Hypertrophic Osteodystrophy

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HISTORY

Hypertrophic osteodystrophy (HOD) was first identified in the veterinary literature in the mid 1930s by Collett(5) and Morell.(5) Initially described as Barlow's disease in the dog, it has subsequently been termed Moller-Barlow's disease of the dog,(18) idiopathic osteodystrophy,(4) canine skeletal scurvy,(13) osteodystrophy II,(21) and metaphyseal osteopathy,(10) among other less frequently used names.(24) A developmental disease process of unknown etiology, HOD affects primarily young, rapidly growing large and giant breed dogs and has been reported to affect the Great Dane, Irish Wolfhound, St. Bernard, Borzoi, boxer, Dalmatian, Irish setter, Weimaraner, German shorthaired pointer, Doberman pinscher, German shepherd, Labrador retriever, collie, greyhound and even the bassett hound and some terrier types.(6,10,12,13,16,17)

CLINICAL SIGNS

Most animals experience the onset of clinical signs between 3 and 4 months of age (range 2 months 8 months).(1,10,13,19,26,27) Clinical signs in minimally affected animals usually relate to a slight limp, with pain exhibited on deep digital palpation of the affected metaphyses. More severely affected animals, however, may exhibit anorexia, weight loss, fever, and depression accompanied by extremely swollen, warm, and painful long-bone metaphyses, with refusal to bear weight on the affected limbs. The disease is episodic in nature and bilaterally symmetric in affliction, with periods of symptomatology of approximately 1 week duration, followed oftentimes by complete spontaneous remissions; multiple recurrences 1 to 6 weeks apart are uncommon, however.(1,10,13,19,26,27) Euthanasia is often requested by owners for those animals experiencing multiple bouts of clinical symptomatology, whereas terminal complications related to prolonged recumbency, anorexia, and hyperthermia (up to 106°F) have been reported in more severely affected animals. (10,21) The disease has been reported only in growing animals with open physes. A review of those cases presented in the literature would indicate that males are afflicted slightly more commonly than females, but there are as yet insufficient data to support such a claim.

Particularly affected are the metaphyseal regions of the long bones distal to the elbow and stifle (i.e., distal radius and ulna and tibia); however, all long-bone metaphyses can be affected, including the metacarpals, as well as the mandible and maxilla, the costochondral junctions of the ribs, the scapula, and even the anterior border of the ilium. (1,13,16,27) These grossly apparent "bony" swellings are the result of a fibrous thickening of the periosteum accompanied by periosteal new-bone formation. In earlier reports, this periosteal proliferation was believed to be related to subperiosteal hemorrhage, the extent of which seemingly determined both the degree of clinical lameness and temperature spike (due to protein resorption following hemorrhage).(1,16) In cases of extreme osteogenic activity, ossification has been reported to occur in the soft tissues outside the periosteum as well.(21) Two authors have also described metastatic calcification of the aorta,
endocardium, lungs, and kidneys at necropsy. (13,22) 

Mildly affected animals are generally presented with complaints of lameness; the physical examination localizes the pain to the metaphyses, and radiography reveals the classic radiolucent line above the epiphysis. (21) More severely affected animals are generally presented for systemic manifestations of the disease, as well as refusal to stand and walk related to excruciating metaphyseal pain. Quite frequently, case histories reveal that diarrhea and upper respiratory symptoms have occurred prior to the initial onset of lameness and HOD-related problems. (10,16,27) This has lead some to speculate on an infectious etiology or sequel. Vaccination status, size relative to littermates, and feeding schedules seemingly have little correlation to degree of affliction; few familial tendencies have been noted. (10,16) Anorexia, listlessness, and depression tend to wax and wane with changes in body temperature, while lameness is seemingly related to both body temperature and the degree of warmth and pain felt in affected metaphyseal regions. (16) Residual skeletal deformities have been reported in more severely affected animals and most probably relate to growth rate discrepancies either within a given metaphysis (e.g., tibia) or between metaphyses of closely related long bones (e.g., radius and ulna). Thus canines afflicted with this disease as puppies have often been noted to be "cow hocked" or to exhibit radiocarpal valgus deviations as adults. (1,10,13,16) Resolution of the disease process is generally accompanied by complete remodeling of affected bones; however, residual radiographic abnormalities of bone shape and texture as well as vestiges of remodeled osteophytes can occasionally be detected in adult animals. (10,27) Hematologic examinations, serum alkaline phosphatase levels, and serum calcium and phosphorus values generally remain within normal ranges, regardless of the severity of clinical symptomatology, with no definable trends noted. (10,13,26) Since the disease has been believed to be linked to vitamin C deficiency, both serum ascorbic acid levels and urine ascorbic acid levels have been noted by multiple authors, with variable and conflicting results. (3,10,13,16,25,27)

