CASE REPORT

Hypertrophic Osteoarthropathy: an Unusual Cause of Knee Pain and Recurrent Effusion

Ishaan Swarup, MD · Douglas N. Mintz, MD · Eduardo A. Salvati, MD

Received: 26 May 2016/Accepted: 22 July 2016/Published online: 30 August 2016
© Hospital for Special Surgery 2016

Keywords hypertrophic osteoarthropathy · knee pain · case report · total knee arthroplasty

Introduction

Knee pain and effusion are a common cause for referral to an orthopedic surgeon. Even though the AAOS recognizes that arthritis is the most common cause for knee pain and disability, other diagnoses should be considered when evaluating patients [14]. Hypertrophic osteoarthropathy is a syndrome characterized by clubbing of the digits, periosteal new bone formation, and synovial effusions [3]. While clubbing of the digits was described by Hippocrates, the clinical triad of digital clubbing, ossifying periostitis, and arthralgias was recognized in the 1800s [6]. Hypertrophic osteoarthropathy is classically described as either primary or secondary. Primary or familial form of hypertrophic osteoarthropathy, also known as pachydermoperiostosis, typically begins in childhood and represents 3% of all cases of hypertrophic osteoarthropathy [3, 4]. Secondary hypertrophic osteoarthropathy is associated with an underlying pulmonary, cardiac, hepatic, or intestinal disease, and it is more common in adults [3].

Electronic supplementary material The online version of this article (doi:10.1007/s11420-016-9522-8) contains supplementary material, which is available to authorized users.

I. Swarup, MD (✉) · E. A. Salvati, MD
Department of Orthopaedic Surgery,
Hospital for Special Surgery,
535 East 70th Street,
New York, NY 10021, USA
e-mail: swarupi@hss.edu

D. N. Mintz, MD
Department of Radiology and Imaging,
Hospital for Special Surgery,
535 East 70th Street,
New York, NY 10021, USA

As a whole, hypertrophic osteoarthropathy is a rare condition. There is a paucity of systematic prevalence studies on hypertrophic osteoarthropathy, but the coincidence of this condition in association with other underlying medical conditions has been described [4]. For example, hypertrophic osteoarthropathy occurs in 5–10% of patients with intrathoracic malignancies, but its prevalence has been reported to be as high as 32% in patients with primary lung cancer [9]. While primary hypertrophic osteoarthropathy occurs in young patients, secondary osteoarthropathy commonly affects patients between the ages of 55–75 [9]. The morbidity and mortality associated with hypertrophic osteoarthropathy is dependent upon its associated medical condition [4].

Patients with hypertrophic osteoarthropathy are most commonly evaluated by primary care physicians, rheumatologists, and other medical specialists. These patients are not typically evaluated primarily by orthopedic surgeons, and as a result, there is limited awareness of the clinical manifestations and medical implications of this condition. Given the association between hypertrophic osteoarthropathy and serious medical conditions, it is important to raise awareness of this condition among orthopedic surgeons. This case report provides an interesting example of a patient who presented for evaluation of his knee osteoarthritis and was found to have hypertrophic osteoarthropathy. In this case report of the incidental and unexpected finding of hypertrophic osteoarthropathy, we present the patient's history, physical exam, synovial analysis, radiographs, and work-up. Our goal is to educate orthopedic surgeons and other professionals about the classic characteristics and clinical relevance of hypertrophic osteoarthropathy. Ultimately, increased awareness of this condition may result in timely referral and management of serious medical conditions.

Case Report

The patient is a 66-year-old man who presented to the arthroplasty clinic with complaints of worsening right knee

pain and recurrent effusion. The pain began 10 months ago and it was significantly affecting his ability to ambulate and perform daily activities. At the time of presentation, he was requiring a walker for ambulation and he was having difficulty sleeping at night. The patient had been evaluated elsewhere, and he was given a diagnosis of osteoarthritis. He had previously undergone two knee aspirations and corticosteroid injections without sustained relief. The patient's medical history was otherwise significant for diabetes and hypertension, as well as a remote history of smoking.

