

Oral lesions associated with renal secondary hyperparathyroidism in an English bulldog

Lesões orais associadas ao hiperparatireoidismo renal secundário em um Buldogue Inglês

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Abstract

Renal secondary hyperparathyroidism is a complex clinical syndrome frequently described in dogs. However, in most cases, lesions are characterized by fibrous osteodystrophy of facial bones, affecting principally the mandible and the maxilla. There are few reports of renal secondary hyperparathyroidism associated with facial tumorous masses in the dog; similar findings in dogs have not been previously described in Brazil. This report describes the clinical, pathological, and radiological findings of this syndrome in a 14-month-old dog with oral tumorous-like lesions. The pathogenesis associated with this disease is also discussed.

Key words: Hyperparathyroidism, kidney, bone, dog

Resumo

Hiperparatireoidismo renal secundário é uma síndrome clínica complexa freqüentemente descrita em cães. Entretanto, na maioria dos casos as lesões são caracterizadas por osteodistrofia fibrosa dos ossos faciais, afetando principalmente a mandíbula e a maxila. Existem poucos relatos do hiperparatireoidismo renal secundário associada a massas tumorais na face de cães; achados semelhantes em cães não foram anteriormente descritos no Brasil. Este relato descreve os achados clínicos, patológicos e radiológicos dessa síndrome em um cão de 14 meses de idade com lesões semelhantes a tumores na cavidade bucal. A patogenia associada a essa doença também é discutida.

Palavras-chave: Hiperparatireoidismo, rim, osso, cão

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Renal secondary hyperparathyroidism (RSHPTH) is a well-recognized clinical entity observed in young dogs due to an increase in the levels of the parathyroid hormone (PTH) with nonendocrine alterations in the metabolism of calcium and phosphorus (FORREST, 2002; PALMER, 1993; TORRANCE, 1998; WEISBRODE, 2007). This syndrome is also referred as renal osteodystrophy, rubber jaw, renal rickets, and renal osteitis fibrosa (PALMER, 1993). In most cases, associated lesions are frequently described in the mandible and maxilla bones (TORRANCE, 1998; FORREST, 2002), but in severe cases gross detectable lesions are present in the nasal and frontal bones of the face and in the zygomatic arch (THOMPSON, 2007). Occasionally, facial swelling and marked demineralization of bones of the head may occur (PALMER, 1993). However, there are few descriptions of oral swelling associated with this syndrome in the dog; two cases have been previously described: one in a Great Dane (NORRIN, 1975), and the other in a Labrador retriever (SARKIALA; DAMBACH; HARVEY, 1994), and there is also the classical text-book reference (THOMPSON, 2007; WEISBRODE, 2007). This report is important since it describes a case of oral lesions associated with renal secondary hyperparathyroidism in a 14-month-old dog. It provides further information so that veterinarians (clinical and pathologist) could include this manifestation as the differential diagnosis for other oral lesions.

A 14-month-old, female, English bulldog, was presented with unusual growths of the maxillary bones; malfunctioning of mastication and swallowing was not observed. Laboratory analyses revealed elevated renal values (urea 250 mg/dl, reference range 21.4 – 42.8 mg/dl; creatinine 6 mg/dl, reference range 0.5 – 1.5 mg/dl). After three months the animal returned because of chewing and eating difficulties. Clinical examination revealed continued growth of multiple nodular masses in the maxillary bone that extended from the canine tooth to the molar area bilaterally. Teeth (mostly molars and premolars) were severely displaced, with severe expansion of oral and

palatal cortical bones. At this time mastication and swallowing were severely affected, and there was marked emaciation, extensive salivation, anorexia, generalized weakness, and increased azotemia (urea 309 mg/dl; creatinine 11 mg/dl).

Radiological evaluation of the head revealed bilateral destruction of the lamina dura around teeth resulting in a floating appearance at the demineralized bony structures of the maxilla and mandible, associated with marked mandibular and maxillary osteopenia (Fig. 1A). The owner opted for euthanasia due to the extensive oral lesions which reduced the animal's alimentary capacity and the terminal stage of the disease; necropsy was performed soon after death. Selected tissues were routinely processed for histopathological evaluation.

Significant gross findings were observed in the oral cavity and kidneys, and to some extent in the ribs. There were several different sized, smooth-surfaced masses within the mouth. These masses were more prominent at the buccal surface of the maxillary bone (Fig. 1B), and resulted in severe teeth displacement. The maxillary bone was less mineralized; the sectioned surface revealed that the tooth was embedded in a firm reddish-brown colored tissue. The size of the right kidney was remarkably reduced relative to the left. Both kidneys were pale, firm, and shrunken; capsular surfaces were remarkably scarred, irregular with several whitish, finely lines located principally at the cortex. The ribs bent easily without much applied force.

