Reactivation of primary hypertrophic osteoarthropathy by bronchogenic carcinoma

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ABSTRACT

This paper reports 2 cases of primary hypertrophic osteoarthopathy (PHO) which evolved into secondary hypertrophic osteoarthopathy (SHO) under the influence of bronchogenic carcinoma. The patients had a clinical picture of primary hypertrophic osteoarthropathy but without any signs of disease activity until in the last several months when a malignant bronchopulmonary condition developed. This activated all the symptoms: joint swelling; enlarged fingers and distal forearms and legs; moist palms and soles; unpleasant odour of perspiration; and deeper folds of the forehead and nasolabial furrow. A bone scan showed increased accumulation of the radioisotope in specific regions of the skeleton. To our knowledge, no similar cases have been described in the literature.

Introduction

Primary hypertrophic osteoarthropathy (PHO) is a more common disease than was believed until recently (1, 2). Over a long period we have diagnosed PHO in a substantial number of patients (3). Secondary hypertrophic osteoarthropathy (SHO) develops most often in different conditions of the lungs and mediastinum such as infections (1),primary tumour of the lungs, metastatic lung tumours, respiratory distress syndrome, bronchiectasis, fibrosis cystica (4), pneumonitis (6), idiopathic lung fibrosis (7), and pneumonia with *Pneumocystis carinii* in AIDS (8), as well as in other diseases involving various organs and body systems (9-20).

However, some of above mentioned conditions can reactivate PHO, causing the secondary form of the disease. This occurred in the two patients reported in this study.

Case reports

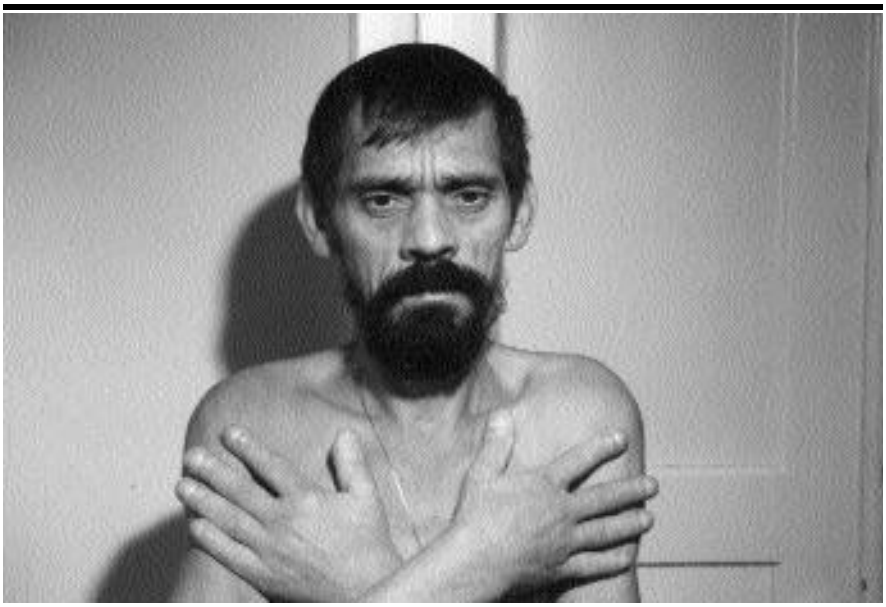
Case 1

G.I., a male born in 1954, unmarried manual worker.

Family history: His father died at the age of 68 from malignant carcinoma of the right hip, while his brother had undergone surgery due to lung cancer. Both the father and brother had clubbed fingers before developing malignant disease.

Personal history: Since childhood G.I. has had clubbed fingers and a peculiar appearance (deeper folds on the forehead and nasolabial furrow). About 45 days before presenting to us he started to cough and also felt pain in his knees, ankles, and radiocarpal joints, and pain in the proximal interphalangeal joints (PIP) of the hands and feet accompanied by swelling without redness (Fig. 1).

Status: Swelling of both feet, ankles and knees, radiocarpal joints and PIP joints, which were moderately painful.



