SECTION 7
HYPERTROPHIC PULMONARY OSTEOARTHROPATHY

Hypertrophic pulmonary osteoarthropathy (HPOA) is a syndrome of thoracic disease accompanied by (1) digital clubbing, (2) periosteal new bone formation and synovitis in the extremities, and (3) nonpitting swelling of the soft tissues at the ends of the long bones. Digital clubbing is invariably present and is a less severe manifestation. Earlier statements that the soft tissue changes of clubbing are not of the same etiology as the bony changes[1,2] are no longer widely accepted.

Asbestosis has been defined by the presence of three or more of the standardized clinical abnormalities, including dyspnea, rales, finger clubbing, reduced vital capacity, and characteristic radiographic shadows.[3] Finger clubbing and the skeletal changes of HPOA may be due to asbestos-related bronchogenic carcinoma and pleural mesothelioma in addition to the pulmonary fibrosis of asbestosis.

Digital clubbing without any bony changes is seen in a wide variety of thoracic and extrathoracic disease (see Fig. 2-96). These include benign and malignant pleural and parenchymal tumors, cyanotic heart disease, chronic obstructive and inflammatory lung disease, diffuse interstitial pulmonary fibrosis of many etiologies, biliary cirrhosis, ulcerative colitis, regional enteritis, subacute bacterial endocarditis, and idiopathic steatorrhea. Moreover, digital clubbing alone may be a familial disease or may be associated with bone changes in thyroid acropachy, leukemic acropachy, and pachydermoperiostosis.[4,5,9]

The full syndrome, digital clubbing and skeletal changes, has been reported in the following thoracic abnormalities: chronic diseases of lung and pleura; benign and malignant pleural tumors; primary carcinoma of the bronchus, thymus, and thyroid; metastases to pleura and lung; bronchiectasis; hemangioma and malignant esophageal tumors; Hodgkin's disease; and occasionally cyanotic heart disease. Extrathoracic causes are known.

An unusual feature is the association between HPOA and fibrous tumors of the lung and pleura. Although 80 percent of patients with HPOA have primary bronchogenic tumors, the overall incidence of HPOA in primary bronchogenic tumors is only about 12 percent.[4,5,9] Fibrous tumors of the lung

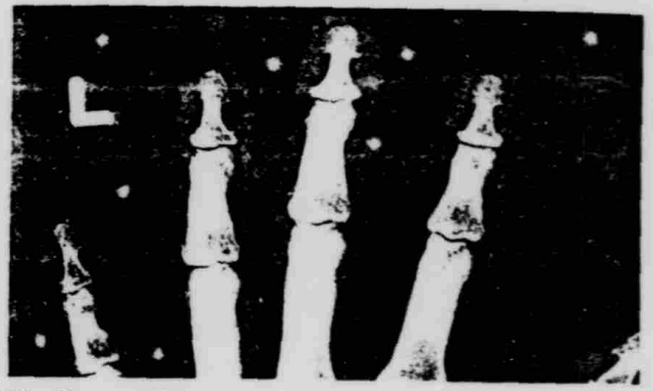


Fig. 2-96. *Digital clubbing in an asbestos worker with pulmonary fibrosis. A rapid increase in clubbing, especially when painful, may indicate development of an associated bronchial carcinoma.*

and visceral pleura, fibroma, fibrosarcoma, and benign and malignant mesothelioma have an incidence of HPOA of between 50 and 67 percent, and metastatic osteosarcoma, fibrosarcoma, and leiomyosarcoma, which have a predominantly fibrous tissue stroma, have a similar high incidence. The reason is unknown.[6]

CLINICAL FEATURES

HPOA usually manifests itself after the underlying disease has been present for some time. Rarely is it the first clue to the disease. Its severity may diminish during treatment of the underlying disease[7] and increase with recurrence. Treatment with adrenergic blocking drugs reduce pain and limb hypervascularity.[8] The clubbing associated with asbestos-induced pulmonary fibrosis is slow to develop and painless; if it is associated with bronchogenic carcinoma or mesothelioma, it may develop more rapidly and be more painful. Clubbing without periostitis is usually painless; if periostitis is present, pain usually, but not invariably, occurs. An adjacent synovitis may cause arthralgia. In descending frequency the distal radius and ulna, tibia and fibula, femur, metacarpals and metatarsals, and proximal and middle phalanges are involved. The terminal phalanges are usually spared (see Fig. 2-97).

