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Original Research Article

Hypertrophic Pulmonary Osteoarthropathy (HPOA) Masquerading as Inflammatory Arthritis

Gopikrishnan Rajeev[1], Ashok Ramakrishnan[2]

[1]Senior Resident, Department of Orthopaedics, Government Medical College, Thiruvananthapuram
[2]Additional Professor, Department of Orthopaedics, Government Medical College, Thrissur

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Corresponding Author: Dr. Ashok Ramakrishnan
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Abstract:

Introduction: Clubbing and Hypertrophic Pulmonary osteoarthropathy (HPOA) are the two manifestations of a clinical syndrome which is referred to as hypertrophic osteoarthropathy (HOA). HPOA involves abnormal proliferation and of skin and periosteal tissues of the extremities. It can be primary (Pachydermoperiostosis) or secondary to chronic lung and heart diseases.

Case report: A 23 year old man presented with complaints of pain and swelling of right ankle. Initially an inflammatory arthritis was suspected but presence of high grade clubbing in all his digits gave way to a suspicion of HPOA. Patient is known case of emphysema with a history of recurrent respiratory illness in childhood.

Conclusion: As is the case with most HPOA cases reported in literature, the clinical presentation mimicks that of an inflammatory arthritis. Close attention has to be paid especially to signs like digital clubbing which can point to a more sinister underlying cause like a primary lung malignancy.

Keywords: Hypertrophic Pulmonary Osteoarthropathy, Periostitis, Clubbing.

Introduction

Hypertrophic Pulmonary Osteoarthropathy(HPOA) or Pierre-Marie-Bamberger syndrome is part of a clinical syndrome of hypertrophic osteoarthropathy(HOA) of which clubbing is a central clinical feature.[1] Patients with HPOA can also present with painful swelling and inflammation of joints especially in the lower extremities. It is characterized by periostosis of tubular bones [1]. The triad of periostitis, clubbing and arthritis has been associated with numerous diseases such as lung cancer, congenital cardiac diseases and infections [2].

It may occur as a primary condition, which is familial and affects mainly males [3]. Idiopathic or primary HOA is a rare familial autosomal dominant condition without an underlying cause. It is also referred to as pachydermo periostosis. Secondary HOA on the other hand is always associated with an underlying disease. In most cases, it is a rheumatic paraneoplastic syndrome secondary to an underlying lung malignancy [4].

Initially, the name HPOA was coined as it was only thought to coexist with an underlying lung condition. However, new studies have shown the coexistence of HOA with non-pulmonary causes like pleural, cardiac and abdominal pathologies. Early identification of HOA is of paramount importance as the commonest association of this syndrome is lung malignancy (large cell and adenocarcinoma of the lung) [5]. Identifying this condition can in turn aid in the early detection of lung malignancies even before the patient becomes symptomatic. Over 80% of adult HOA cases have associated malignancies [6,7]. Hypertrophic osteoarthropathy may affect upto 10% of patients with adenocarcinoma of the lung [8].

Case Presentation

A 23 year old man presented to the Orthopaedic outpatient department with complaints of pain and swelling in the right ankle following a trivial trauma sustained 1 year back. The patient was initially given NSAIDs but the pain nor the swelling did not resolve.

Clinical examination revealed a firm globular swelling over his lateral malleolus measuring about 5-6cm in diameter (Fig 1) which was tender to palpation. Activities like walking and prolonged standing were noted to aggravate his symptoms. He was also found to have clubbing bilaterally with drumstick appearance involving all his digits (Fig2).No evident nail changes were noted.

Considering that the patient was a young male, he was initially treated as a case of inflammatory arthritis and the clubbing was thought to be a coinci-

dental finding. Routine blood workup and screening for inflammatory markers were sent, including CRP, RA Factor, anti CCP and ANA profile. Routine blood workup was normal and the patient was negative for all inflammatory markers. This, in addition to the fact that the patient did not respond adequately to conventional pain medications, gave rise to the possibility of an alternate, non-inflammatory diagnosis. The patient also gives a history of recurrent respiratory illness in childhood and is also regularly consulting a pulmonologist for treatment of emphysema. The clubbing now seemed to be part of a syndrome rather than an incidental finding.