Microscopic alterations were restricted to the oral masses and the kidneys. Oral lesions revealed osteolytic activity of the trabeculae of the alveolar bone associated with extensive and severe proliferation of loose fibrous connective tissue that consisted mainly of spindle-shaped cells, resulting in almost total substitution of normal bone (Fig. 1C). The connective tissue was severely hemorrhagic and consisted of randomly distributed giant cells, located adjacent to trabecular bone. Two types of giant cells were observed: the predominant type consisted of

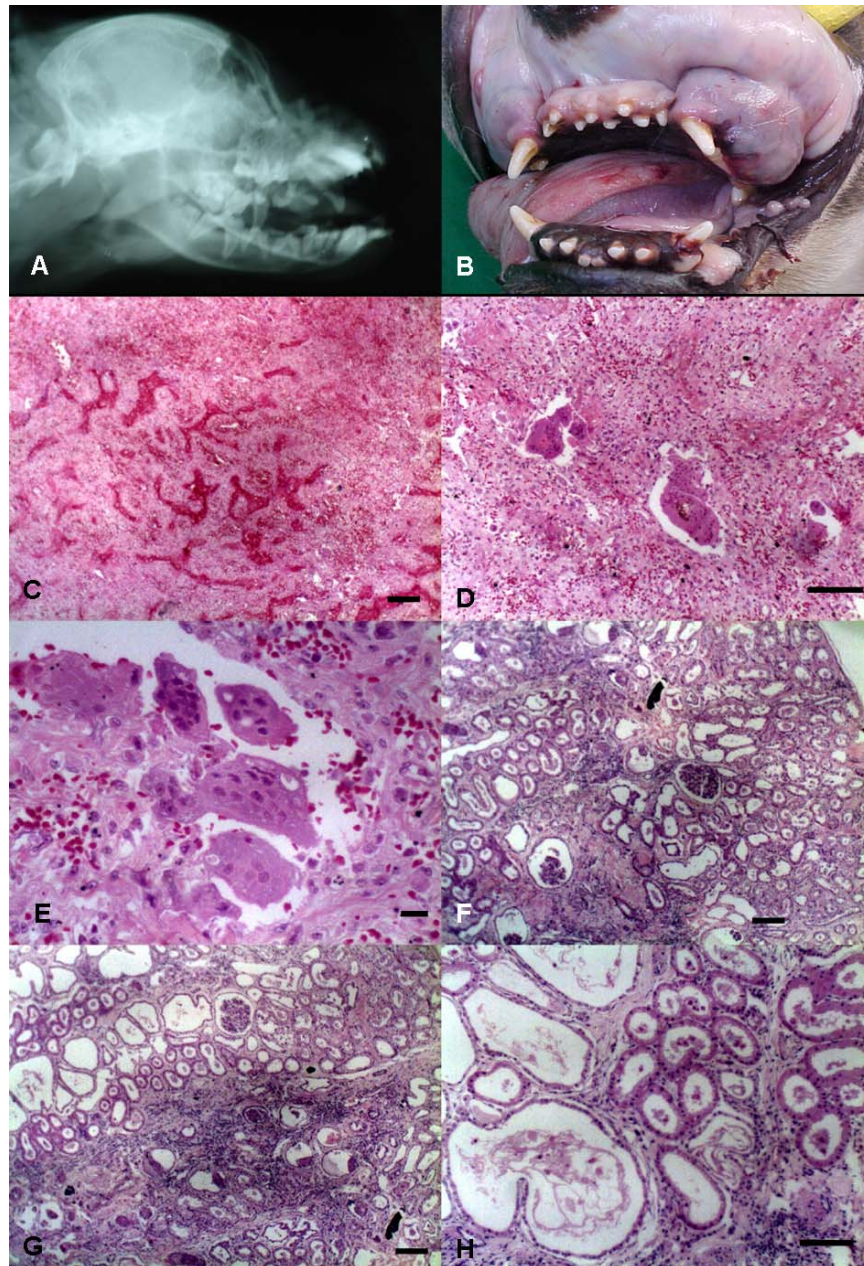


Figure 1. Composite photograph of secondary renal hyperparathyroidism in a 14-month, English Bulldog.

A. Radiographic image of lateral view of head; there is mandibular and maxillary osteopenia and marked loss of lamina dura around teeth.

B. Gross image of oral cavity; observe proliferative mass around the maxillary and canine areas.

C. Microscopic image of maxillary bone. Note extensive proliferation of fibrous connective tissue substituting bone and moderate multifocal hemorrhage. HE. Bar = 100 μ m.

D. Microscopic image of maxillary bone. Note multinucleated giant cells adjacent to trabecular bone. HE. Bar = 100 μ m.

E. Microscopic image of maxillary bone. There are several multinucleated giant cells of different sizes (ranging from 10 - 150 μ m extension) with peripheral and random distribution of nuclei. HE. Bar = 10 μ m.

F. Chronic renal insufficiency: kidney, cortical zone. Observe reduced number of glomeruli, glomerulosclerosis and dilation of renal tubules. HE. Bar = 100 μ m.

G. Chronic renal insufficiency: kidney, cortical zone. Note marked influx of mononuclear inflammatory cells, proliferation of interstitial connective tissue and mineralization. HE. Bar = 100 μ m.

