American Journal of Medical Case Reports, 2021, Vol. 9, No. 8, 397-401
Available online at http://pubs.sciepub.com/ajmcr/9/8/4
Published by Science and Education Publishing
DOI:10.12691/ajmcr-9-8-4

A Case of Paraneoplastic Arthralgias

David Pisarcik[1,*], Gabriel Kousourou[2], Nagadarshini Vinod[2]

[1]Department of Medicine, Indiana University, Indianapolis, IN, USA
[2]Department of Rheumatology, Indiana University, Indianapolis, IN, USA
*Corresponding author: dapisa@iu.edu

Received March 08, 2021; Revised April 15, 2021; Accepted April 25, 2021

Abstract Hypertrophic Osteoarthropathy (HOA) is a rare condition that presents with arthralgias, digital clubbing, and abnormal periosteal bone deposition seen on x rays. The secondary form of HOA may be associated with an underlying malignancy, thus highlighting the importance of early clinical recognition. We present the case of a 44-year-old woman who presented with several weeks of lower extremity swelling, arthralgias, and digital clubbing who was later found to have non-small cell lung cancer. Diagnosis can be challenging due to variable presentations that can often mimic other forms of inflammatory arthritis. Treatment is focused on addressing the underlying cause. Nonsteroidal anti-inflammatory drugs (NSAIDS) are commonly used for pain relief while intravenous bisphosphonates have been trialed with some success in case reports.

Keywords: *paraneoplastic syndrome, arthralgias, clubbing, periostosis, hypertrophic osteoarthropathy*

Cite This Article: David Pisarcik, Gabriel Kousourou, and Nagadarshini Vinod, "A Case of Paraneoplastic Arthralgias." *American Journal of Medical Case Reports*, vol. 9, no. 8 (2021): 397-401. doi: 10.12691/ajmcr-9-8-4.

1. Introduction

Hypertrophic osteoarthropathy (HOA) is distinguished by a triad of digital clubbing, abnormal deposition of periosteal bone (periostosis), and arthralgias [1]. HOA is classically diagnosed based on clinical and radiographic findings. There are two forms of HOA, primary and secondary. Primary HOA is much less common and is hypothesized to be caused by genetic abnormalities related to impaired metabolism of prostaglandin E2 (PGE2) [2]. Secondary HOA is largely considered a paraneoplastic syndrome from non-small cell lung cancer but it has also been reported in a variety of other conditions including sarcoidosis, pulmonary tuberculosis, cystic fibrosis, cyanotic heart disease, and cirrhosis among others [3,4]. While the exact mechanism of HOA pathogenesis is incompletely understood, it is believed that elevated levels of PGE2 lead to stimulation of vascular endothelial growth factor and platelet-derived growth factor causing increased bone formation [5].

2. Case Presentation

A 44-year-old female with a past medical history of hypertension, gastroesophageal reflux disease, and generalized anxiety disorder presented with a six-week history of symmetric polyarthralgias. The patient complained of pain and swelling affecting her bilateral hands, wrists, elbows, knees, ankles, and feet. She had associated morning stiffness that lasted an average of two hours. She reported using topical diclofenac gel, naproxen, and hydrocodone-acetaminophen as needed with some improvement in her pain. Review of systems was notable for generalized fatigue and chronic cough that the patient attributed to smoking. She reported a history of smoking one pack of cigarettes per day for the last ten years.

On physical exam, the patient had normal vital signs. The lungs were clear to auscultation bilaterally without rales, rhonchi, or wheezes. Her oxygen saturation was 100% on room air. Cardiac and abdominal exams were unremarkable. Clubbing of the distal phalanges was noted on examination of the hands. She had mild swelling of the knees and distal lower extremities. Her ankles and metatarsal phalangeal joints (MTPs) were tender to palpation bilaterally. No synovitis was detected on exam.

Labs were notable for anemia with a hemoglobin of 7.9 g/dL, elevated inflammatory markers with an ESR of 103, and a mildly elevated alkaline phosphatase of 163U/L. Antinuclear antibody, rheumatoid factor and anti-CCP testing were negative. Complement levels including C3 and C4 were elevated at 222 and 43 respectively. X rays of the bilateral hands and wrists showed mild periosteal reaction along the ulnar aspect of the bilateral ulnar shafts and the left first metacarpal bone (Figure 1 and Figure 2). X rays of the bilateral lower extremities and feet showed smooth, thin, periosteal reaction along the mid-distal shafts of the bilateral tibias and the shafts of the bilateral left fourth and fifth metatarsals (Figure 3 and Figure 4).

