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Research Article

# Hypertrophic Osteodystrophy in the Dog: 18 Cases

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**Abstract:** Hypertrophic osteodystrophy was diagnosed in 16 male and 2 female puppies aged between 2.5 and 8 months. All animals had stiff and stilted gait, painful swellings in the metaphyseal areas of the antebrachium and tibia, pyrexia, weakness and diarrhoea as common symptoms. Radiological examination of the affected areas showed extraperiosteal bone proliferations. With chronicity, the new bone formation spanned the entire diaphysis from the distal to the proximal metaphysis. Two dogs were treated with parenteral administration of analgesics, corticosteroids, vitamin C, and antibiotics in addition to dietary management. These 2 puppies, which had shown a clinical improvement during the long therapy period, died immediately after the cessation of drug administration. Fifteen animals recovered completely. These 15 puppies underwent dietary management only. The other dog was euthanised without any treatment at the owner's request. In the histopathologic examination of 2 dogs, in which a necropsy was performed, epiphyseal plates were structurally normal. However, primary and secondary spongiosa immediately below were observed to have been destroyed, extending up to the metaphyseal zone, and resorption had occurred in some areas. In the periostal zone, extraperiostal ossification, foci of bone destruction due to the osteoclastic activity, development of fibrous tissue, and infiltration by numerous neutrophils were observed.

Key Words: Hypertrophic osteodystrophy, dog

## Köpeklerde Hipertrofik Osteodistrofi: 18 Olgu

**Özet:** Yaşları 2,5 ile 8 ay arasında değişen 16 erkek 2 dişi yavru köpekte hipertrofik osteodistrofi tanısı konuldu. Hayvanların hepsinde; ağrılı ve zahmetli yürüyüş, antebrachium ve tibia'larının metafiz bölgelerinde ağrılı şişkinlikler, beden ısısında artış, zayıflık ve diare gibi semptomlarla karşılaşıldı. Hastalıktan etkilenmiş bölgelerin radyolojik görüntülerinde ekstraperiostal kemik üremelerinin varlığı tespit edildi. Kronik olgularda, kemiklerin diafizinden başlayan proksimal ve distal metafize kadar uzanan kemik üremeleri gözlendi. İki köpek, parenteral kortikosteroid, ağrı kesici, C vitamini ve antibiyotik uygulanması suretiyle tedaviye alındı. Bu köpekler uzun tedavi süresince iyileşme gösterdiler, ancak tedavinin kesilmesinden hemen sonra öldüler. Onbeş köpek sorunsuz iyileşti. Bu 15 köpek sadece diyet düzenlenmesi ile sağaltıldılar. Diğer bir olgu herhangi bir sağaltım uygulanmadan hasta sahibinin isteği üzerine ötenazi edildi. Nekropsileri yapılan iki köpeğin histopatolojik incelemesinde epifiz plağı normal görünümdeydi. Ancak, hemen altında başlayan primer ve sekunder spongioz kemiğin, metafizyal kemik alanına kadar nekroze olup, yer yer rezorbe olduğu gözlendi. Periostal bölgede, ekstraperiostal kemik üremeleri ve yine bu alanlarda osteoklastik aktiviteye bağlı kemik yıkımlanmaları, bağ doku artışı ve nötrofil lökosit infiltrasyonu izlendi.

Anahtar Sözcükler: Hipertrofik osteodistrofi, köpek

## Introduction

Hypertrophic osteodystrophy (HOD) is a bony disease affecting the metaphyseal areas of long bones in young growing dogs of large breeds between 2 and 8 months of age. The disease has been also referred to as skeletal scurvy, infantile scurvy, Moeller Barlow's disease, osteodystrophy type I, osteodystrophy type II, hypo or avitaminosis C, metaphyseal osteopathy and metaphyseal dysplasia (1-4).

HOD was first reported in 1935 in Europe and later in 1957 in the USA, in 1962 in England, in 1967 in South Africa, in 1971 in Chile, in 1973 in Australia (5) and in 1992 in Ankara (6).

The cause of HOD is uncertain (3,4,6), but hypovitaminosis C (7-10), infective agents (5,11-13) and overnutrition (5,10) have been suggested as aetiological factors. Although a reduced serum vitamin C concentration is found in some affected dogs, it is not

considered the real cause because the bone lesion suspected in hypovitaminosis C is osteoporosis, whereas HOD is characterised by excessive bone formation and retarded resorption. It can be found in almost every painful disease, which indicates completely different causes. Consequently, low vitamin C-values associated with HOD are assessed as secondary (6,7,14-16). The proposal of an infectious aetiology is not proven but the presence of an infectious disease may accelerate the onset and development of HOD. In many affected animals diarrhoea is seen, while some have tonsillitis, pyoderma or pneumonia (1,4,5).

