

THE CLINICAL PICTURE

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Hypertrophic osteoarthropathy: Uncommon presentation of lung cancer



FIGURE 1. Digital clubbing.



FIGURE 2. Radiography of the ankles showed a lamellar type of periosteal reaction (arrows).

A 43-YEAR-OLD WOMAN presented to the clinic complaining of bilateral ankle joint pain for 2 months. She denied a history of fever, weight loss, addictions, cough, or trauma. On physical examination, she had swelling of the ankle and wrist joints and digital clubbing (**Figure 1**). Active movement of the ankles and wrists was restricted due to pain. The examination was otherwise unremarkable.

Radiography of both ankles showed a lamellar type periosteal reaction suggestive of periostitis (**Figure 2**). Computed tomography of the chest revealed a spiculated mass over the right lower lobe. Biopsy study of the mass was positive for squamous cell carcinoma. She was referred to the oncology center for further management.

■ FEATURES OF HYPERTROPHIC OSTEOARTHROPATHY

Digital clubbing is one of the oldest signs in clinical medicine. It is characterized by bul-

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bous enlargement of the terminal segments of the fingers and toes due to proliferation of subungual connective tissue. It usually appears as a painless finger deformity and is clinically appreciated as a loss of the normal angle between the nail bed and proximal nail fold.

Hypertrophic osteoarthropathy is a symptomatic form of clubbing associated with proliferative periostosis of the distal end of long tubular bones, commonly those adjacent to the wrist and ankle joints.¹ The laminated appearance of these bones on radiography is due to the excess connective tissue secondary to new osteoid material deposited under the periosteum.

There is evidence to suggest that clubbing and hypertrophic osteoarthropathy represent different stages of the same disease process.² In most cases, finger deformity is the first manifestation; as the disease progresses, periostosis becomes evident.

Hypertrophic osteoarthropathy can be classified as primary or secondary. The primary

form, also known as primary pachydermoperiostosis, is rare and constitutes only 3% of all cases.³ The exact cause is not yet known; it occurs as a hereditary disease with autosomal dominant inheritance with variable penetrance. Congenital clubbing without periostosis is of no clinical significance.⁴

■ **CONDITIONS ASSOCIATED WITH CLUBBING**

Primary bronchogenic carcinoma is the most common cause of clubbing and hypertrophic osteoarthropathy. In one retrospective series, 4.5% of patients with lung cancer had radiologic evidence of hypertrophic osteoarthropathy.⁵ Other malignancies associated with this condition are mesothelioma, hepatocellular carcinoma, and certain types of gastrointestinal adenocarcinoma.

Other conditions associated with clubbing include:

- Cardiovascular disease such as congenital cyanotic heart disease and infective endocarditis
- Gastrointestinal conditions such as cirrhosis, primary sclerosing cholangitis, Crohn disease, and ulcerative colitis
- Infections such as lung abscess and empyema.

Clubbing is generally bilaterally symmetrical. Asymmetric clubbing is rare and usually indicates impaired regional blood flow due to vascular disease. Unilateral clubbing or hypertrophic osteoarthropathy restricted to 1 upper

limb can result from an anomaly of the aortic arch or from a subclavian or brachial artery aneurysm. Clubbing affecting predominantly the lower limbs has been reported in coarctation of aorta and patent ductus arteriosus.⁶ Rare cases of unidigital clubbing are reported in sarcoidosis.⁷

The importance of recognizing hypertrophic osteoarthropathy cannot be overemphasized. If any of the manifestations of the syndrome become evident in a previously healthy person, a thorough evaluation for an underlying disease should be done.

Clubbing should be differentiated from pseudoclubbing, which is seen in conditions such as hyperparathyroidism and scleroderma. The central mechanism for nail deformity in pseudoclubbing is acro-osteolysis with the resulting collapse of the subungual soft tissues. The important features differentiating it from true clubbing are preservation of the angle between the nail bed and proximal nail fold and asymmetric finger involvement.⁸

■ **MANAGEMENT**

The management of primary hypertrophic osteoarthropathy focuses on relieving the symptoms of periosteitis. Secondary forms require a detailed evaluation to rule out the underlying disease. In refractory cases, a bone-modifying agent (eg, zoledronic acid),⁹ octreotide,¹⁰ nonsteroidal anti-inflammatory drugs, or vagotomy¹¹ may help. ■

Management focuses on relieving the symptoms of periosteitis

■ **REFERENCES**

1. Martínez-Lavín M, Matucci-Cerinic M, Jajic I, Pineda C. Hypertrophic osteoarthropathy: consensus on its definition, classification, assessment and diagnostic criteria. *J Rheumatol* 1993; 20:1386–1387.
2. Martínez-Lavín M. Digital clubbing and hypertrophic osteoarthropathy: a unifying hypothesis. *J Rheumatol* 1987; 14:6–8.
3. Jajic Z, Jajic I, Nemcic T. Primary hypertrophic osteoarthropathy: clinical, radiologic, and scintigraphic characteristics. *Arch Med Res* 2001; 32:136–142.
4. Walker HK, Hall WD, Hurst JW, eds. *Clinical Methods: The History, Physical, and Laboratory Examinations*. 3rd ed. Boston, MA: Butterworths; 1990.
5. Izumi M, Takayama K, Yabuuchi H, Abe K, Nakanishi Y. Incidence of hypertrophic pulmonary osteoarthropathy associated with primary lung cancer. *Respirology* 2010; 15:809–812.
6. Anoop TM, George KC. Images in clinical medicine. Differential clubbing and cyanosis. *N Engl J Med* 2011; 364:666.
7. Singh A. Unidigital clubbing. *Am J Med* 2008; 121:e15.
8. Santiago MB, Lima I, Feitosa AC, Braz Ade S, Miranda LG. Pseudoclubbing: is it different from clubbing? *Semin Arthritis Rheum* 2009; 38:452–457.
9. Tachibana I, Gehi D, Rubin CD. Treatment of hypertrophic osteoarthropathy with underlying pulmonary adenocarcinoma using zoledronic acid. *J Clin Rheumatol* 2015; 21:333–334.
10. Birch E, Jenkins D, Noble S. Treatment of painful hypertrophic osteoarthropathy associated with non-small cell lung cancer with octreotide: a case report and review of the literature. *BMJ Support Palliat Care* 2011; 1:189–192.
11. Nguyen S, Hojjati M. Review of current therapies for secondary hypertrophic pulmonary osteoarthropathy. *Clin Rheumatol* 2011; 30:7–13.

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