**RADIOGRAPHIC FINDINGS**

Radiographic changes in the early stages of the disease occur in the metaphyses of the long bones and are usually bilaterally symmetric. Occasionally other bones such as the mandible, ribs, or scapula are affected. Irregular radiolucent lines are seen in the metaphyses (Fig. 50-1). Although the epiphyses and growth plates usually are normal, irregular widening of the growth plate may occur as the disease progresses. Subsequently, subperiosteal or extraperiosteal new-bone formation of the metaphyses occurs, which may progress to involve the entire diaphysis (Figs. 50-2 and 50-3). The disease may manifest itself in a variety of ways depending on the stage when first observed. (10,20,27) The initial radiographic examination may reveal metaphyseal lesions and periosteal bone formation or metaphyseal lesions with soft tissue swelling only or periosteal new bone in the absence of metaphyseal lesions.

**FIG. 50-1** Radiograph of the distal radius and ulna of a 4-month old Great Dane with hypertrophic osteodystrophy. Note the irregular radiodensity of the metaphysis proximal to the growth plate and the radiolucent line immediately above it that extends across the entire width of the metaphysis.

**FIG. 50-2** Radiographs of the radius and ulna of a 5-month-old Great Dane with hypertrophic osteodystrophy. (A) First radiographic diagnosis of hypertrophic osteodystrophy; (B) 12 days later; (C) 22 days after onset; (D) 65 days after onset. Note the progression of the subperiosteal and extraperiosteal new bone formation.

**FIG. 50-3** Macerated bony specimens from dogs with hypertrophic osteodystrophy. (A) Long bones of a dog affected for 6 weeks. (B) Long bones of a dog affected for 4 months.
PATHOLOGY

Although death may occur naturally, euthanasia as a result of the disease is more common. Grossly, the most striking lesion tends to occur in the distal radius and ulna. Hemisection of an affected bone reveals a transverse band of disrupted trabeculae immediately adjacent to the growth plate (Fig. 50-4). This corresponds to the lucent zone observed radiographically. The zone of calcified cartilage and attenuated primary trabeculae appears as a yellowish white band interposed between the disrupted metaphysis and the growth plate. In terminal cases, the growth plate may be irregularly widened. This apparently is caused by failure of endochondral calcification due to disruption of the metaphyseal blood supply. Periosteal bone formation produces a collar of bone around the metaphysis. The nature and location of the lesions and the frequent absence of classic hypertrophy in this disease support Grondalen's suggestion that the term metaphyseal osteopathy is more accurate than hypertrophic osteodystrophy.

Histologically, the metaphyseal lesions are characterized by the following changes as one progresses from the growth plate toward the diaphysis (Fig. 50-5):

1. Irregular widening of the growth plate, when present, is due to increased length of the columns of hypertrophied chondrocytes.
2. The calcified cartilage spicules immediately adjacent to the growth plate frequently are devoid of osteoid on their surfaces and are surrounded by hemorrhage and massive cellular infiltration comprised predominantly of neutrophils and mononuclear cells.
3. The band of trabecular disruption consists of hemorrhage, hemosiderin deposits, fibrosis, necrotic trabeculae, and inflammatory cells.
4. Osteoclastic resorption of the adjacent metaphyseal trabeculae is focally extensive. In some cases multifocal perivascular infiltrations of neutrophils in this area are suggestive of osteomyelitis.
5. There may or may not be subperiosteal hemorrhage or reactive new-bone formation.