It is suggested that overnutrition by high dietary calcium intake, and high protein and energy intake induce hypercalcitonism and these changes are caused by hypercalcitonism (1,7,8).

The effect of sex is not known but males seem to be affected more often (1,17).

The disease is seen in metaphyseal areas of long bones, mainly in the distal radius-ulna and tibia. Depending on the severity of the lesion, it may span the entire diaphysis from the proximal to the distal metaphysis, and even the costochondral junction of the ribs, mandible and vertebral bodies can be affected (2,17,18).

As a result of radiological investigations, the presence of HOD is divided into 2 forms (1). The radiographic findings of HOD in the late form are characterised by subperiosteal and extraperiosteal new bone growth with chronicity, and the new bone formation may span the entire diaphysis from the proximal to the distal metaphysis (3,4).

The most striking histopathologic abnormalities of HOD are found in the primary spongiosa of the metaphyses. The calcific cartilaginous lattice of the primary spongiosa is elongated, and the trabeculae are impacted. Necrosis, failure of osseous tissue deposition onto the calcified cartilage lattice, and trabecular microfractures are associated with acute suppurative inflammation in the intertrabecular areas. The aforementioned abnormalities are thought to result in metaphyseal infraction and separation of the epiphysis. The inflammation of the osteochondral complexes, marrow, and periosteum are thought to cause defective bone formation (osteodystrophy) secondarily (2,3,5,18).

Affected animals exhibit lameness and reluctance to move because of painful swellings of the metaphyses of long bones, and systemic signs including depression, anorexia and variable hyperthermia. Many affected dogs may recover clinically in time but some may have one or several relapses during the following weeks before complete recovery. In some cases, however, relapses and remissions occur repeatedly and the resulting pain, cachexia and debility may cause death (1,3,4,17,18).

HOD can be confused with panosteitis, pulmonary osteoarthropathy, hypervitaminosis D, rickets and Moeller Barlow's disease. Differential diagnosis requires radiographic examinations (9,15,17,18).

Treatment of HOD is directed toward controlling the fever and reducing pain. For this purpose, while some authors (11) recommend rest and analgesics, others suggest the use of vitamin C, corticosteroids and antibiotics together with such a treatment (2,4,10). Most dogs may recover from systemic signs in a week but bony changes require 2-3 months for resorption (1-6,18).

The purpose of this study was to report seen in 18 cases of HOD for detailed clinical observations.

## Materials and Methods

The material of the study was 16 male and 2 female puppies aged between 2.5 and 8 months, which were brought to our clinics between 1990 and 2002. All of these animals were large breed puppies (2 German shepherds, 2 Anatolian sheep dogs, 1 Doberman, 1 Great Dane and 12 cross-bred dogs). Twelve of these puppies had previously been taken to different private veterinary clinics for rickets treatment and, due to treatment failure, they were brought to our clinics.

All of the dogs underwent clinical and then periodic radiological examinations. Radiographic examinations were performed by taking 2 view radiographs of the affected extremities. Of the animals kept under clinical observation in our clinics, because of economic reasons blood chemistry was performed in 4, and in 2, which died, a histopathological examination was performed. Fifteen animals underwent dietary management only and healed completely. Due to severe pain 2 dogs were treated with analgesics, vitamin C, antibiotics and corticosteroids in addition to dietary management. These 2 puppies, which had shown a clinical improvement

during the long period of therapy, died immediately after the cessation of drug administration and the other was euthanised without any treatment by a private veterinarian on the owner's request. Systemic necropsies of 2 dogs were performed. Samples were taken from the humerus, antebrachum, femur and tibia, fixed in 10% formalin and then decalcificated. They were processed routinely and embedded in paraffin wax. They were sectioned at 5 µm by rotary microtome and stained with hematoxylin and eosin. Additional Mallory's Triple Staining was carried out on the processes and an examination under a light microscope was performed (19).

## Results

The findings observed in the animals were evaluated clinically, radiologically, haematologically and histopathologically.