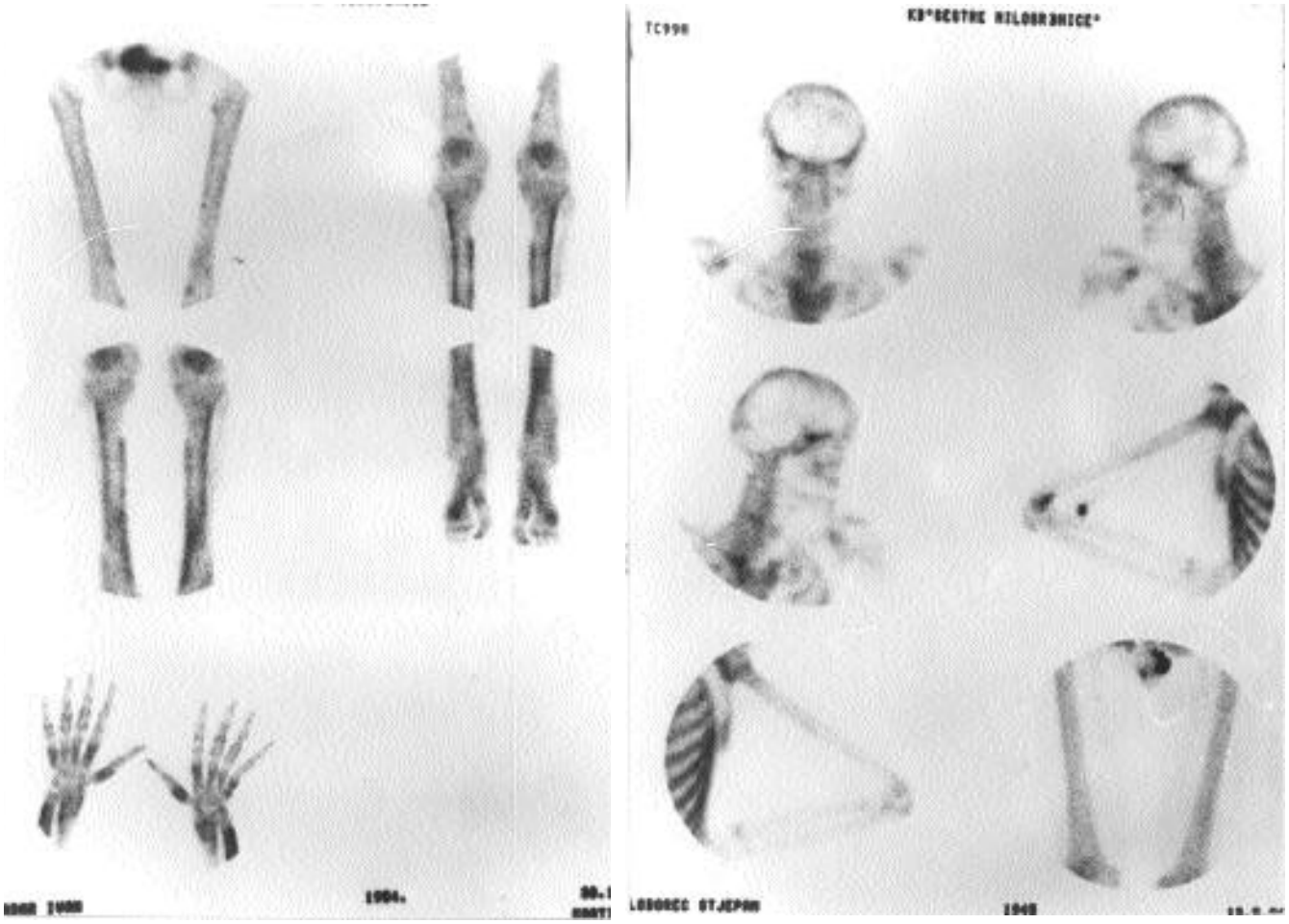


Fig. 2. Bone scan of patient (case no. 1) with hypertrophic osteoarthropathy.

Clubbing of the fingers and toes, erythematous and moist palms, deeper nasolabial furrows and folds of the forehead. Irritated cough.

Laboratory (pathological) findings: ESR 117 mm/h; leukocytes 11.2 x 10^9/L; hemoglobin 115 g/L; thrombocytes 716 x 10^9/L; alkaline phosphatase 142 U/L; serum proteins: albumins 35.1%, alfa1 6.1%, alfa2 21.0%, beta 15.3%, gamma 22.5; Ig A 5960 mg/L; CRP 138 mg/L; Ceruloplasmin 430 mg/L; and Haptoglobin 5760 mg/L.

Radiological findings: Periostal reaction in the tibia, fibula, ulna, radius, humerus and femur. Suspect shadow on upper part of the right lung.