PATHOGENESIS

The role of vitamin C in the etiology of HOD has remained obscure. The disease was initially termed canine skeletal scurvy due to some clinical and radiographic similarities it shares with infantile skeletal scurvy in humans. The reporting of diminished vitamin C levels in urine and serum of a few affected animals, coupled with a return to "normal" values upon spontaneous recovery and the apparently "prompt" response to vitamin C therapy in certain clinical cases, has done much to circumstantially implicate it as a primary factor in the development of this disease process. Since dogs have been proven capable of synthesizing their own vitamin C, a more reasonable explanation has been offered that suggests a transient derangement of vitamin C metabolism, including failure of synthesis, storage, or utilization. The distinct predilection for certain breeds and ages has also been postulated to reflect a particular susceptibility of large breeds to such a derangement in general, and more specifically to transient liver malfunction. However, in reality HOD encompasses as many clinical,
pathologic, radiologic, and histologic distinctions from infantile skeletal scurvy as it does similarities.(13,14) Past methods of measurement of both urine and serum vitamin C levels have been open to question; regardless, many affected animals tested in these previous reports had, in fact, normal values.(7) Clinically, as many (if not more) animals treated with vitamin C do not respond to the treatment regimen as do respond, unlike humans. Finally, vitamin C may, in fact, be contraindicated in animals affected with HOD, since its supplementation has recently been proven to result in relatively higher serum calcium levels, which may, through an enhancement of hypercalcitoninism, significantly diminish bone resorption.(11,15,25) Thus, much work needs yet to be done in this area.

Evidence also has been presented that overnutrition may be the major etiologic factor in this disease.(7,11,21) That oversupplementation of vitamins, especially vitamin D, minerals, and energy are factors in the pathogenesis of HOD is supported by its occurrence in pups that have received massive dietary supplements.(2,22) Observations of dystrophic mineralization in the endocardium, aorta, and kidneys further support this concept.(21-23) In spite of this evidence, overnutrition is not a consistent finding in dogs with HOD, and in those in which it is, dietary correction alone seldom leads to remission of the clinical signs.

Finally, as mentioned above, because of the frequency with which affected animals have exhibited prior systemic signs of illness, an infectious etiology has been postulated.(10) In truth, the disease's etiology remains unknown. The possibility of HOD occurring in animals afflicted by other metabolic bone diseases (e.g., panosteitis, retained endochondral cores, osteochondrosis) must always be kept in mind.

**TREATMENT**

The treatment regimens administered for HOD have been as diverse as the tentatively diagnosed etiologies. Antibiotics, analgesics, antihistamines, glucocorticoids, parathormone, vitamin C, and dietary changes (especially mineral and vitamin D supplements) have all been tried; the results have been equivocal with all regimens.(10,16) The many spontaneous remissions of symptomatology so characteristic of untreated animals have made all treatments appear somewhat successful and allowed no proof of uniform cure. There is some justified belief that mineral, vitamin C, and vitamin D supplements should be avoided because they may accelerate the rate of dystrophic calcification as well as diminish the rate of bone remodeling.(2,10,16,25) Since there is apparently no significant difference in the recovery rates between intensively treated and untreated animals, guidelines for therapy must of necessity remain vague.(1,10) Dietary imbalances, if detected, should be corrected. Analgesics to control pain may be of benefit, beginning with salicylates and phenylbutazone, reserving corticosteroids for the more refractory cases. Finally, good nursing care to prevent decubitis, the stimulation of appetite (to include force feeding), and fluid replacement to offset dehydration may all be necessary.

The prognosis for any animal will naturally relate to the degree of affliction. Generally, the overall prognosis for affected animals is favorable, and relapses are rare.(10) Freedom from the disease appears certain only when an animal reaches skeletal maturity.

**REFERENCES**


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