**Clinical findings:** All the animals were brought to our clinics mainly because of debility, reluctance to move, swellings on limbs and severe pain on palpation. Closer examinations revealed that all puppies had a painful and hard swelling around their carpal and tarsal joints; these swellings were enlarged along the antebrachium and tibia and reached the cubiti and genu joints (Figures 1 and 2). The gait of the dogs was stiff and stilted. They felt severe pain when they were lifted up to place them on the examination table. Their facial expressions showed the severity of pain they felt. Most of them were exhausted and weak. Five of the dogs also had diarrhoea. Body temperatures varied between 40 and 41 ºC. In 13 of the animals, which were observed very closely, these clinical symptoms decreased during the therapy and relapsed when the medication was stopped. However, the swellings were not parallel to the clinical improvement. In 14 animals, which recovered completely, the bony swellings gradually decreased and finally disappeared in 7-8 months.

**Radiological findings:** Intensive bone proliferations, especially over the distal metaphyseal areas of the radius-ulna and tibia, were seen in all dogs. All diaphyses of affected bones were coated by proliferations in 6 cases. One of the dogs that completely healed had bony proliferations of the costachondral junction of ribs at the beginning. The resorption and loss of bony proliferations were followed radiologically by taking periodic radiographs over 8 months (Figures 3 and 4).

**Haematological findings:** Haematological examinations were performed in only 4 cases when a severe disease was present. This examination revealed significant lymphocytosis. Serum alkaline phosphatase

Figure 1. Severe swelling of the distal antebrachium due to hypertrophic osteodystrophy (HOD) in an 8-month-old male cross-bred dog.

Figure 2. Stiff and painful gait in a dog with HOD.

was above the normal value. Total protein and albumin were decreased, while calcium and phosphorus were high and imbalanced. Vitamin C levels, however, could not be determined by our facilities.

**Histopathological findings:** In the post-mortem examination, histologically, the epiphyseal plates were structurally normal. Primary and secondary spongiosa immediately below were observed to have been destroyed, extending up to the metaphyseal zone, and resorption had occurred in some areas. In the trabeculae were determined widespread destruction, osteolysis and foci of fracture due to the osteoclastic activity. The destroyed trabeculae were replaced by fibrous tissue. The blood vessels were dilated with erythrocytes and mild to moderate infiltration of neutrophils and few lymphocytes were present within these areas. In the periostal zone, extraperiostal ossification, foci of bone destruction due to the osteoclastic activity, development of fibrous tissue and infiltration by numerous neutrophils were observed (Figures 5-8).

