

## Severe Calcification of Mucocutaneous and Gastrointestinal Tissues Induced by High Dose Administration of Vitamin D in a Puppy

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**ABSTRACT.** A three-month-old male Bull Terrier was referred to the Animal Medical Centre, Nihon University with chief complaints of subacute emesis and lethargy. Severe leukocytosis, high CRP, hypercalcemia and hypochloremia were detected. Moreover, severe calcification of gingival mucosa and abdominal skin, and abnormalities of the skeletal system were discerned. Abdominal X-ray and endoscopic examination revealed ulcer and hemorrhage on the mucosal membrane of the stomach. This might have been due to injections of high dose vitamin D at 3 and 2 weeks ago by another practitioner, according to the detailed history of medication. After two months, a gastrointestinal and skin disorder disappeared, although calcification of the stomach membranes remained and abnormality of the skeletal system had worsened. Therefore, vitamin D should be carefully administered to a puppy.

**KEY WORDS:** puppy, severe calcification, vitamin D toxicosis.

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It is not clear why calcification of mucocutaneous and gastrointestinal tissues occurs, but it is well known that high dose administration of vitamin D induces hypercalcemia. Because we had an opportunity to examine a puppy, which suffered from calcification of some tissues caused by high dose administration of vitamin D, we report it in this paper.

A three-month-old, 3.5 kg, male Bull Terrier was referred to the Nihon University Animal Medical Centre with subacute emesis, unequal abdominal pain, skin ulcer, polyuria, polydipsia and lethargy. The slightly emaciated patient puppy had usually licked many kinds of metals and plastic substances in its surroundings. Physical examination revealed a severe calcification of the gingival mucosa and abdominal skin, and systemic skeletal abnormalities (Fig. 1). A diagnosis of cholecalciferol toxicosis was suggested by serum biochemical abnormalities; profound hypercalcemia (observed Ca, 16.4 mg/dl; reference range of 7.9 to 12.2 mg/dl in our hospital for less than 6 month old puppies), lower normal phosphorus concentration (5.0 mg/dl; reference range of 5.1 to 10.4 mg/dl), BUN (29.6 mg/dl) and creatinine (0.5 mg/dl). Increased neutrophils in number and high CRP were found on blood examination. Urine analysis indicated hypercalciuria (>16 mg/dl). Moreover, the serum 1-alpha-25 OH<sub>2</sub> Vitamin D value of the puppy was high (51.1 pg/ml). Abdominal radiography revealed that the barium administered 4 days before, remained in the stomach and a part of the descending colon. Gastric folds were observed as stripe-shaped calcification on radiography (Fig. 2a). Endoscopic examination showed ulcerous lesions and punctate hemorrhage on the mucosal membrane of the stomach, and food block covered with barium (Fig. 2b).

The puppy was treated with antibiotics (orbifloxacin, 15 mg/head, sid), gastrointestinal mucous membrane protectant

(sucralfate, 200 mg/head, bid), H<sub>2</sub> receptor-blocker (famotidine, 5 mg/head, bid) and prednisolone (1.5 mg/head, sid). Calcification of the gingival mucosa had disappeared, and his serum calcium level and CRP value were within the normal range in two weeks, but a low rectal temperature and aggravated depression were observed at two weeks after the first examination in our hospital. At that time, the hypothyroidism was suspected because of hypothermia, low serum phosphorus, high total cholesterol (392 mg/dl) and low serum T4 and fT4 (tT4, 0.49 µg/dl; reference range of 0.85 to 10.5 µg/dl, fT4, 0.22 ng/dl; reference range of 0.5 to 3.0 ng/dl in our hospital for dogs, respectively). Levothyroxine analogue (250 µg/head, bid) was also administered, improving the clinical findings in a few days. After two months, a gastrointestinal and skin disorder had disappeared, although calcification of the stomach membranes remained and abnormality of the skeletal system had worsened. The left forelimb was slightly twisted with a differences in length between the radius and cubitus. Calcification had developed at the synovial membrane of the major joint such as a stifle.

The abdominal radiography and endoscopy performed in our hospital revealed the calcification in the stomach but not in the kidneys, though renal calcification is a common finding in hypercalcemia as well as mild glomerulonephropathy in dogs [1, 2].

