PRIMARY HYPERTROPHIC OSTEOARTHRPATHY (PHO)
AND CHANGES IN THE JOINTS

Clinical, X-ray, Scintigraphic, Arteriographic and
Histologic Examination of 19 Patients

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ABSTRACT. Nineteen patients with PHO with onset in
crudement are presented. In 7 cases the syndrome was found
in other family members too. In clinical, X-ray scintigra-
graphic, arteriographic, and plethysmographic investiga-
tions, joint affection was found in 14 patients. Clubbing
of the fingers and toes was seen in all the patients and a
periostal reaction was found in the long bones in 11 pa-
tients. Arteriography was carried out in 5 patients and
showed hypervascularization and arteriovenous anas-
tomoses in the clubbed fingers. The gas analysis of the
arterial blood did not show any pathological changes. The
histological finding showed poorly vascularized and
oedematous periarticular tissue and ossification in the
periostal area, while in the synovial membrane, slight,
nonspecific inflammatory changes were seen.

PHO causes considerable difficulties in the dif-
ferential diagnosis of diseases of the locomotor sys-
tem. We therefore wanted to widen our knowledge
of the clinical picture of this syndrome by making
a detailed investigation and contribute to the
pathogenesis of PHO.

MATERIAL AND METHODS

In the period from 1972 to 1978 19 patients were observed
(all men) suffering from PHO. The average age of the
patients was 40 years and 7 months, and their age ranged
from 25 to 56 years.

A detailed personal and family history was recorded for
every patient. Clinical examination of the locomotor sys-
tem, haematological and blood chemistry tests (creatinine,
BUN, bilirubin, alkaline phosphatase, transaminase) were
made. Examination of lungs and heart, X-ray of hands and
feet, and long bones were performed. Scintigraphy of
affected joints, hands, feet and long bones were made in
13 patients. Spirometry, gasanalysis of blood, body
plethysmography and arteriography of the arm in 5
patients. Histological investigations of the synovial tissue
were carried out in 5 and histological investigation of the
periostal tissue from the tibia in 4 patients.

Hippocrates knew about hypertrophic osteoar-
thropathy, but the first to describe it in modern
times was Friedrich (1868). Clubbing of the fingers,
nail and joint affections were described by Bam-
berger (1889) and Marie (1890), while Grönberg
wrote in 1927 about the periostal affections of
the skeleton. The condition is known in the litera-
ture as primary or idiopathic hypertrophic osteo-
arthropathy (PHO), pachydermoperiostosis and
Bamberger–Marie’s syndrome. The secondary or
acquired hypertrophic osteoarthropathy is the most
frequent type and is associated with chronic in-
trathoracic diseases (bronchiectasis, tuberculosis,
empyema, tumours), some chronic heart diseases,
and gastrointestinal and liver diseases.

PHO is a syndrome described during the last 30
years in a small number (13) of patients (1, 3, 5, 8,
11, 18, 27, 29, 30), whereas secondary or ac-
quired hypertrophic osteoarthropathy has been
more frequently described in the literature (4, 7, 10,
13, 15, 20, 21, 23, 27).

Fig. 1. Example of one of the pedigrees. The mother,
two sons and a grandson suffer from PHO. ●, Affected;
○, healthy.
RESULTS

The family history of 7 patients revealed that one or more members of the family had been suffering from PHO. Of 10 members in those 7 families, 4 were women and 6 men (in Fig. 1 one of the families).

According to the history in all these patients clubbing of the fingers had been present since childhood, and other symptoms had appeared at different periods of their lives.

Clinical, X-ray and scintigraphic investigations revealed affections of the joints in 14 out of 19 of our patients (Fig. 2). The incidences of the affections were as follows: ankles (8), knees (5), hips (2), finger joints (1) and wrists (1). In 2 patients several joints were affected but the affection was asymmetrical. Periarthritis was seen in 8 patients in the ankles, without oedema outside the joint area.

Clubbing of the fingers (Fig. 3) and toes (Fig. 2) was found to a varying degree in all 19 patients.

Periosteal new bone formation on the long bones was found in 11 patients, mostly in the distal ends of

Fig. 2. Bilateral talo-crural arthritis with clubbing toes.

Fig. 3. Clubbed fingers on both hands.

Fig. 4. Periosteal new bone formation on tibia and fibula.
the tibial and fibular diaphysis (Fig. 4). Roughness of the terminal phalanx of the finger (tuberositas phalangis distalis) was marked in all the patients (Fig. 5) and in one patient the X-rays revealed degenerative changes of both hip joints (Fig. 6).

Arteriography of the hands showed hypervascularization of the soft tissue of the distal parts of the fingers in 5 patients. Formation of arteriovenous anastomoses and rapid filling of the veins were observed (Fig. 7). Scintigraphy showed a more intensive tracer accumulation in the area of the affected joints, of the clubbed fingers and the periosteal new bone formation 10 out of 13 patients (Fig. 8).

The histology of periarticular tissue of one patient revealed a firm, slightly cellular and poorly vascularized oedematous tissue (Fig. 9). Histology of the tibial periosteum of one patient revealed a thickened periosteal zone consisting of numerous, partly hyaline, firm connective bundles. The blood vessels were increased in number, and the arteries were of medium size with a thickened media (Fig.

