

## Calvarial hyperostosis syndrome in a young Weimaraner dog

### *Calvarium hyperostosis syndroom bij een jonge weimaraner*

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## ABSTRACT

**Calvarial hyperostosis syndrome (CHS) is a rare, non-neoplastic, proliferative bone disease of the flat bones of the skull. The lesions of CHS are initially painful, but self-limiting with skeletal maturity. Therefore, treatment is aimed at relieving pain. Until recently, CHS has only been described in young Bullmastiffs and the etiology is still unknown. In this report, CHS is described in a six-months-old, male Weimaraner with the typical presentation of an asymmetrical swelling affecting the frontal, parietal and sometimes occipital bones of the skull.**

## SAMENVATTING

Calvarial hyperostosis syndroom (CHS) is een zeldzame, goedaardige, proliferatieve botaandoening van de platte beenderen van de schedel. Het proces is aanvankelijk pijnlijk maar geneest vanzelf als het skelet volgroeid is. De behandeling is daarom gericht op pijnbestrijding. Tot voor kort werd CHS enkel beschreven bij jonge bullmastiffs en voorsnog is de etiologie onbekend. In deze casuïstiek wordt een zes maanden oude weimaraner beschreven met CHS met de typische presentatie van een asymmetrische zwelling van de frontale, pariëtale en soms occipitale beenderen van de schedel.

## INTRODUCTION

Calvarial hyperostosis syndrome (CHS), previously also called idiopathic calvarial hyperostosis (Fischetti et al., 2006) is a non-neoplastic, proliferative bone disease of the flat bones of the skull. CHS has been reported to share clinical, radiographic and histopathological characteristics with canine craniomandibular osteopathy (CMO) (Pastor et al., 2000; Huchkowsky, 2002; Mathes et al., 2012). They are all self-limiting diseases in young patients, with pain at the onset of the disease. Therefore, no specific treatment is needed and the animal is supported with analgesia when necessary. Some dogs with CHS have concurrent fever, lameness and lymphadenopathy (McConnell et al., 2006). Diagnosis can be made based on clinical presentation, radiographs and histology results (Dennis et al., 1993; Pastor et al., 2000; Fischetti et al., 2006; Mathes et al., 2012).

Until recently, CHS has only been described in young Bullmastiffs, more often in male than female dogs (Pastor et al., 2000; Fischetti et al., 2006; McConnell et al., 2006). A report of similar changes found in a young Pitt Bull terrier could be classified as CMO

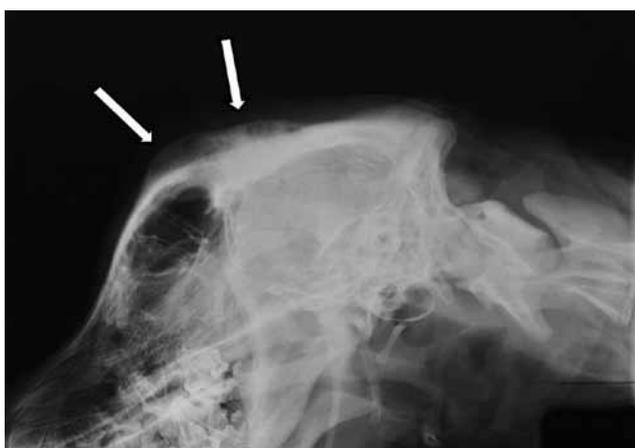
based on the bilateral involvement of the mandibles (Thompson et al., 2011; Mathes et al., 2012). Mathes et al. (2012) described CHS in an English springer spaniel with bony changes located in the left caudal maxillary and frontal bones causing a left exophthalmos. This is an unusual presentation of CHS. To the authors' knowledge, this is the first description of CHS in another breed than Bullmastiff with the typical presentation of an asymmetrical swelling affecting the frontal, parietal and sometimes occipital bones.

