Severe pulmonary mineralization in a dog with pituitary-dependent hyperadrenocorticism: a case report

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Abstract: A 7-year-old, spayed female Chihuahua with dyspnea, intermittent cyanosis, and dermal plaques was diagnosed with hyperadrenocorticism. Thoracic radiographs showed markedly hyperdense alveoli in multiple lung lobes. Computed tomography (CT) images showed lung mineralization confined to the lung parenchyma and pituitary macroadenoma. Pulmonary mineralization secondary to hyperadrenocorticism is commonly found on histopathologic examination. However, those lesions are rarely identified radiographically. We describe obvious pulmonary mineralization secondary to hyperadrenocorticism found on radiographs and present the first report regarding CT imaging of the mineralization. Pulmonary mineralization should be considered when a dog affected by hyperadrenocorticism shows diffuse lung mineralization on radiographs.

Keywords: computed tomography, dog, hyperadrenocorticism, mineralization, radiography

Pulmonary mineralization is a common pathologic finding in dogs with hyperadrenocorticism [1]. However, ante mortem diagnosis of pulmonary mineralization is extremely difficult, as it generally does not induce remarkable change on radiography. Calcification of the tracheal rings and bronchial walls can be observed radiographically in dogs with hyperadrenocorticism, but these can also be age-related changes [2,3]. Compared with airway calcification, pulmonary mineralization is usually seen as a generalized interstitial lung pattern, not as diffuse mineral densities.

Due to the low sensitivity of radiography for pulmonary mineralization, 3 dogs with hyperadrenocorticism have previously been diagnosed using nuclear scintigraphy with 99m-technitium-methylene diphosphonate [4,5]. In human medicine, not only is nuclear scintigraphy used, but high-resolution computed tomography (CT) is also recommended for the definitive diagnosis of pulmonary mineralization [2,6]. Pulmonary mineralization may contribute to hypoxemia in dogs [4], thus CT study should be considered in any dog with suspected pulmonary mineralization from hyperadrenocorticism. Though CT imaging is widely available in veterinary medicine, to the authors' knowledge, there are no reports on CT imaging of pulmonary mineralization in dogs with hyperadrenocorticism. Here, we describe a case of pulmonary mineralization secondary to pituitary-dependent hyperadrenocorticism (PDH) as visualised by radiography and CT study.

A 7-year-old, spayed female Chihuahua presented in respiratory distress with cutaneous lesions. Erythematous, palpable, and firm papules as well as well-demarcated plaques with ulceration and crusting were observed on the thorax and abdominal region (Fig. 1A). Respiratory signs including dyspnea, panting and cyanosis under stress had been observed for months. Previous diagnostic examination or treatment had not been pursued in this dog because the clinical signs were mild. A complete blood count showed mild thrombocytosis (614 K/µL; normal range, 148–484 K/µL) with a stress leukogram demonstrating neutrophilia and eosinopenia. Serum chemistry showed a marked elevation of alkaline phosphatase (1,597 U/L; normal range, 23–212 U/L).
Radiography revealed mineralization with alveolar infiltrate and radiolucent bronchi within the lung lobes, particularly in the caudal lobes, as well as mineralization of tracheal rings (Fig. 1C and D). Dorsal cutaneous and subcutaneous radiopaque changes were also present, suggesting mineralization. Abdominal ultrasonography revealed bilateral mineralization of the renal cortices and bilateral adrenal gland enlargement (left = 6.7 mm, right = 5.7 mm). Hepatomegaly was consistent with cutaneous calcinosis cutis. The overlying epidermis and follicular epithelium were hyperplastic, and the dermis was densely fibrotic, with some areas of mature granulation tissue. Histopathologic examination was consistent with cutaneous calcinosis cutis.

Hyperadrenocorticism was confirmed and trilostane was administered at a dose of 1 mg/kg orally every 12 hours. Despite treatment, the respiratory signs persisted. The dog was euthanised due to respiratory distress 60 days after the diagnosis. Unfortunately, necropsy could not be performed due to the owner’s wishes.

Pulmonary mineralization is rarely found by radiography as compared with the mineralization of the airway which is usually seen in aging animals. Although about 90% of hyperadrenocorticism cases have pulmonary mineralization on histopathologic examination, only a few cases have been identified on radiographs [1,4]. Even in those dogs, the generalised interstitial lung pattern seen was not specific to pulmonary mineralization. Interstitial infiltrate can be seen in other conditions such as chronic bronchitis, cardiogenic and non-cardiogenic pulmonary oedema, eosinophilic broncho-pneumopathy, lung fibrosis and more. In the present case,
marked hyperdense alveoli were identified in multiple lung lobes and the density of the alveoli was notably high, indicating the possibility of pulmonary mineralization rather than other conditions.

In humans, bone scintigraphy and CT scans are used to confirm pulmonary mineralization [6,7]. CT allows the identification of minimal changes in lung density as it discriminates a density difference of 0.25% to 0.5%, as compared to radiography, which can detect a density difference of about 10% [3]. CT study was performed in our case due to the availability of the imaging modality. In this dog, not only were there mineral density changes of multiple lesions, but also increased density of overall lung fields. In general, lung densities are considered to be normal between −700 and −850 HU [8]. When hyperinflation or emphysema occurs in the lung, the lung density falls below −850 HU. When the lung density is above −700 HU, infiltrative parenchymal disease is suspected. In this dog, the density of the lung parenchyma was about −370 HU due to the interstitial infiltrate, which was not observed on radiography. Moreover, discrete lesions with mineral density were observed in multifocal areas on CT images. The lesions were coalesced mineralized alveoli which contained gas-filled bronchi in some areas. The dog in this case presented with dyspnoea and cyanosis under stress and finally died secondary to respiratory distress. In addition to marked mineralized alveoli, diffuse parenchymal infiltrates could have aggravated the respiratory condition in this case.

About 33% of dogs with pulmonary mineralization showed hypoxemia (PaO\textsubscript{2} < 53 mmHg) in a previous study [4]. In hyperadrenocorticism, respiratory failure, such as panting and dyspnoea, is one of the most common clinical findings. However, thrombosis is another potential complication of the hyperadrenocorticism, with pulmonary thromboembolism (PTE) being most common in dogs [9]. The radiographic features of PTE can be nonspecific ranging from normal appearance to interstitial infiltrate. Chronic thrombi in the pulmonary vessels can be seen as mineral densities, but they are confined to the vascular lumen, not the alveoli. In dogs, clinical signs of pulmonary mineralization are difficult to differentiate from signs of PTE, but the typical CT features, such as increased mineral density of the pulmonary alveoli, can be pathognomonic for pulmonary mineralization.

Lack of the histopathologic examination of the lungs lim-
its this case. However, the presumptive diagnosis of pulmo-
mary mineralization secondary to PDH could be made in this
case based on the evidence: 1) PDH confirmed by ACTH
stimulation testing, adrenal hyperplasia and a pituitary mass,
2) generalised mineralization of the cutaneous tissue con-
firmed as calcinosis cutis on histopathologic examination,
and 3) CT confirmed the mineralization to the pulmonary
alveoli and ruled out PTE as the cause of mineral densities in
the lung.

We report a dog diagnosed with dystrophic pulmonary
mineralization and calcinosis cutis secondary to PDH. To the
best of our knowledge, this is the first case of obvious pul-
monary mineralization visualised as mineral density on radi-
ography in a dog with PDH, and the first description of CT
features associated with pulmonary mineralization. Pulmo-
nary mineralization should be considered when a dog affected
by hyperadrenocorticism exhibits respiratory failure and diff-
use interstitial infiltrates or mineralization on radiography.

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