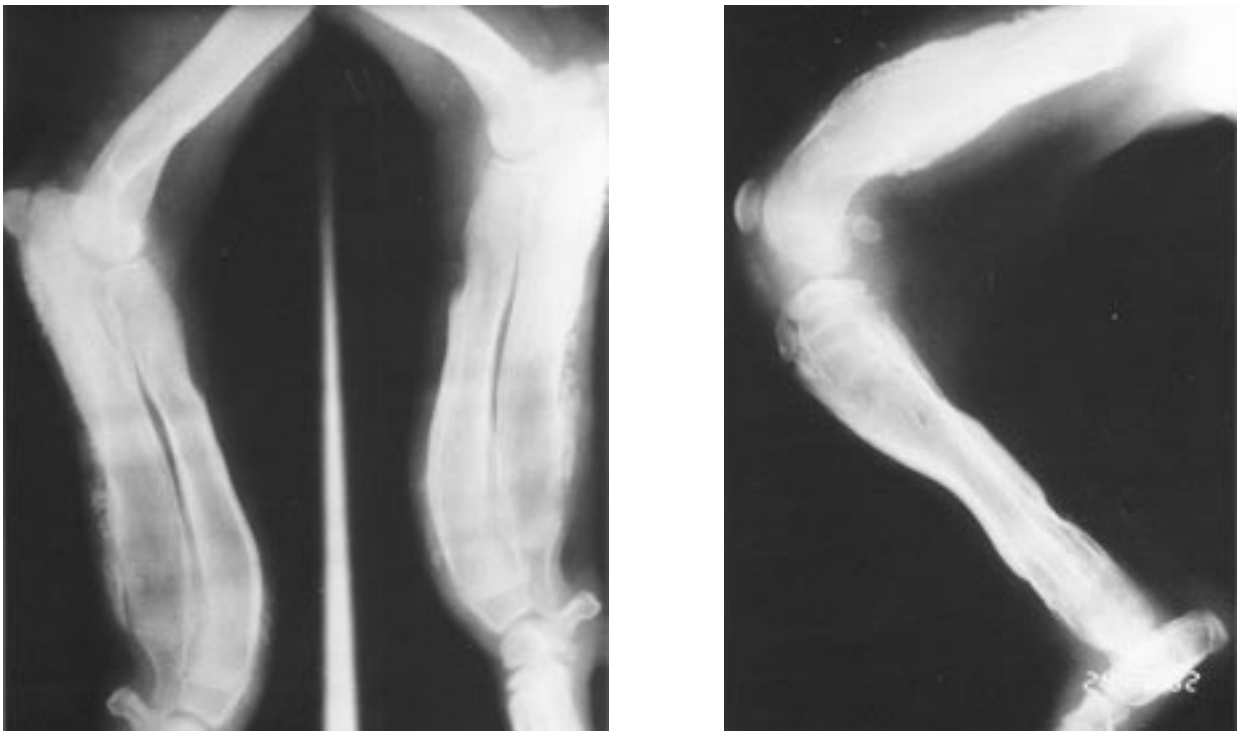
## Discussion

This disease affecting the skeletal system is rare in young, growing dogs of large breeds. As the disease resembles rickets at the beginning, it is usually diagnosed as rickets by mistake. The first dog brought to our clinics was in the same situation. Detailed examinations and check-ups, however, revealed the disease to be HOD. It is also seen that the radiological presence of HOD differs from that of rickets. In particular the presence of thickened metaphyseal areas and subperiosteal or extraperiosteal new bone formation of long bones makes the radiological diagnosis easier. Increased bony proliferations and spanning of these proliferations proximally is also valuable proof (2,17,20,21) because the disease affects young growing dogs and the absence of pulmonary involvement separates HOD from pulmonary osteoartropathy (3,5,22).

However, the exact aetiology is not known. It is considered that overnutrition is the most important factor. Overnutrition, especially excessive calcium intake, can lead to hypercalcaemia, hypercalcitonism and hypoparathyroidism with retarded bone resorption. Inhibition of cartilage maturation, a known effect of excessive calcitonin, can result in retarded chondrolysis. Coupled with excessive dietary protein and energy intake it can also result in HOD (1,7,8).

The cases that were diagnosed and treated as rickets at the beginning followed a more deterioriative course; this can be attributed to excessive calcium intake (7,8). Twelve of the dogs underwent rickets treatment at the beginning in private veterinary clinics. This observation supports the importance of overnutrition. Cessation of calcium therapy and use of a poor feeding regimen provide complete healing after a long period of time.

The role of hypovitaminosis C in HOD is not proven since reduced serum vitamin C concentrations in affected animals vary with stress caused by the pain seen in HOD (6,10,11,14). However, several authors have proposed vitamin C as a causative factor, since vitamin C deficiency prevents the formation of collagen and delayed enchondral bone formation results in HOD (1). In



A B

Figure 3. Medio-lateral radiograph of both antebrachium (A) and tibial and femoral (B) involvement of the same dog with severe HOD.