X ray of the chest showed a 3.1 cm right upper lobe lung mass. The patient subsequently underwent CT of the chest which revealed a solid right upper lobe lung mass with spiculated borders and innumerable smaller bilateral lung nodules (Figure 5 and Figure 6). The patient underwent CT guided lung biopsy with final pathology demonstrating non-small cell carcinoma, likely adenocarcinoma.

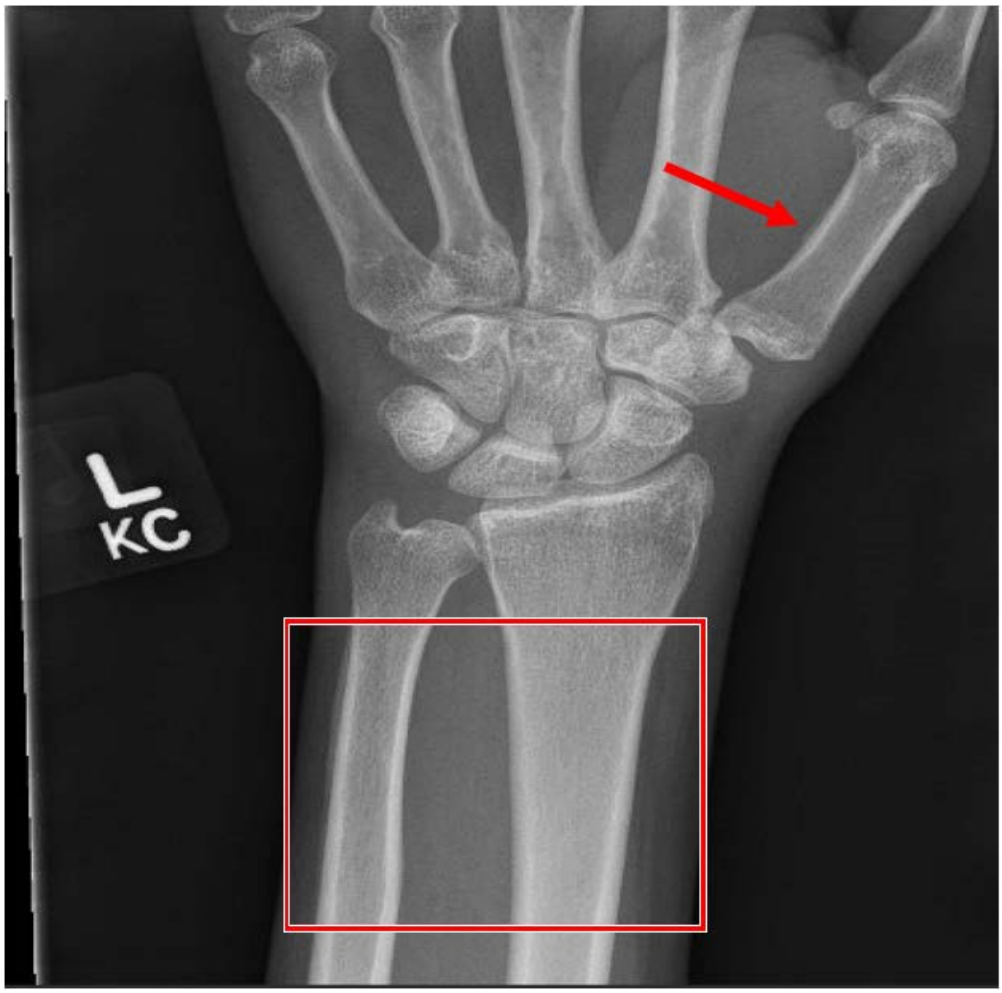

Figure 1. X ray of the left wrist and hand with periosteal reaction along the ulnar shaft and first metacarpal bone.

