these elodont incisors and the molecular signals regulating their maintenance (Harada et al., 1999 and Harada et al., 2002). A "niche" is defined as the micro-environment that favours the presence and division of stem cells, forming daughter cells (Perez-Moreno *et al.*, 2003). Recently, the new term "apical bud" was proposed to refer to this stem cell compartment of continuously growing teeth, as it corresponds to the transient bud of teeth with limited growth and can therefore be seen as a permanently maintained bud at the apex of continuously growing teeth (Ohshima *et al.*, 2005). After cell division of stem cells in the apical bud of elodont teeth, one daughter cell remains in the stem cell compartment and the other gives rise to differentiated cells, i.e., odontoblasts, ameloblasts and cementoblasts (Ohshima *et al.*, 2005). The length of the clinical crown of the upper incisors is therefore maintained by a combination of cell proliferation at the apical end and attrition of the incisal edge (Ohshima *et al.*, 2005).

Odontomas represent the most common type of odontogenic tumour in man (Chang *et al.*, 2003) and are considered by many to be odontogenic hamartomas rather than true neoplasms (Neville *et al.*, 2002; Head *et al.*, 2003). Hamartomas are defined as benign tumour-like lesions composed of an overgrowth of mature tissue that normally occurs in the affected part of the body but with disorganization and often one element predominating (Anreoli *et al.*, 2000). In the case of odontomas, the tumour may consist of either multiple, small tooth-like structures (compound odontoma) or a conglomerate mass of odontogenic hard and soft tissue (complex odontoma) (Neville *et al.*, 2002; Head *et al.*, 2003). Odontomas have been diagnosed in mice (Ida-Yonemochi *et al.*, 2002), dogs (Eickhoff *et al.*, 2002; Felizzola *et al.*, 2003; Papadimitriou *et al.*, 2005), prairie dogs (Phalen *et al.*, 2000), horses (DeBowes and Gaughan, 1998), cows (Tetens *et al.*, 1995) and in an elephant (Raubenheimer *et al.*, 1989). The so-called "odontogenic dysplasia in ageing rodents and lagomorphs" is defined as the disorganized development of the continuously erupting incisor teeth of rodents and lagomorphs, due to inflammation, trauma, toxicosis or age (Head *et al.*, 2003).

The pathogenesis of these odontoma-like lesions in rodents is not clear, but various postulates have been proposed for both spontaneously developing and experimentally induced lesions. Osteopetrosis is an autosomal recessive disease with abnormal recruitment of osteoclasts, and patients with this disease usually suffer from disturbed tooth eruption and the formation of odontoma-like masses. This has been postulated to be the result of reduced bone resorption (Schour *et al.*, 1949) and a disordered

extracellular matrix remodelling capacity in such tissue (Ida-Yonemochi *et al.*, 2002). According to these and other similar postulates, the formation of these tumours is the result of crowding of the odontogenic tissue rather than excessive proliferation thereof (Schour *et al.*, 1949; Philippart *et al.*, 1994; Nakajima *et al.*, 1996; Ida-Yonemochi *et al.*, 2002). Due to the reduced resorption ability of bone, osteopetrotic mice with odontoma-like periapical masses have bone trabeculae invading the tooth germs in early odontogenesis, leading to a further postulate to account for the lesions (Ida-Yonemochi et al., 2004 and Ida-Yonemochi et al., 2002). This was recently confirmed and subsequently explained by a study showing penetration of bone trabeculae into the epithelial cords of young tooth germs, creating daughter germs that each matured independently, forming their own hard and soft tissue components and resulting in odontoma-like tumours (Ida-Yonemochi *et al.*, 2002).

Trauma with damage to surrounding bone caused by chewing on cage bars or falling from a height has been proposed as a cause of odontomas in prairie dogs (Phalen *et al.*, 2000). Traumatic intrusion of the elodont incisor on impact or even local infection in the vicinity of the apical bud might theoretically cause damage to the continuously developing odontogenic tissue and its follicle, as well as to the surrounding alveolar bone. The authors suggest that the variation in pathological changes observed in the nine tree squirrels of the present study was due to the various degrees of trauma sustained by the odontogenic tissue. Chronic mild trauma such as that caused by cage biting might distort the epithelial cords, causing minor anatomical abnormalities in the teeth (i.e., irregular enamel formation on the labial surfaces). The formation of large odontoma-like masses probably resulted from severe traumatic incidents, such as falling from a height; indeed, this was confirmed by the owner of squirrel 6 which suffered a heavy fall a few weeks before the clinical examination. Severe trauma may damage the odontogenic tissue and surrounding follicle to such an extent that the epithelial cords are disrupted completely, creating daughter germ cells, each being capable of continuous development forming its own hard and soft tissue components but in a haphazard manner, leading to the formation of hamartomatous masses (Ida-Yonemochi *et al.*, 2002). A possible mechanism of this type is illustrated in Fig. 6.
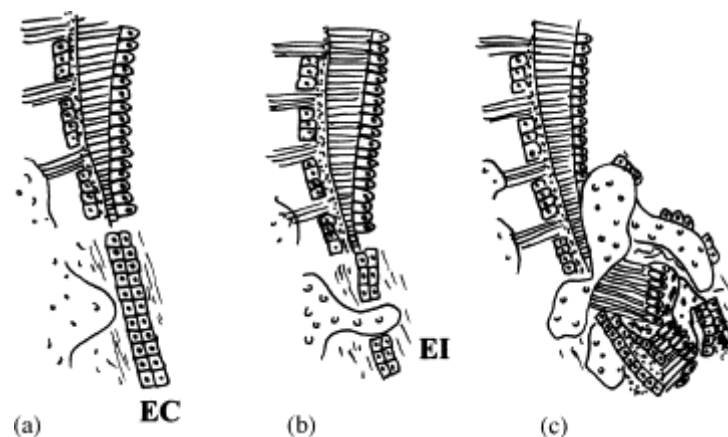

Fig. 6a–c. A line diagram to demonstrate the possible pathogenesis of elodontomas. Following trauma to the normal developing elodont tooth, bone regeneration may cause bone trabeculae to disrupt the epithelial cords (EC) but these may also have been torn by bone trabeculae on impact (a), resulting in several odontogenic epithelial islands (EI) (b). Each daughter island of epithelium, due to its continuously proliferating nature in elodont teeth, continues to form dental hard tissue, resulting in a haphazardly arranged mass of odontogenic hard and soft tissue (c).

Due to the continuously developing nature of rodent incisors with specialized apical buds, which is totally different from the cervical loop or Hertwig's root sheath of developing teeth with limited growth potential, the authors believe the term odontoma to be inappropriate when referring to these lesions. The debatable hamartomatous *vs* neoplastic nature of odontomas in brachyodont teeth warrants a separate term to describe lesions with similar histological features in elodont teeth. We therefore propose the term "elodontoma" to replace the term odontoma in respect of hamartomatous jaw lesions in squirrels and similar species with elodont teeth. Elodontoma would then be defined as a hamartoma of continuously developing odontogenic tissue and alveolar bone at the periapical bud of elodont teeth.

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