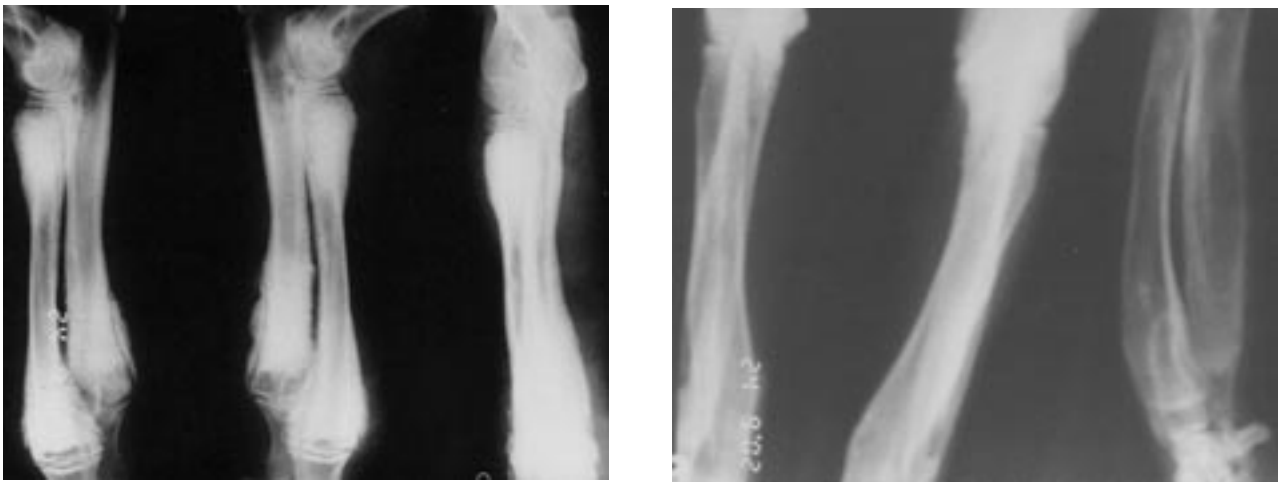


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Figure 4. A 6-month-old male cross-bred puppy with HOD. A) Medio-lateral of both and latero-lateral radiographs of right antebrachium. B) Bone lesions regressed after 3 months in the same dog.

contrast, some authors consider that vitamin C treatment of dogs with HOD is contraindicated, as it can only aggravate the osseous lesions in HOD (10).

It is reported that the temperature elevation in the course of HOD may be due to protein resorption following extensive haemorrhage rather than infection (9). Furthermore, while the elevated temperature is

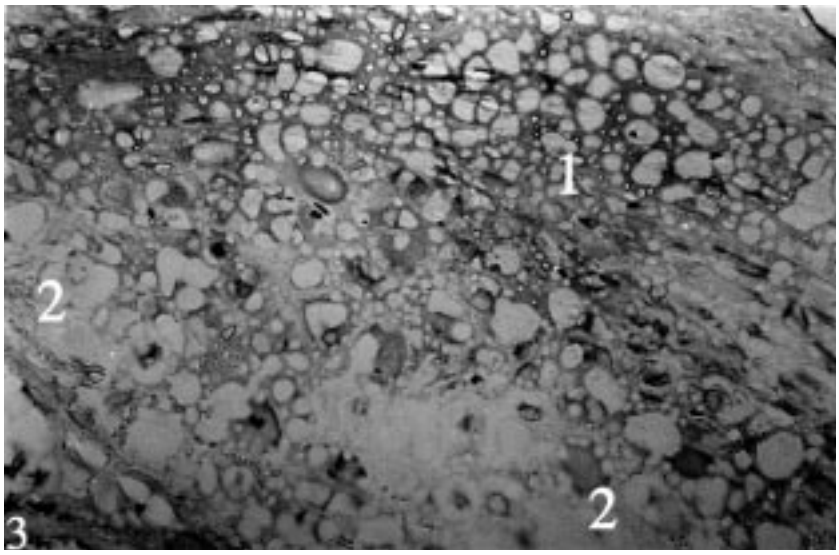


Figure 5. Epiphyseal plate (1), primary and secondary spongiosa including foci of necrosis and resorption in some areas (2), metaphyseal bone revealing signs of destruction (3), [H.E., 200x].

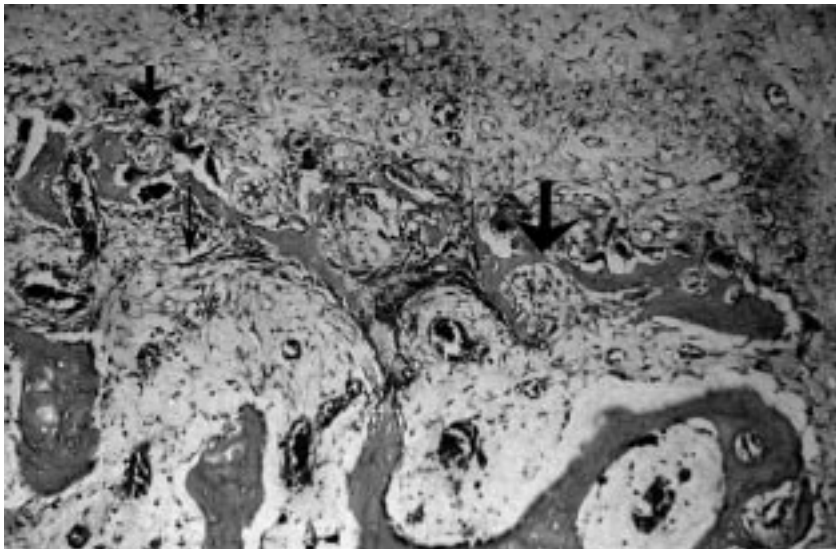

Figure 6. Osteoclasts (short arrow), destroyed zone (thick arrow), fibrous tissue (thin arrow), [H.E., 100x].

decreased by aspirin, the antibiotics' effect on hyperthermia support this theory. The diarrhoea frequently seen in affected dogs may be caused by altered intestinal absorption. The clinical symptoms observed in our 2 cases over a long time were parallel to the observations of other authors (3-5). The idea that males are more frequently affected (1,17) is supported by the fact that most of our cases were male.