The incidence of digital clubbing in industrial surveys of asbestos workers

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Fig. 2-97. *Left femur in an asbestos worker with severe pulmonary fibrosis who had clubbing. Tibia and fibula were also involved. Lateral femoral border (single arrowhead) shows a lucent line between diaphysis and periosteal lamellae. Laterally the new bone is wavy and has been incorporated into the shaft. Note sparing of the bone end.*

is variable. Using measurements derived from casts of the hyponychial angle of both index fingers, clubbing was present in 4 percent of Belfast insulation workers; using clinical assessment only, the percentage was approximately double.[19,20] Clubbing usually precedes the periostitis by several months, but occasionally the two may develop together.

PATHOLOGICAL FEATURES

The affected soft tissues show proliferation, edema, and increased vascularity. The overgrowth of vascular connective tissue precedes periosteal new bone formation. The increase in blood flow is related to an overgrowth of connective tissue and not to periostitis.[3,5,8] Periosteal new bone that is laid

down becomes incorporated into the shaft; the rate of formation of endosteal bone is increased. The mechanism of lamellated periosteal reaction in areas of venous stasis, a form of hypervascularity, has been studied in dogs.[11] It appears that the most superficial subperiosteal lamella produces perpendicular buds of bone that elevate the periosteum. The inner osteogenic layer of periosteum then forms a new superficial lamella beneath the elevated periosteum. This new superficial layer is connected to the next deeper layer by bony buds or bridges. The process continues by new bud formations, periosteal elevation, and further lamella formation. When the sequence is rapid and filling in appositional bone formation lags behind, the lamella become radiographically visible.

Rarely, there may be sterile joint effusions that may be recurrent. Synovial biopsy shows some synovial cell hypertrophy without inflammatory cells in the effusion.

PATHOPHYSIOLOGY

There are three main theories concerning the etiology of HPOA: neuronal, hormonal, and vascular.

Neuronal

Flavell suggested a neurogenic theory.[12] A reflex originates either in the diseased lung or in the adjacent pleura. The afferent limb is thought to be either the vagus or possibly the intercostal nerve. The distal limb is unknown. It may be the sympathetic nervous system. Thoracic or cervical vagotomy, mediastinal dissection which damages the vagus, and adrenergic blocking drugs which reduce sympathetic activity reduce blood flow in affected hands and lessen pain but cause no discernible improvement in bony changes, which may actually worsen despite reduction of pain. Because of double innervation of the lung, unilateral denervation may result in bilateral relief. Transaction of the intercostal nerves may also be followed by regression of the arthropathy.[13] Since involved organs are all served by the ninth or tenth cranial nerves, a reflex arc appears to be a reasonable hypothesis.[14]

Hormonal

An etiologic role has been postulated for estrogens, growth hormone, and vasoactive substances. Increased estrogen levels were seen in some patients with HPOA and bronchogenic carcinoma.[15] The level decreased after removal

of the tumor, but estrogens were not found in the tumor itself. The blood level could be due to increased adrenal excretion or abnormal hepatic function affecting metabolism of estrogenic precursor. The levels of estrogen tended to be higher in the presence of periostitis but not directly related to it; estrogen unrelated to the presence or absence of digital clubbing.

The large digits of patients with clubbing, reminiscent of acromegaly suggested a possible role for growth hormone as an etiologic agent. No proof exists that HPOA is related to increased production of growth hormone. Some malignant tumors synthesize and secrete a growth-hormone-like substance, and plasma levels may revert to normal after resection of the mass.

In a patient with squamous cell carcinoma of the cervix and adenocarcinoma of the pulmonary hilus, irradiation of the uterine cancer produced regression of hypertrophic osteoarthropathy prior to thoracotomy to obtain a tissue diagnosis of the hilar mass. This is additional evidence suggestive of a hormonal etiology.[7]

Vascular

Vasoactive substances such as 5-hydroxytryptamine and the kinins also have been incriminated. Arteriovenous shunts may allow these substances to bypass the pulmonary circulation where they are normally inactivated and exert their effect peripherally. This theory may be acceptable for digital clubbing in cyanotic heart disease but seems untenable as an explanation in other conditions associated with HPOA.