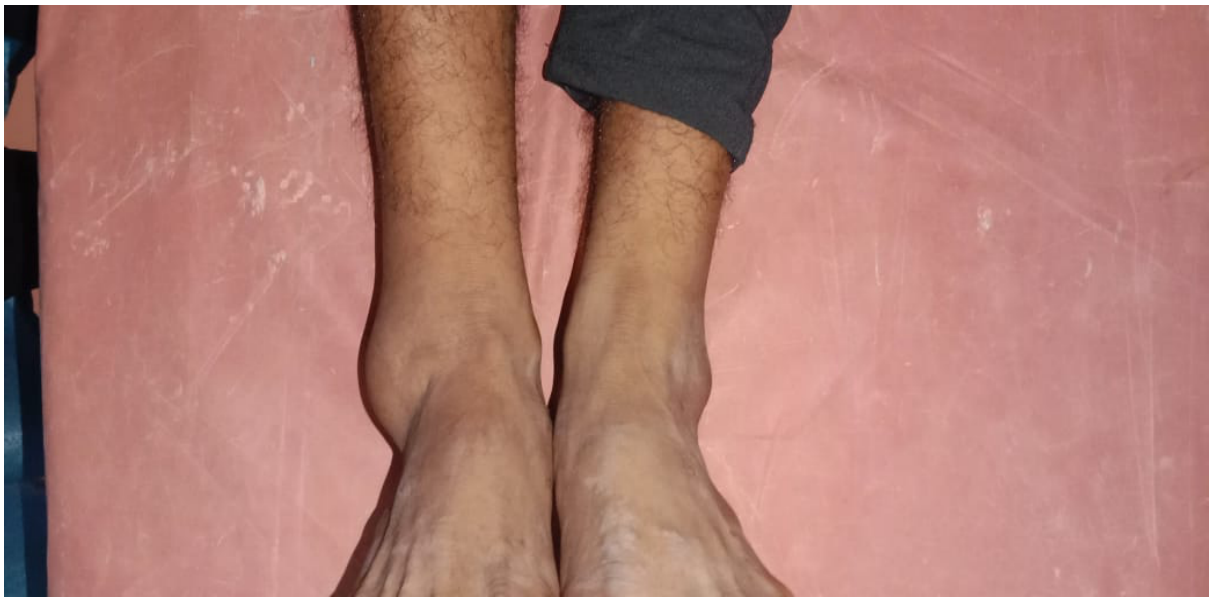

Figure 1: The patient presented with swelling of his right ankle which was associated with pain which increased on prolonged standing. Clinically,it was suggestive of an inflammatory cause