Bone lesions tend to localise in the distal metaphyseal areas of the antebrachium and tibia and the costachondral junction of ribs because these sites grow actively. Other long bones are less affected by the disease since they do not have active bone growth, including the antebrachium and tibia (2,6,16,17).

Our radiological findings were similar to other author's observations (1,6,20,21,23). In 6 cases, lesions

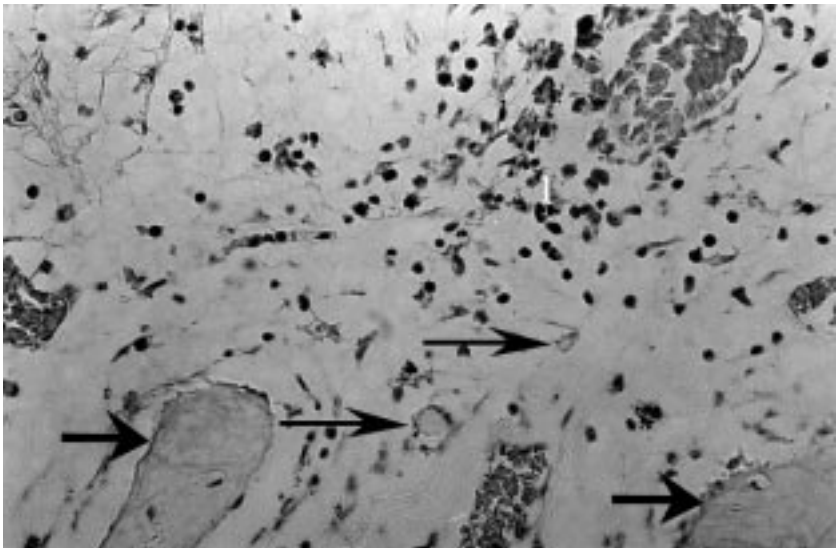


Figure 7. Neutrophils (1), bone fractures destroyed (thin arrow), trabeculae (thick arrows), [H.E., 400x].

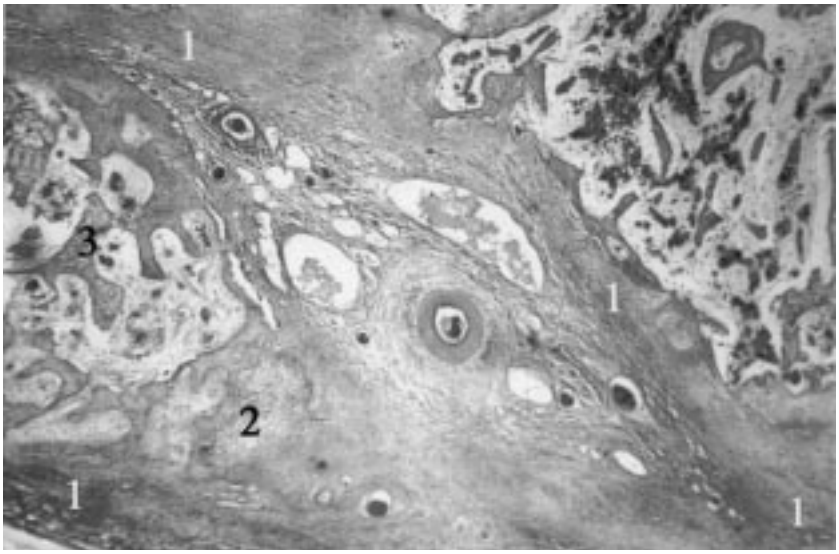


Figure 8. Extraperiostal ossification, periosteum (1), hyaline cartilage (2), trabeculae (3), [Mallory's Triple 40x].

situated over distal metaphyseal areas spanned the entire diaphysis.

Blood analysis was performed in only 4 cases and the results were similar to the literature data (1-3). There were high calcium and phosphorus levels and the Ca/P balance changed in favour of phosphorus.

In 2 cases histological studies were performed after death and the findings were parallel to the literature (12). Histological examinations confirmed previous clinical and radiological diagnoses and were the same as the literature information (1,3).

We considered that the 18 evaluated cases of HOD could be utilised in future studies of this subject.

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