On physical exam, the patient walked with an antalgic gait. He had a large knee effusion, and his knee range of motion was from 10° to 120° and painful. He was neurovascularly intact distally. Radiographs revealed bilateral medial joint space narrowing and marginal osteophytes consistent with moderate osteoarthritis. His radiographs were also significant for an incidental finding of bilateral and symmetric periosteal reaction consistent with hypertrophic osteoarthropathy (Fig. 1). This finding was present on the tibia, femur, and patella, and it could be appreciated on both radiographic views. Given the patient's large knee effusion, an arthrocentesis was performed and approximately 30 mL of straw-colored synovial fluid was aspirated. Synovial fluid analysis revealed a white blood cell count of 175 cells/mm³ and no crystals. Gram stain revealed no

organisms and cultures were negative for 14 days.

After consultation with our radiologist, the finding of hypertrophic osteoarthropathy was further discussed with the patient. Upon further questioning, the patient stated that he had recently discovered enlarged cervical lymph nodes and experienced involuntary weight loss. He was referred to his medical doctor for further evaluation, and he underwent advanced imaging. A lung mass was discovered, and a recent biopsy confirmed adenocarcinoma of the lung (Fig. 2). The patient is currently awaiting treatment for this new diagnosis.

Discussion

In this case report, a patient with worsening knee pain and recurrent effusion presented to our arthroplasty clinic for total knee replacement. The patient's history, exam, and radiographs were not consistent with isolated osteoarthritis, and additional questioning and work-up resulted in a diagnosis of secondary hypertrophic osteoarthropathy. The patient's timely diagnosis resulted in prompt referral and treatment of his underlying adenocarcinoma of the lung.

Hypertrophic osteoarthropathy is characterized by a constellation of symptoms and it is typically associated with an underlying medical condition [3]. Patients with hypertrophic osteoarthropathy due to neoplastic or inflammatory pulmonary conditions typically report pain and swelling in joints and long bones. Joint symptoms can range from mild to severe arthralgias, and it can involve the small and large joints [1]. Range of motion may be decreased and effusions may develop in large joints [7]. Arthrocentesis reveals a non-inflammatory fluid with cell counts less than 500 cells/mm³ consistent with the findings in our patient [13]. Radiographs show periosteal thickening, as well as a thin line of new bone separated from the subjacent cortex by a radiolucent area. These changes begin in the proximal and distal diaphysis, and then extend to involve the metaphysis [3]. These characteristic radiographic features were clearly present in our patient's radiographs (Fig. 1), including a faint radiolucent line beneath the new

Fig 1. These AP and Merchant views of bilateral knee reveal a thick and symmetric periosteal reaction characteristic of hypertrophic osteoarthropathy.

Fig 2. The chest PA radiograph documents a lesion in the left lobe.

periosteal bone in the distal diaphysis and metaphysis. It has been noted that thicker and more extensive reaction are indicative of long-standing disease [12].

While the etiology of hypertrophic osteoarthropathy is unknown, several mechanisms have been suggested as contributing to its development. Previous theories on increased vagal stimuli from tumors and decreased clearance of signaling molecules from the lung have been largely abandoned since they are not consistently present in patients with hypertrophic osteoarthropathy [3]. More recent studies have suggested that megakaryocytes and large platelet particles that are fragmented in their passage through normal lung bypass the lung in cases of hypertrophic osteoarthropathy and subsequently reach the distal extremities where they can interact with endothelial cells. This platelet-endothelial interaction results in the release of platelet-derived growth factor and other factors resulting in the proliferation of connective tissue and periosteum [3]. This phenomenon results in the characteristic radiographic findings of hypertrophic osteoarthropathy.

Secondary hypertrophic osteoarthropathy has been associated with malignant and nonmalignant diseases. The most common malignant condition associated with hypertrophic osteoarthropathy is lung cancer, more specifically non-small cell lung cancer such as squamous cell or adenocarcinoma [4]. In this case report, our patient was diagnosed with adenocarcinoma of the lung. Other malignancies associated with hypertrophic osteoarthropathy include gastrointestinal cancer, renal cell cancer, pancreatic cancer, melanoma, breast phyllodes tumor, thymic cancer, and Hodgkin's lymphoma [9]. Nonmalignant diseases associated with hypertrophic osteoarthropathy include chronic respiratory diseases, inflammatory bowel disease, thyroid disease, and congenital heart diseases [3].