Fig. 5. Markedly developed distal phalangeal tuberositas.

Fig. 6. Bilateral coxarthrosis.
Spirometric and body plethysmographic findings were within physiological limits. The concentration of respiratory gas in the arterial blood was within normal limits too.

The haematological findings in all our patients were normal. Liver function tests were pathological in 2 patients due to liver lesion and chronic alcoholism. In one patient transient deviations of liver function tests were noted. Physical and X-ray examinations of the heart and lungs and the ECG did not reveal any signs of pathological changes.

**DISCUSSION**

The cause of PHO is unknown. Not only human beings but animals too (14) are affected. The condition has been described even in the body of a 7½-month-old child (16). In a certain number of patients it is very difficult to differentiate between the primary and secondary form, as differentiation depends on the course of the disease and on the causative factor (28).

Clubbled fingers, watchglass nails, affection of large joints (synovitis recidivans), periartthritis of knees, ankles, and wrists, sweating from the distal parts of the extremities and (less frequently) thickening and greasiness of the facial skin are the main symptoms of this syndrome. However, not all the signs of the syndrome are always present and need
not be marked in every patient. Thus in the literature clubbing of the fingers has been described as an isolated phenomenon (2, 12, 25). A prolonged observation can be helpful in diagnosing the syndrome and therefore the proposition of Touraine et al. (26) who distinguish three forms of the syndrome: the complete, incomplete, and the forme fruste (16) is understandable. According to our obser-

**Fig. 9.** Periarticular oedematous connective tissue with scanty supply of blood vessels (H+E, ×32).

**Fig. 10.** Thickened periosteum built of bundles of firm connective tissue. In the central part, two arteries with markedly thickened walls (Mallory, ×32).
vations, affections of the joints appear regularly in this syndrome. The question is only: when do they appear and how skillfully are they diagnosed.

Joint affections become manifest by the intermittent appearance of oedema, pain, and tenderness. The oedema may remain even after the acute attack has passed. It appears in the form of a thickening of the synovial membrane and articular capsule. This may in later stages of the disease result in erosion of the joint cartilage, and the process can lead to

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Fig. 11. Synovial tissue after synovectomy of the knee.

Fig. 12. Synovial membrane with tasseled surface. Covering cells mostly reduced in number and of atrophic appearance. Stroma well vascularized, containing mainly perivascular mononuclear infiltrates (H+E, ×32).
changes in subchondral bone. Hence in some cases knee synovectomy may be indicated. This operation has been carried out in 3 of our patients. In addition, hypotrophy and general muscle weakness is regarded as signifying the disease in its advanced stage or as a result of the joint affection.

Some authors have described localized oedema as pretibial myxedema (3), which we have not observed.

According to Vogl et al. (28) the syndrome can appear in both men and women, before and after puberty. In our group of 19 patients there were no women and in all cases the onset of the disease was prepubertal. It then progressed to the complete syndrome (periarthritis, synovitis, clubbed fingers, ossification, etc.) before the age of 30.

Four of our patients consumed more than 1 dl of alcoholic spirits a day, and 2 of them underwent liver function tests, with pathological results. However, these patients had had clubbed fingers since childhood. Later on they developed periostitis and other symptoms of the disease. Thus it seems unlikely that the liver affection is involved in the pathogenesis of PHO.

The familial appearance of the syndrome has been described earlier. De Sève et al. (24) found clubbing of the fingers in the brother and father of a patient, while Vogl et al. (28) found it in the father of one patient. Franceschetti et al. (6) found in the literature 15 cases of the syndrome in the relatives of patients. They are of the opinion that the disease is inherited recessively or as an irregular dominant with a predisposition for males. McKusick (17) maintains that it is a problem of autosomal dominant heredity with a greater domination for males. We have found the familial phenomenon of the syndrome in 17 patients.

It has been established that clubbing of the fingers and the periosteal ossification is a result of the increased need for peripheral circulation in secondary hypertrophic osteoarthropathy (19), while in PHO the peripheral circulation has been reported not to be increased. However, in all 5 of our patients in whom arteriography of the hands was performed, signs of an increased need of arterial circulation in the tissues were observed.

Pathological changes appeared in the skeleton and in soft tissues, as well as in the synovial membrane. Bone affections consist of irregular periosteal ossification in the entire circumference of the distal parts of long bones, and in the ligament and tendon attachments. New bone is formed between the cortex and the periosteum. Subsequently it forms an osseous mass with the cortex. In soft tissues the changes consist of slight inflammatory infiltration and oedema of the synovial membrane, periosteal tissue and elastic fibres (9), which was confirmed by our observations.

In the differential diagnosis hypothyreosis should be taken into consideration primarily, less frequently cardiac oedema, rheumatoid and gouty arthritis, malignancy, syphilis, tuberculous periostitis, osteomyelitis sclerotics, xanthomatosis and blastomycesis. Thyroid acropathy almost always appears with exophthalmos and myxedema of the leg. Periosteal affections often appear on the phalanges and on the metacarpal bones. Oedema of cardiac decompensation are neither painful nor sensitive to palpation and develop on the distal third of the leg. In rheumatoid and gouty arthritis it is the joint which is primarily affected.

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Scand J Rheumatology 9:2


Submitted for publication September 25, 1979

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