## CASE HISTORY

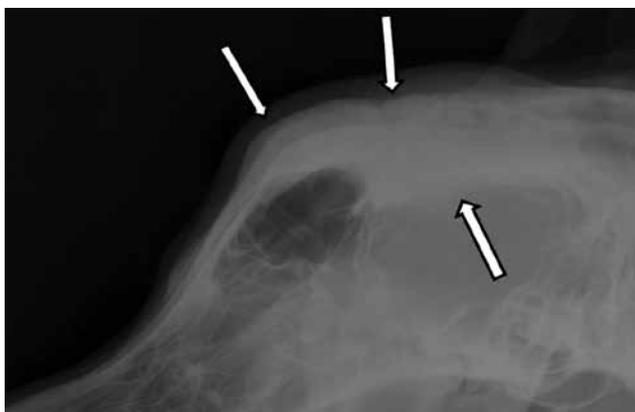
A four-months-old, male Weimaraner was presented to the referring vet for an asymmetrical swelling, initially painful, on the right frontal aspect of the head (Figure 1). The right-left lateral radiograph of the skull demonstrated a soft tissue swelling and smooth thickening of the frontal bone with an irregular structure (Figure 2). Fine needle aspirate biopsies (FNAB) of the bony changes were sent to the University Veterinary Diagnostic Laboratory, Utrecht University, the Netherlands. The FNAB revealed inflammatory cells,



**Figure 1.** Photograph of the dog with asymmetrical swelling of the forehead, taken when he was twelve months of age.



**Figure 2.** Lateral radiograph of the head of the dog. A smooth, periosteal thickening of the frontal bone with an irregular structure is present.



**Figure 3.** Lateral radiograph of the head of the dog. A layer of thick exuberant, proliferative new bone is present at the frontal bone and parietal bone with loss of trabecular pattern of the frontal bones and sclerosis.

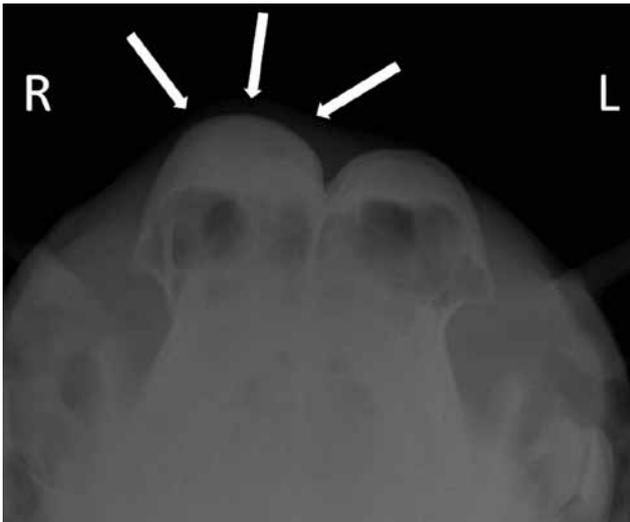
osteoblasts and osteoclasts, which was interpreted by the cytologist as indicative of bony involvement. Because the likelihood of a benign process, it was decided to treat the dog with 4mg/kg carprofen (Dolagis®, Sogeval S.A., Laval, France) once daily for a total of 36 days.

The dog was referred to Dierenkliniek Emmeloord (the Netherlands) because the dog experienced another episode of pain and an increase of the swelling one month after cessation of the medication. On presentation, the dog had a firm swelling of the right side of the frontal bone. Although at presentation not painful anymore, the swelling had enlarged to a degree that it was extending over the median to the left side of the frontal bone. The dog was in good body condition and had no other physical abnormalities.

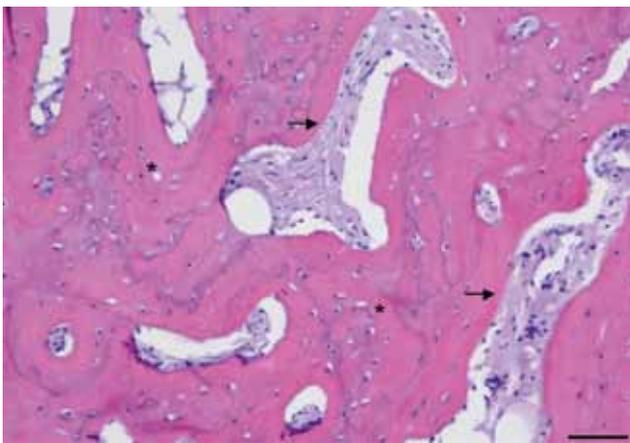
Radiographic examination of the skull included right-left lateral, dorsoventral and rostral-caudal projections. There was loss of the trabecular pattern of the frontal bones, and sclerosis was present (Figure 3). A layer of thick exuberant proliferative new bone formation was located at the right frontal bone and right parietal bone, mild proliferation was present on the left side (Figure 4). The border of the new bone formation was partly irregular. There was no evidence of adjacent cortical lysis. The new bone formation extended only dorsally (periosteal), and there was no evidence of extension into the cranial cavity. The tympanic bullae were not involved. Compared to the lateral radiograph of the referring veterinarian, the new bone formation had subjectively increased in thickness and density and had extended more caudally.