The medical history revealed that this patient had been administered intramuscularly 500,000 units of vitamin D analogue (the daily requirement for a 3 to 5 kg puppy was 80 units/head) [3] as a treatment for rachitis because of only revealing a slight pain in the left forearm, but the practitioner did not do any clinical examinations or even radiography. At our first examination, the alteration in the epiphyses was

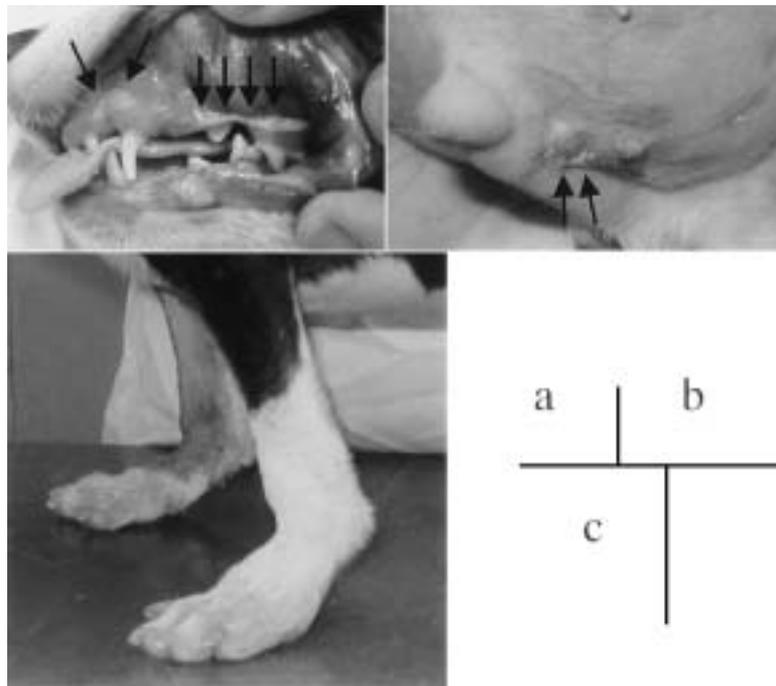


Fig. 1. Calcification of gingival mucosa of the patient puppy. Band-like mineralization (arrows) on the upper gingival mucosal membrane (a). Erosive lesion with cream colored calcium board (arrow) of abdominal skin (b). The knuckles showed an abnormal angle, which indicated calcification and inflammation confirmed by radiography (c).

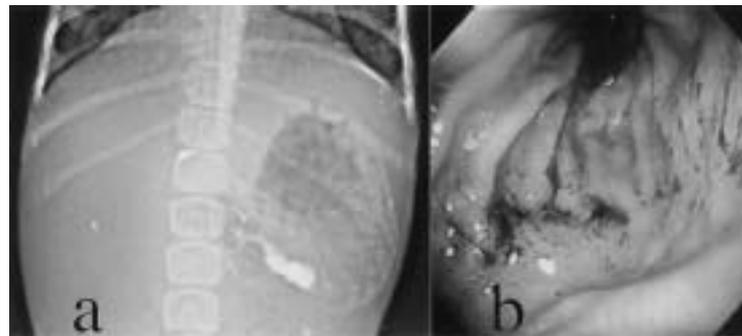


Fig. 2. Stripe-shaped calcification and remaining barium on the stomach mucosa detected by radiography (a). Barium clearly on the mucosal membrane of the stomach with punctate hemorrhage in the pyloric region (b).

not listed in the radiographic findings (Fig. 3). The puppy began to vomit from two days after the first injection of vitamin D analogue, and was admitted to an animal hospital. During a 5-day hospitalization, the patient puppy was treated under an uncertain diagnosis with antibiotics and antiemetics, and recovered. Sixteen days after the first injection of vitamin D, the patient puppy was given a second injection of the vitamin D analogue when he was admitted for the examination for dermatitis with skin mineralization. He began to vomit severely, on the day after the second vitamin D administration. At last, he was referred to our hospital seven days after the second injection of vitamin D

analogue.

Vitamin D toxicosis causes osteoclastic activity and increases calcium uptake from the intestinal membranes, which may result in hypercalcemia. Increased serum calcium was considered to induce mineralization in the stomach membrane, gingival mucosa, skin and synovial membrane of major joints.

A severe adverse reaction was induced, although only a small amount of medicine was administered. The formula was for domestic animal use and contained highly concentrated cholecalciferol.

Vitamin D toxicosis has been reported in dogs when they



Fig. 3. Radiographic findings in his forearms. The patient puppy presented differ from the rachitis, since the epiphyses of his radius were indicated with no change.

ingested a cholecalciferol-containing rodenticide [2, 4] or topical antipsoriatic vitamin D analogue ointment [5].

Therefore, attention should be paid to vitamin D toxicosis in dogs, especially when vitamin D analogues are administered.

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