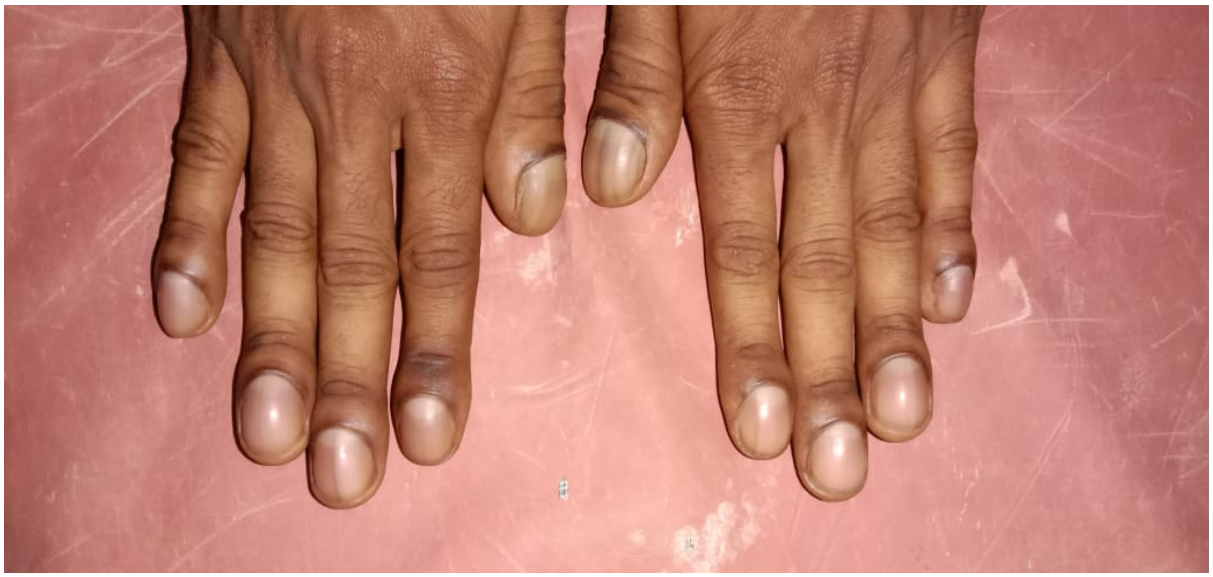

Figure 2: High grade clubbing was noted bilaterally in all digits. This,along with the history of respiratory illness,gave rise to high index of suspicion for HPOA

Plain radiographs of the ankle were taken and showed soft tissue enlargement around the lateral malleolus with associated periostitis features of the distal fibula (Fig 3). CT scan of the ankle did not reveal any obvious bony abnormality. MRI revealed an enhancing heterogenous soft tissue lesion around the distal fibula extending down till the lateral aspect of calcaneum (Fig 4).There was associated cortical thickening with cortical erosions and edema of the distal fibula suggestive of periostitis. Radiologically confirmed periostitis, clubbing and the history of underlying respiratory illness all gave rise to a high index of suspicion for Hypertrophic Pulmonary Osteoarthropathy (HPOA). The patient was promptly referred to a pulmonologist to identify any underlying lung pathology.

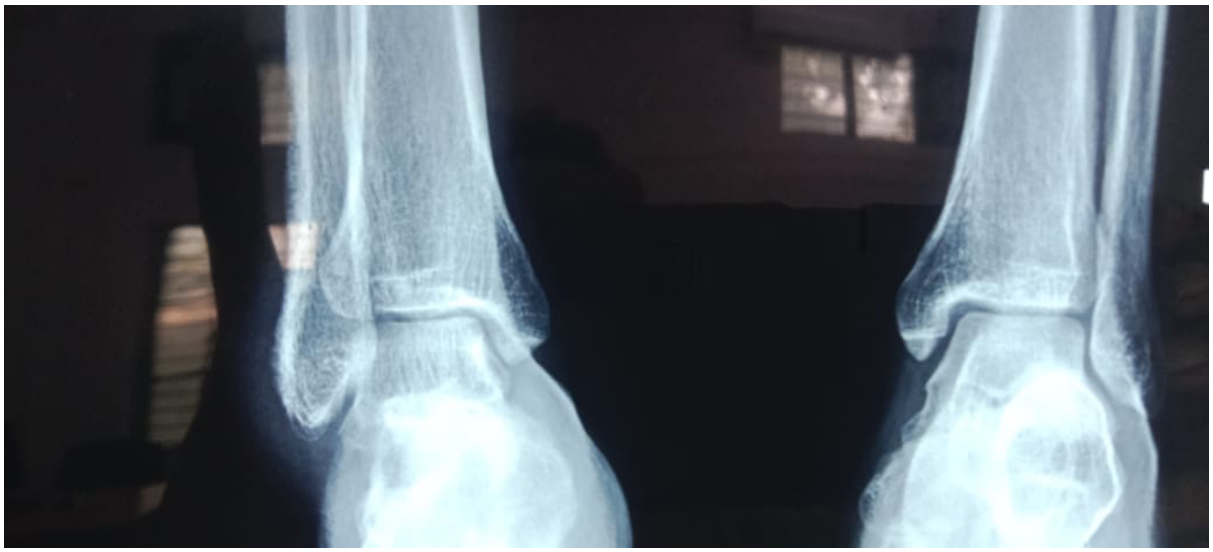

Figure 3: Plain radiographs showing soft tissue swelling and periosteal thickening around the distal fibula which is due to periostitis associated with HPOA