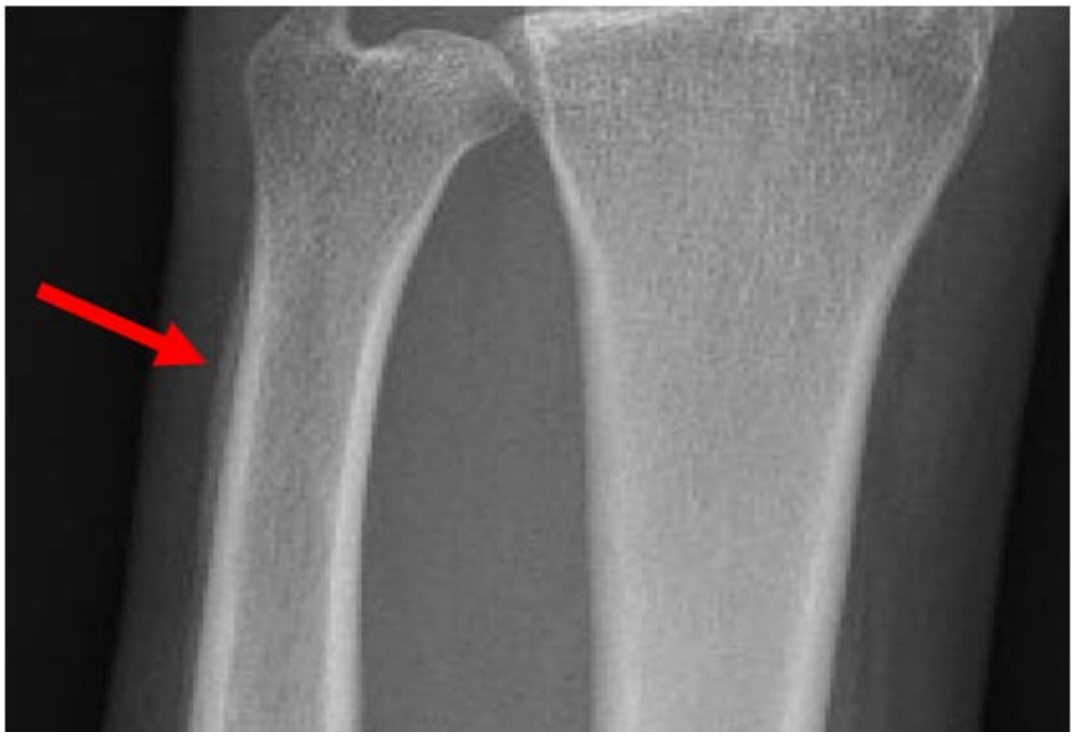

Figure 2. Closer look at the periosteal reaction seen along the distal left ulnar shaft