Pulmonary functional tests (Vitalograf): Obstruction in the small airway passages, FDT negative.

Bronchoscopy: Obstructive infiltrative proliferative mass in the upper lobe of the right lung

Pathohistology: Dg. Bronchogenic squamous cell carcinoma.

Bone scan: Pathological radioisotope (Tc-99) accumulation in the projection of the 6th rib, right scapula, thoracic vertebrae D III, DIV, DXI and DXII, lumbar vertebra L IV, iliac bones, both knees and metatarsal bones (Fig. 2). A bone scan performed 2 years ago showed normal findings.

Case 2

L.S., a male born in 1945, married clerk.

Family history: His sister also suffers from PHO.

Personal history: Since his childhood he has had clubbed fingers, folds on the forehead, a deeper nasolabial furrow, and thickening of the distal parts of the legs. A year before coming to our hospital (1996), simultaneously with the occurrence of an irritative cough he noticed that his fingers started to enlarge, and erythema, perspiration of the palms, the angle between the nails, and eponychium and convexity of the nails increased.

Status: Clubbing of the fingers was very pronounced. Both palms and fingers were sweaty and warm, with pronounced periungual erythema. The nails were markedly bent in the transverse and longitudinal direction. Schamrot's test was positive. The legs were thickened in the lower third with perimalleolar edema. The other joints were normal and there were no pulmonary findings.

Laboratory (pathological) findings: ESR 96 mm/h, erythrocytes 3.80 x 10^{12} /L, hemoglobin 110 g/L, thrombocytes 611 x 10^9/L.

Radiological findings: Periostal reaction in the tibia, fibula, radius, ulna.

Lungs: Tumorous shadow in the left lung.

Bone scan : Increased radioisotope (Tc-99) accumulation in the skull, right scapula, humerus, radius, ulna, cervical spine, femur, tibia, fibula and tarsal bones. A bone scan performed 5 years

ago did not show increased binding of the radioisotope.
Bronchoscopy: Tumorous mass in the lower part of left lung.
Pathohistology: Dg. Bronchogenic squamous cell anaplastic carcinoma.

Discussion

Malignant bronchopulmonar conditions can develop in any subject, as well as in patients with PHO. PHO usually develops in childhood or, at the latest, during adolescence, but is rarely accompanied by severe symptoms (1, 2). PHO has familial aggregation and usually several family members have signs of the disease (3). A genetic connection is indicated in our patients, both of whom had a close family member with PHO. Some degree of genetic predisposition may also be involved in malignant conditions.
SHO has been linked to a number of causes, but to the best of our knowledge the transformation of PHO into SHO under the influence of bronchogenic carcinoma has never been reported in the literature (21-25).
Our first patient (G.I.) smoked 20-30 cigarettes a day, which could have enhanced the development of the carcinoma and the earlier activation of hypertrophic osteoarthropathy symptoms. However, his father died from bone malignancy, while his brother (still living) had been treated for lung tumour. We don't know whether their symptoms of hypertrophic osteoarthropathy worsened during the malignant process, but this might have been the case.
In the second patient (L.S.) the malignant process of the lungs also activated the symptoms of the present but inactive hypertrophic osteoarthropathy. His sister also had the same disease since childhood.
After the appropriate therapy, symptoms and signs of hypertrophic osteoarthropathy in both patients decreased.
In many cases rheumatologists fail to establish a diagnosis of hypertrophic osteoarthropathy, although the symptoms may be obvious. They usually do not pay much attention to the onset or worsening of symptoms of the disease, which may be related to the activation of some other (usually lung) disease. Clinical findings are essential to guide diagnostic procedures. Apart from finding the cause of activation of the disease, the most sensitive diagnostic tool for HOA is a bone scan. It is more often positive before a periostal reaction can be detected on plain X-rays (3).
A malignant bronchogenic process activated the quiescent hypertrophic osteoarthropathy in our 2 patients, causing the development of the secondary form of the disease. These cases highlight the importance, in cases of relapsing PHO, of searching for a possible provoking factor, particularly in the bronchopulmonary region.