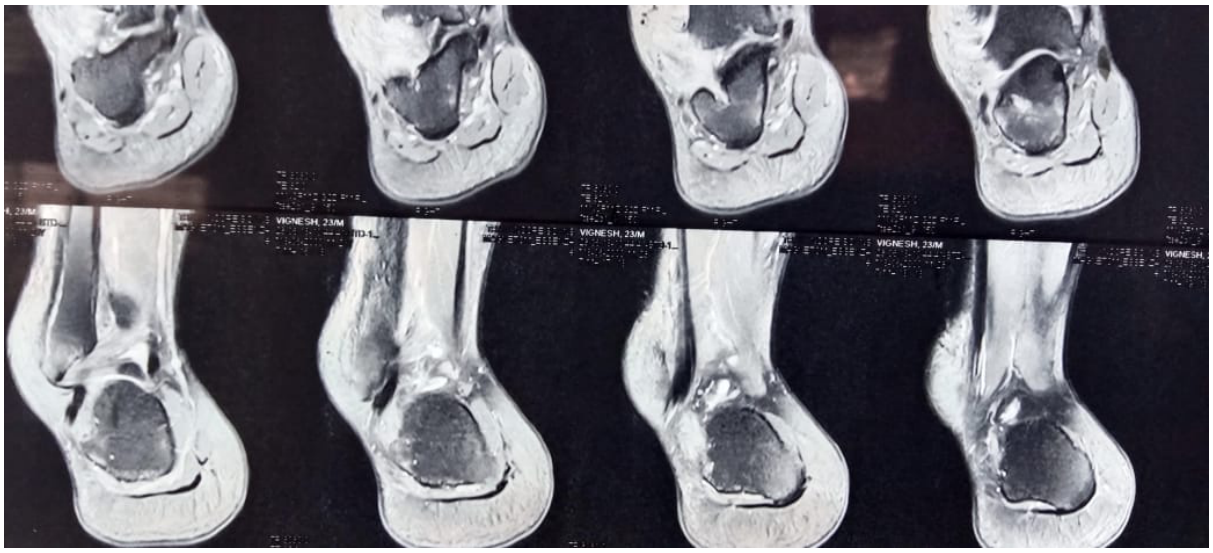

Figure 4: MRI showed cortical thickening in the distal fibula with an associated soft tissue lesion around it extending distally upto the lateral aspect of calcaneum

A detailed workup was done in tandem with the cardiologist and pulmonologist to identify the underlying pathology. CECT of the thorax showed changes suggestive of paraseptal emphysema in bilateral apical lobes.

No mass lesions/nodules/pleural effusion was present. Echocardiography was also done which showed normal cardiac dimensions with good systolic and diastolic functions.

Therapeutic Intervention

An open biopsy was taken from the lesion under local anaesthesia and the specimen sent for histopathological examination (HPE).

HPE report revealed normal fibrocollagenous tissue with congested blood vessels. No granulomatous changes or features suggestive of a metastatic lesion were found. (Fig. 5).