Based on the radiographic changes, a likely diagnosis of CHS was made. Jamshidi-needle biopsies of the skull were taken and submitted for histopathological analysis to the Laboratory of Pathology and Histology, GD Deventer (the Netherlands). The biopsies were decalcified in Osteosoft® (Merck KGaA, Darmstadt, Germany) for 48 hours and further processed to 4 µm-thick microscopic sections. Microscopically, the biopsies showed a periosteal bone proliferation that resulted in lamellar bone (Figure 5). The presence of fibrovascular stroma, devoid of inflammation, was noted in between the bony lamellae.

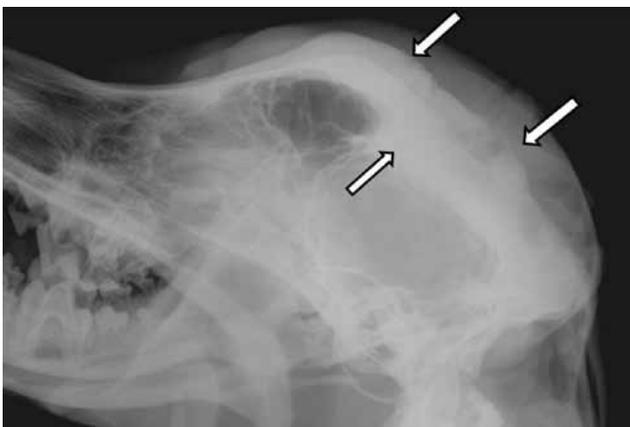
The dog was presented again three weeks later with aggravation of the swelling, marked pain and reduced appetite. Clinically, the swelling had extended over the nose, the complete right frontal bone and the parietal bone. The overlying skin was a little erythematous, the right submandibular lymph node was enlarged, body temperature was 38.5°C and the dog experienced no pain when opening the mouth. A slight blepharospasm of the right eye and hyperemic conjunctiva were present. Radiographs of the skull were repeated. The proliferative new bone formation located at the right frontal bone and right parietal bone had mildly increased in thickness (Figure 6). No other radiographic changes were visible. The dog was sent home with 0.1mg/kg meloxicam (Metacam®, Boehringer Ingelheim GmbH, Ingelheim/Rhein, Germany) once daily for one week. The dog responded well



**Figure 4.** Rostro-caudal view of the head of the dog. The exuberant, proliferative new bone formation is indicated with the arrowheads. Mild periosteal thickening of the contralateral side is present.



**Figure 5.** Microscopic features of the bone biopsies. The mass is composed of fully differentiated lamellar bone (asterisk), containing fibrovascular stroma devoid of inflammatory changes (arrow). HE stain, the bar represents 100  $\mu\text{m}$ .



**Figure 6.** Lateral radiograph of the head of the dog. The layer of proliferative new bone formation present at the frontal and parietal bone has mildly increased in thickness.

and was pain-free within four days. During the following seven months the swelling of the skull slowly decreased.

## DISCUSSION

In this case report, CHS in a young Weimaraner is described. CHS shows overlap and differences with CMO in clinical, radiographic and histopathological characteristics. CHS seems to only affect young dogs, four to ten months of age (Pastor et al., 2000; Fischetti et al., 2006; Mathes et al., 2011). It is an asymmetrical, non-neoplastic, proliferative bone disease of the flat bones of the skull. The lesions of CHS are self-limiting with skeletal maturity, with pain at the onset of the disease. Some dogs with CHS have concurrent fever, lameness and lymphadenopathy (McConnell et al., 2006). No specific treatment is needed and the animal is supported with analgesia when necessary (Pastor et al., 2000; Fischetti et al., 2006; McConnell et al., 2006; Mathes et al., 2011). Until recently, CHS was only described in young Bullmastiffs, but now the lesion has also been described in an English springer spaniel and a Weimaraner (Pastor et al., 2000; Fischetti et al., 2006; McConnell et al., 2006; Mathes et al., 2011).