RADIOGRAPHIC FEATURES

Periosteal new bone is most pronounced in the diaphyses. In descending order of involvement are the distal radius and ulna, distal tibia and fibula, femur, metacarpals, matatarsals, and proximal and middle phalanges. Periostitis may not involve the phalanges and metacarpals even when digits are severely clubbed. In such patients the distal radius and ulna may show periostitis and should be included in the radiograph. The radiographic appearance has been classified[8] as (1) simple periosteal elevation with translucency between it and the cortex, (2) onion skin type, (3) localized small areas of periostitis, (4) long segments with wavy contour, and (5) wide cortex, a result of incorporation of periostitis in the shaft. The duration of the disease to some extent controls the radiographic appearance. Long-standing asbestos-related pulmonary fibrosis may allow incorporation of periostitic lamella to produce a wide shaft; the shorter life expectancy of patient with asbestos-related mesothelioma or bronchogenic carcinoma may allow production of shorter and

narrower segments of periostitis. Synovitis is usually not detectable radiographically. Difficulties in diagnosis may arise when HPOA is the presenting clinical symptom; the etiological factor must then be found. The arthralgia usually has no radiographic signs, and if present without periostitis, it may be a problem in diagnosis. The periostitis is usually symmetrical, but when asymmetric,[17] it may be a diagnostic problem.

SCINTIGRAPHIC FEATURES

Scintigraphic features of HPOA have been the subject of many case reports.[18,19] Technetium 99m diphosphonate is commonly used. It is selectively deposited in the new periosteal lamellae either by chemisorption onto hydroxyapatite crystals or by complexing with receptors such as alkaline phosphatase. In patients with asbestos-related malignant diseases, it is important to differentiate the scintigraphic appearance of HPOA from that of metastatic disease, which is usually medullary. An associated uptake in areas of synovitis may be helpful in suggesting HPOA; the distribution of HPOA in the distal portion of limbs is unusual for metastatic disease. HPOA affecting proximal parts of the limbs is occasionally seen, however, and metastatic bronchogenic carcinoma to digits is rare but recorded. The occasional asymmetry of HPOA may cause a problem. Differentiation of metastic disease from HPOA is important in planning therapy. CT scans with appropriate manipulation of window height and width holds promise in the detection of cortical metastases.

All conditions that cause digital clubbing or generalized periostitis enter into the differential diagnosis. Periostitis in adults is seen in pachydermoperiostosis (idiopathic hypertrophic osteoarthropathy), thyroid and leukemic acropachy, vitamin A excess, collagen disease, and periarteritis nodosa.

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ILO U/C INTERNATIONAL CLASSIFICATION OF RADIOGRAPHS OF THE PNEUMOCONIOSES

Leslie Preger

The grading system of changes in chest radiographs of those exposed to asbestos is of use in clinical assessment, compensation adjudication, evaluation of quality of dust control in epidemiologic surveys, and identification of those individuals who have radiographic evidence of pulmonary fibrosis and therefore must be informed of the need to change occupation.

An internationally accepted system is now available, the ILO U/C 1971 system,[1] which is applicable to coal workers' pneumoconiosis (CWP), silicosis and asbestosis. The historical development of the system is of interest. The first internationally accepted classification of the radiographic appearance of the pneumoconioses was made in 1950 in Sydney by the ILO (International Labor Organization). This was restricted to findings resulting from coal and silica, and like all later classifications, it was strictly descriptive and avoided any interpretive comments or inferences. In 1958, a meeting in Cincinnati of several interested organizations from North America and the International Union Against Cancer (UICC) decided that the patterns characteristic of asbestos exposure be added so that the system of grading would be applicable to the radiographic patterns seen in those exposed to asbestos as well as coal and silica. This became known as the U/C classification. At about the same time the ILO realized that the ILO 1950 classification was unsuitable for asbestosis in which the typical parenchymal opacities are linear or irregularly shaped and