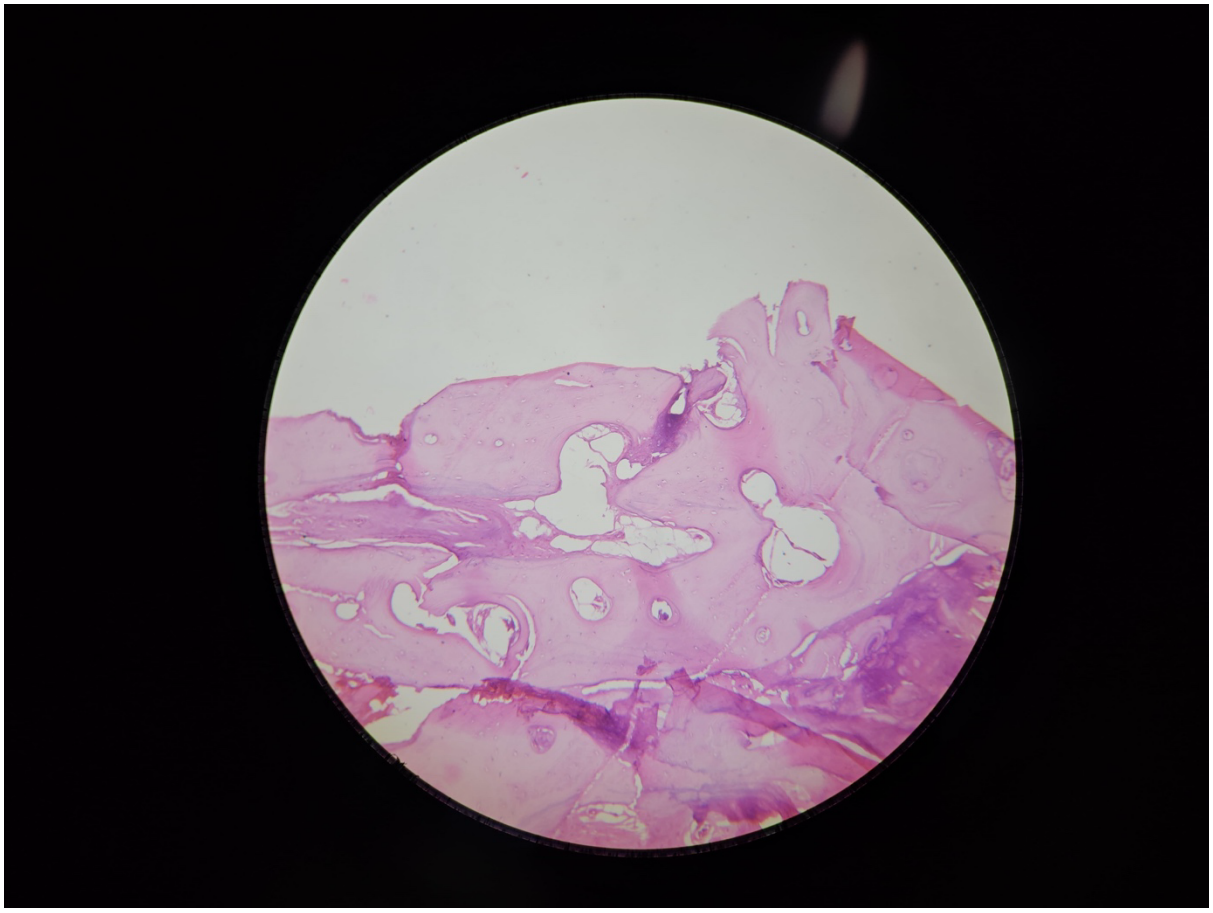

Figure 5: Histopathology revealed normal appearing bone with surrounding fibrocollagenous proliferation. No evidence of any metastatic lesions or granulomatous changes were found.

Correlating his clinical, radiological and histopathological findings, a diagnosis of HPOA secondary to emphysema was made. The patient was managed with analgesics and further excision of the lesion was not done.

Followup and Outcomes

Once a diagnosis of HPOA was made, the patient was referred to a pulmonologist for management of the underlying emphysema. The patient did not respond to any of the conventional pain medications suggesting that it is not a case of inflammatory arthritis. The resolution of inflammation and swelling in a case of HPOA depends on the prompt management of the underlying cause.

Discussion

Hypertrophic osteoarthropathy, also known as Pierre Marie Bamberger syndrome, is a condition characterized by the triad of digital clubbing, periosteal reaction of long bones and painful tenderness of the extremities, especially the lower extremities, sometimes with non-inflammatory synovial effusions of the large joints [1]. Digital clubbing is often present but can be isolated or part of the syndrome of HPOA.

Diagnosis of HOA tends to be difficult since its clinical presentation can mimic that of other diseases, especially inflammatory conditions like rheumatoid arthritis. The presence of rheumatic disease does not necessarily rule out HOA as it is known to coexist with certain rheumatological conditions [9,10].