H. Chronic renal insufficiency: kidney, cortical zone. Compare severely dilated renal tubules with their normal counterparts. HE. Bar = 10 μ m.

huge (> 100 µm in extension), irregular, eosinophilic giant cells with extensive cytoplasm and randomly distributed nuclei; others were smaller (< 50 µm), regular in shape, with nuclei arranged at the periphery (Fig. 1D-E). Chronic end stage renal uremic-associated lesions were observed in both kidneys, and were located predominantly at the cortex; but the right kidney was more affected than the left. Right kidney lesions consisted of severe multifocal interstitial fibrosis; marked dilation of renal tubules; significant reduction in the number of glomeruli; discrete foci of osseous metaplasia; severe multifocal proliferation of glomerular membranes; discrete multifocal glomerulosclerosis; moderate multifocal tubular and glomerular proteinuria; moderate, multifocal metastatic mineralization of tubular basement membranes and some vessels, and severe multifocal interstitial influx of mononuclear inflammatory cells (Fig. 1F-G). Lesions of the left kidney were similar to those of the right, but cortical tubular dilation was more diffuse and severe with comparatively reduced interstitial fibrosis and influx of mononuclear inflammatory cells.

A diagnosis of renal secondary hyperparathyroidism (RSHPH) was based on clinical, radiological, gross, and histological findings observed in this dog; similar cases have been described in young dogs (NORRDIN, 1975; SARKIALA; DAMBACH; HARVEY, 1994; THOMPSON, 2007; WEISBRODE, 2007). Unfortunately the serum levels of calcium, phosphorus, vitamin D, or PTH of this dog were not determined, so the specific hormonal dysfunctions associated with the clinical syndrome in this dog are not known. Nevertheless, the findings observed in this case are strongly indicative of secondary hyperparathyroidism due to chronic renal insufficiency demonstrated by progressive azotemia with corresponding histological findings consistent of renal uremic lesions (MAXIE, 1993). In the two previously described cases both dogs demonstrated elevated PTH, urea, and creatinine values, with calcium being normal (NORRDIN, 1975; SARKIALA;

DAMBACH; HARVEY, 1994). However, serum phosphorus was reported as normal (NORRDIN, 1975) and increased (SARKIALA; DAMBACH; HARVEY, 1994).

The end stage renal uremic-associated lesions observed in this case, particularly in the right kidney, were similar to those previously described (NORRDIN, 1975), where these lesions were characterized as renal cortical hypoplasia. However, we prefer to consider the renal alterations observed in this dog as being associated with chronic uremia rather than hypoplasia. This is because the term renal cortical hypoplasia is not appropriate and should be avoided since it is considered inconsistent with actual recognized concepts of renal embryology and anatomy (MAXIE, 1993). Although the kidneys of dogs may be reduced in size this does not necessarily imply that there is concomitant renal hypoplasia; additionally, most small kidneys of domestic animals diagnosed as hypoplastic may in fact be dysplastic or scarred (MAXIE, 1993). In veterinary medicine, the criteria for the diagnosis of renal hypoplasia are not well established. When this abnormality occurs there is quantitative reduction in the mass of metanephric parenchyma, and in these cases, the affected kidney should be weighed and compared with the other to confirm this diagnosis (MAXIE, 1993).

The loss of lamina dura observed around the teeth in this case with marked mandibular and maxillary osteopenia are consistent with RSHPH in dogs and normally results in a floating appearance to the remaining teeth within the demineralized bone (DRAZNER, 1987; FORREST, 2002; THOMPSON, 2007). Similar radiological evidences were also described in a dog with this syndrome (SARKIALA; DAMBACH; HARVEY, 1994). In severe cases there is further destruction of alveolar socket bone, osteitis fibrosa cystica of the mandibular and maxillary bones, resulting in softening of the mandibular bones and the formation of the rubbery jaw syndrome (DRAZNER, 1987).

These oral secondary renal hyperparathyroidism-induced lesions observed in this case are not

frequently seen in dogs. To the authors' knowledge similar cases have not been previously described in dogs in Brazil. Therefore, this unusual manifestation of RSHPTH in dogs must be differentiated from oral tumors such as the central (VALENTINE et al., 1988) and the peripheral giant cell granulomas (VALENTINE; ECKHAUS, 1986), the giant cell reparative granuloma (BLASCHKE, 1994), the giant cell epulis (SCHNECK, 1975), and the giant cell tumor of bone (THOMPSON; POOL, 2002).

Additionally, the pathological findings observed in this dog are comparable to what is known as "brown tumor" of humans (MAFEE et al., 2003). Brown tumor is a rare clinical non-neoplastic reactive growth that is associated with primary, secondary, and/or tertiary hyperparathyroidism, and is more frequently described in aged persons (BLASCHKE, 1994; TAKESHITA et al., 2004). These lesions are solitary or multiple (BLASCHKE, 1994), slow growing and aggressive (MAFEE et al., 2003), and have been observed in the ribs, clavicles, pelvic bones, and the maxillary bones of affected individuals (TAKESHITA et al., 2004). This syndrome is a misnomer since there is no neoplastic potential in this growth (MAFEE et al., 2003); and the name is due to the brownish discoloration of the affected tissue seen grossly imparted by excessive hemorrhage and hemosiderosis (BLASCHKE, 1994).

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