Treatment for hypertrophic osteoarthropathy centers around the management of the underlying condition. In many cases, radiographic findings may regress and symptomatic improvement may be achieved after treatment of the underlying malignancy [4, 10, 11]. Other management options for joint pain and effusion include indomethacin, nonsteroidal anti-inflammatory medications, and pamidronate [2, 5]. While some patients may still benefit from total knee arthroplasty due to a concomitant diagnosis of osteoarthritis, the underlying condition should be addressed first.

Hypertrophic osteoarthropathy is a known cause of pain and effusion in the knee, and it may also cause similar symptoms in patients after total knee arthroplasty [8]. Hypertrophic arthropathy should be considered in patients presenting to arthroplasty clinic with increasing knee pain and recurrent effusion, especially in the setting of an atypical history, physical exam, or radiographs. Patients with this characteristic radiographic appearance should be closely questioned about associated medical conditions and promptly referred for additional evaluation and management. In this case report, we present an interesting case of a relatively uncommon condition seen in orthopedic practice. This case report will help to increase awareness of the characteristics and clinical relevance

of hypertrophic osteoarthropathy, and it may help to provide timely and life-saving care to future patients.

Compliance with Ethical Standards

Conflict of Interest: Ishaan Swarup, MD, Douglas N. Mintz, MD and Eduardo A. Salvati MD declare that they have no conflict of interest.

Human/Animal Rights: All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5).

Informed Consent: Informed consent was waived from all patients for being included in the study.

Required Author Forms Disclosure forms provided by the authors are available with the online version of this article.

References

- Altman RD, Tenenbaum J. Hypertrophic osteoarthropathy. In: Kelley W, Harris ED Jr, Ruddy S, Sledge C, eds. *Textbook of Rheumatology*. 5th ed. Philadelphia: WB Saunders; 1997: 1514–1520.
- Amital H, Applbaum YH, Vasiliev L, Rubinow A. Hypertrophic pulmonary osteoarthropathy: control of pain and symptoms with pamidronate. *Clin Rheumatol*. 2004; 23: 330–332.
- Fauci AS et al., eds. *Harrison's Principles of Internal Medicine*. New York, NY: McGraw-Hill Medical; 2008.
- "Hypertrophic Osteoarthropathy." Web. 11 May 2016. <http://emedicine.medscape.com/article/333735-overview>.
- Leung FW, Williams AJ, Fan P. Indomethacin therapy for hypertrophic pulmonary osteoarthropathy in patients with bronchogenic carcinoma.
- 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(8): 1386–1387.
- Martínez-Lavín M. Hypertrophic osteoarthropathy. In: Klippel JH, Dieppe PA, eds. *Rheumatology*. 2nd ed. London: Mosby; 1998. 8.46.1–4.
- Meeker J, Lachiewicz PF. An Unusual Cause of Late Pain and Effusion After Total Knee Arthroplasty: Pulmonary Hypertrophic Osteoarthropathy: A Case Report. *JBJS Case Connector* Os-90.2 (2008): 390–92.
- Nguyen S, Hojjati M. Review of current therapies for secondary hypertrophic pulmonary osteoarthropathy. *Clin Rheumatol*. 2011; 30(1): 7–13.
- Ooi A, Saad RA, Moorjani N, Amer KM. Effective symptomatic relief of hypertrophic pulmonary osteoarthropathy by video-assisted thoracic surgery truncal vagotomy. *Ann Thorac Surg*. 2007; 83: 684–685.
- Pezzetta E, Vallet C, Christodoulou M, Ris HB. [Hypertrophic osteoarthropathy of the lung and lung cancer: treatment by resection of the primary tumor]. *Rev Pneumol Clin*. 2006; 62: 255–257. French.
- Pineda CJ, Martínez-Lavín M, Goodbar JE, Sartoris DJ, Clopton P, Resnick D. Periostitis in hypertrophic osteoarthropathy: relationship to disease duration. *AJR Am J Roentgenol*. 1987; 148(4): 773–778.
- Schumacher HR Jr. Articular manifestations of hypertrophic pulmonary osteoarthropathy in bronchogenic carcinoma. *Arthritis Rheum*. 1976; 19(3): 629–636.
- "Total Knee Replacement-OrthoInfo - AAOS." Total Knee Replacement-OrthoInfo—AAOS. Web. 16 May 2016. <http://orthoinfo.aaos.org/topic.cfm?topic=a00389>.