CMO predominantly affects the mandibular rami, tympanic bullae, mandibular joints and sometimes the occipital and parietal bones with usually bilateral and symmetrical changes (Huchkowsky, 2002; Pastor et al., 2006; Mathes et al., 2012). It affects young, immature dogs and is self-limiting once the dog reaches skeletal maturity, similar to CHS. Clinically, the dogs have discomfort when eating or opening their mouth, they may experience periods of pain and pyrexia, and they may have excessive salivation, bilateral firm swelling of the mandible and sometimes muscle wastage (Dennis et al., 1993; Huchkowsky, 2002). It has been reported in many breeds (Dennis et al., 1993; Huchkowsky, 2002; Mathes et al., 2012) and in West Highland White terriers an autosomal mode of inheritance has been suggested (Padgett and Mostosky, 1986). CHS radiographically shows a similar type of bone reaction of the calvarium as CMO, but in contrast, the lesion in CHS is usually focal, unilateral and the mandible is not involved (Pastor et al., 2000; Mathes et al., 2012). Furthermore, CMO differs histologically from CHS (McConnell et al., 2006). Histology of CMO consists of interconnected trabeculae of woven bone, proliferative endosteal new bone and abundant osteoclasts on the bone surface. The medullary cavities (mandibles, tympanic bullae and occipital bones) become filled with loose connective tissue and few foci of dense infiltrations of inflammatory cells (Pastor et al., 2000; Huchkowsky, 2002). Histology of CHS consists of a minimal cellular fibrovascular tissue in the intratrabecular space, sometimes with a (sparse) neutrophil infiltrate, but in other cases, devoid of inflammation depending on the stage of the disease at the time histological biopsies

were taken (Pastor et al., 2000; Fischetti et al., 2006). CHS does not affect the medullary cavity and is solely localized (sub)periostally (Pastor et al., 2000; Fischetti et al., 2006; Mathes et al., 2011). Dennis et al. (1993) reported a case of CMO only involving the cranium, but unfortunately histology was not performed. Hence, this might have been a case of CHS, similar to the case described by Mathes et al. (2006).

Differential diagnosis other than CMO for this type of lesion are trauma, fracture, subperiosteal hematoma, osteomyelitis, osteoma multilobular tumor of bone and chondroma rodens (Dennis et al., 2010).

The etiology is unknown but does not appear to be traumatic, neoplastic, or degenerative. Possible factors are infectious, nutritional, metabolic and genetic (Pastor et al., 2000; Fischetti et al., 2006). As CHS has been described in an English springer spaniel (Mathes et al., 2011) and now, in the present case, also in a Weimaraner, a genetic basis for this disease is less likely.

Concurrent long bone involvement has been reported in two cases of CHS; one had post-mortem evidence of osteomyelitis and the other one appeared responsive to antibiotics (Pastor et al., 2000; McConnell et al., 2006). This would favor the hypothesis of a bacterial cause in some cases.

A disorder presenting similar features to CHS exists in humans and is called human infantile cortical hyperostosis (HICH), also called Caffey disease. It is a genetic disorder, which causes an episode of massive subperiosteal new bone formation in long bones, mandible and clavicles in infants from ten weeks to five months of age (Pastor et al., 2000; Gensure et al., 2005; Shandilya et al., 2013). Clinical signs may consist of painful swelling of the involved bones, often accompanied by a systemic fever. Most cases show spontaneous regression after a few months (Gensure et al., 2005; Shandilya et al., 2013). HICH is unlike CHS, a bilateral, symmetrical disease (Pastor et al., 2000), but pathologically, both disorders are similar in being predominately inflammatory subperiosteal or periosteal diseases (Fischetti et al., 2006). Radiographic changes consist of marked periosteal new bone formation with cortical thickening, typically involving the diaphyses of the long bones, mandibles and clavicles. There is no evidence of abnormal medullary bone (Gensure et al., 2005; Shandilya et al., 2013). Periosteal detachment of the underlying bone could be the key pathological process in the onset of episodes of cortical hyperostosis (Gensure et al., 2005; Shandilya et al., 2013). The study of Gensure et al. (2005) finding a COL1A1 mutation in HICH, raises the question if a collagen abnormality would make the periosteum more vulnerable to detachment from the underlying bone. There is a high incidence of HICH as a complication of prostaglandin E1 (PGE1) and E2 (PGE2) therapy for the treatment of ductal dependent cardiac lesions. As high as 63% of all infants receiving PGE1 infusion for more than 60 days show radiographic changes (Gensure et al., 2005; Shandilya et al., 2013).

## CONCLUSION

Calvarial hyperostosis syndrome (CHS) seems to be more widely spread among different breeds than just Bullmastiffs and should be considered in all young dogs with asymmetrical, periosteal proliferation of the flat bones of the skull. The lesion is self-limiting. Further study is required for a better understanding of the possible underlying cause(s). At the time of writing this report, 2.5 years later, the dog was still symptom-free and had not experienced any recurrent episodes; however, a very slight swelling of the cranium is still noticeable to date.

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