References

1. RIMOIN DL: Pachydermoperiostosis (idiopathic clubbing and periostosis. Genetic and physiologic considerations. *N Engl J Med* 1965; 272: 923.
2. OLLENDORF CH, FIRSCHEIN IL, ALPERT M: Familial clubbed fingers. *Arch Derm* 1961; 83: 166.
3. JAJIC I, JAJIC Z: Sindrom hipertrofiène osteoartropatije. In *Medicinska Knjiga*, 1st ed., Zagreb, 1997: 1-180.
4. STENSETH JH, CLAGETT OT, WOOLNER LB: Hypertrophic pulmonary osteoarthropathy. *Dis Chest* 1967; 52: 62.
5. SONSORES R, SALAS J, CHAPELA R *et al.*: Clubbing in hypersensitivity pneumonitis. *Arch Intern Med* 1990; 150: 1849.
6. GALKS B, GROSSMAN RF, DAY A *et al.*: Hypertrophic pulmonary osteoarthropathy in four patients with interstitial pulmonary disease. *Chest* 1985; 88: 94.
7. KANEMATSU T, KITAICHI M, NISKIMURA K *et al.*: Clubbing of the fingers and smooth-muscle proliferation in fibrotic changes in the lung in patients with idiopathic pulmonary fibrosis. *Chest* 1994; 105: 336.
8. MAY T, RABAUD C, AMIEL C, *et al*.: Hypertrophic pulmonary osteoarthropathy associated with granulomatous pneumocystis carinii pneumonia in AIDS. *Scand J Infect Dis* 1993; 25: 771-3.
9. MCLAUGHLIN GE, MCCARTHY DJ, DOWNINGDF: Hypertrophic osteoarthropathy associated with cyanotic heart disease. *Ann Intern Med* 1167; 67: 579-87.
10. TREVER RW: Hypertrophic osteoarthropathy in association with congenital cyanotical heart disease. *Ann Intern Med* 1958;48:660-8.
11. FLCKIGER M: Vorkommen von trommelschlagefornirung Fingerendphalangen ohne chronischen Veranderungen an der Lungen oder am Herzen. *Wien Med Wschr* 1884; 34: 1457.
12. GILBERT A, FOURNIER L: La cirrhose hypertrophique avec icter chez l'enfants. *Rev Mald l'enfance* 1895; 13: 309.
13. PEYMAN MA: Alcholasia of cardia, carcinoma of oesophagus and hypertrophic pulmonary osteoarthropathy. *Br Med J* 1959; 1: 23.
14. SINGH A, JOLLY SS, BANSAL BB: Hypertrophic osteoarthropathy associated with carcinoma of the stomach. *Br Med J* 1950; 2: 581.
15. JAFFE IS: Nasopharyngeal carcionam. Unusual case reports. *Arch Otolryng (Chicago)* 1964; 80: 450.
16. CURTI LG, SICCARDI M, SANTIANELLO EB, FRESCO G: Full-brown hyperthroidism associated with vitiligo and acropachy. Report of one case. *Thyroidology* 1992; 4: 111-4.
17. ALLOWAY LA, NASHEL DJ, ROHATGIPK: Sarcoidosis and hypertrophic osteoarthropathy. *J Rheumatol* 1992; 19: 180-1.
18. CULLEN DR, MASKERY PJ: Clubbing of the finger and hypertrophic osteoarthropathy in pregnancy. *Lancet* 1966; 2: 473.
19. TRIVEDI SA: Neurilenoma of the diaphragm causing severe hypertrophic pulmonary osteoarthropathy. *Broj J Dis Chest* 1958; 52: 214.
20. MAS ESTELLES F, ANDRES V, VALLCANERA A *et al.*: Plasma cell granuloma of the lung in childhood: Atypical radiologic findings and association with hypertrophic osteoarthropathy. *Pediatr Radiol* 1995; 25: 369-72.
21. GINSBURG J: Hypertrophic pulmonary osteoarthropathy. *Postgrad Med J* 1963; 39: 639.
22. BERMAN B: Pulmonary hypertrophic osteoarthropathy. *Arch Intern Med* 1963; 112: 947.
23. SCHUMACHERHR: Articular manifestation of hypertrophic osteoarthropathy in bronchogenic carcinoma. A clinical and pathological study. *Arthritis Rheum* 1976; 19: 629-35.
24. STENSETH JH, CLAGETT OT, WOOLNER LB: Hypertrophic pulmonary osteoarthropathy. *Dis Chest* 1967; 52: 62.
25. DAVIES RA, DARBY M, RICHARDS MA: Hypertrophic pulmonary osteoarthropathy in pulmonary metastatic disease. A case report and review of the literature. *Clin Radiol* 1991; 43: 268-71.