In addition, periosteal reaction, commonly considered to be the radiological hallmark of HOA can also be present in other disorders like polyarteritis nodosa [11], familial Mediterranean fever [12], Takayasu's arteritis [13], psoriatic arthritis and reactive arthritis [14]. Positive laboratory findings are often absent but cases with extensive new bone formation may show an elevated erythrocyte sedimentation rate (ESR) and serum alkaline phosphatase values. Inflammatory markers like rheumatoid factor and anti-nuclear antibody are usually negative [2].

Periosteal reaction is the result of new bone deposition in response to different physical and chemical stimuli and can develop either as a localized or as part of a systemic disease [16]. In HOA, periosteal reaction tends to have a symmetric distribution and the earliest lesions occur at the diaphysis of long bones of lower extremities, typically tibia and fibula [17].

The etiology of HOA remains unclear. Numerous theories including the role of reflex vagal stimula-

tion, growth factors, hormonal and immune mechanisms have been proposed [15]. The stromal and vascular changes leading to digital clubbing have been postulated to be due to the release of vascular endothelial growth factor (VEGF) and platelet derived growth factor (PDGF) after impaction of platelets in the distal vasculature [18]. Although the pathogenesis of HOA is unclear, this condition has been linked to an increased production of prostaglandin E2 (PGE2) as evidenced in two studies conducted by Kozak et al [19,20].

In these studies, both primary and secondary HOA patients were found to have higher urinary levels of PGE compared to healthy individuals [20]. Increased levels of PGE2 might be responsible for secondary overexpression of vascular endothelial growth factor (VEGF), thus inducing neoangiogenesis, new bone formation and edema [19]. Thus VEGF inhibitors such as a monoclonal anti-VEGF antibody and bisphosphonates have been shown to induce relief of bone pain in patients with HOA [21].HOA is a rare differential diagnosis to be considered in cases of inflammatory arthritis. Patients with inflammatory or reactive arthritis usually respond well to NSAIDS, intra articular or systemic corticosteroid therapy or even achieve spontaneous recovery. In cases of HOA, the prognosis and management depends solely on the management of the underlying disease. Excision of tumors or chemotherapy has been shown to resolve clubbing in some cases [22]. Trials with intravenous pamidronate showed significant reduction of pain in HOA with some cases achieving complete resolution of symptoms after a single intravenous dose [23,24]. The mechanism underlying the therapeutic effect of bisphosphonates in HOA remains unclear.

Neither the clubbing nor the inflammation resolved in our case. The pain and inflammation persisted even after a long course of NSAIDs. He was referred to a pulmonologist as soon as HPOA was suspected. Only treatment of the underlying lung pathology can lead to resolution of symptoms in a case of HPOA.

Conclusion

This case report presents a case of HOA masquerading as inflammatory arthritis. HOA is a rare differential in the setting of an inflammatory arthritis, especially in the elderly. Associated clinical signs like digital clubbing should raise the possibility of HOA.

Partial or poor response to initial treatment should prompt the clinician to probe for a non-inflammatory cause. Whenever a case of HOA is diagnosed, malignancy should be thoroughly searched for as the most common association of HPOA is large cell adenocarcinoma of the lung [5]. This must be done even if the clinical and radiological evaluation suggests an infectious or interstitial lung disease. Also, new studies with bisphosphonates have shown promising results with regards to control of HOA related bone and joint pain.

Essentially, resolution of symptoms in HPOA depends on the prompt diagnosis and management of the underlying pathology. This case report aims to alert the orthopaedicians to the existence of this rare entity and how it can closely resemble inflammatory arthritis.

Clinical Message

Patients presenting with joint pain and swelling mimicking inflammatory arthritis should be carefully examined. History of respiratory illnesses and features like digital clubbing are not to be missed. An underlying respiratory/cardiac pathology may need to be looked for. Prompt diagnosis and treatment of the underlying pathology can often result in complete resolution of inflammation in HOA.

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