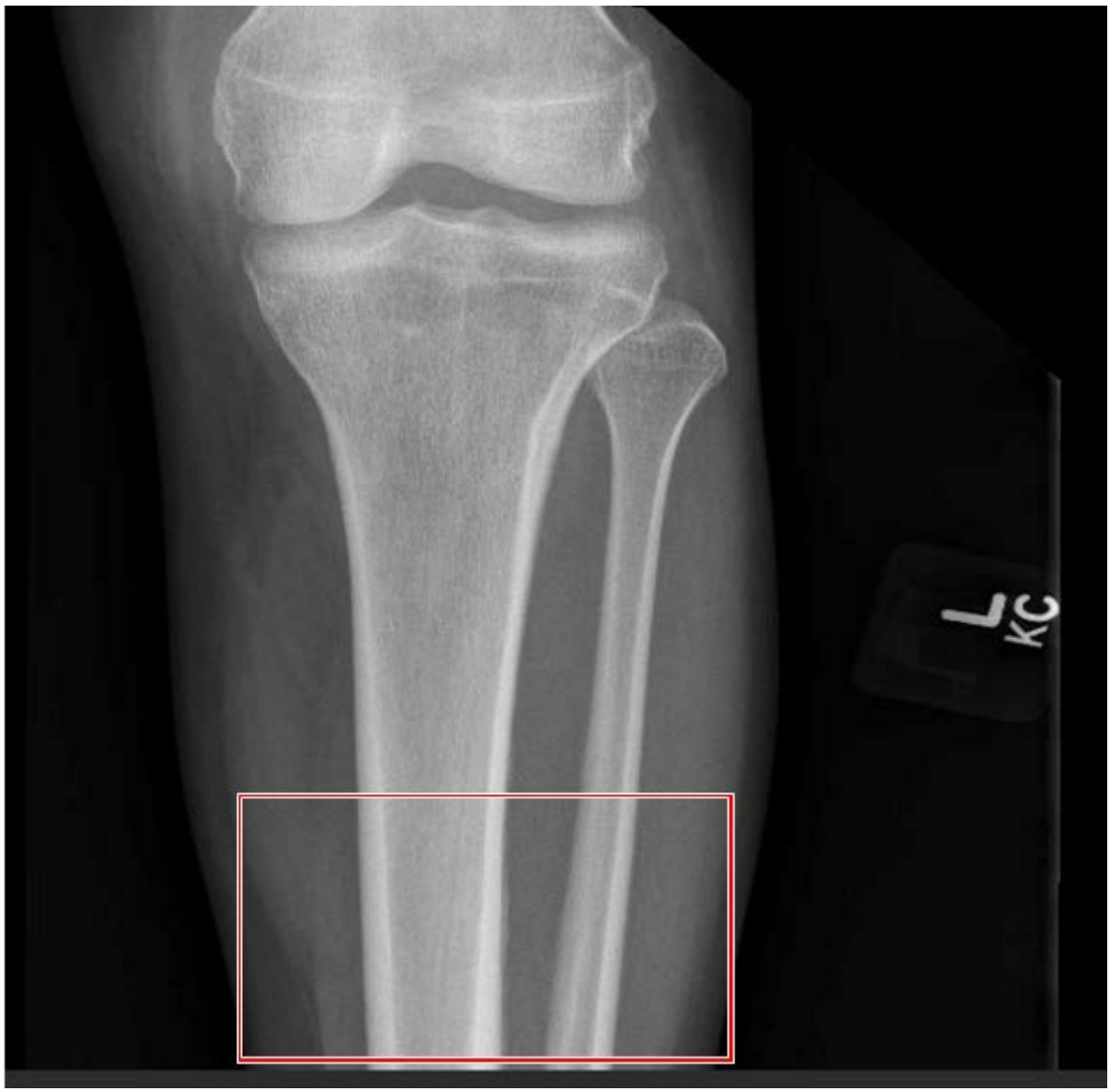

Figure 3. X ray demonstrating a thin periosteal reaction along the shaft of the left tibia and fibula

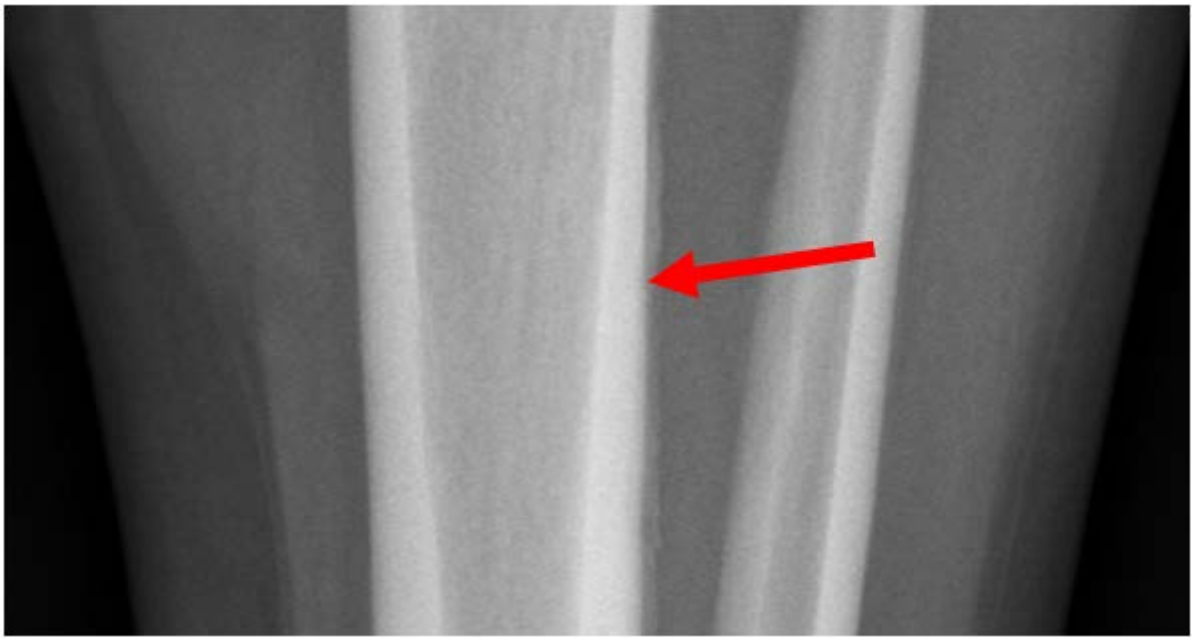

Figure 4. Closer look at the periosteal reaction seen along the shaft of the tibia

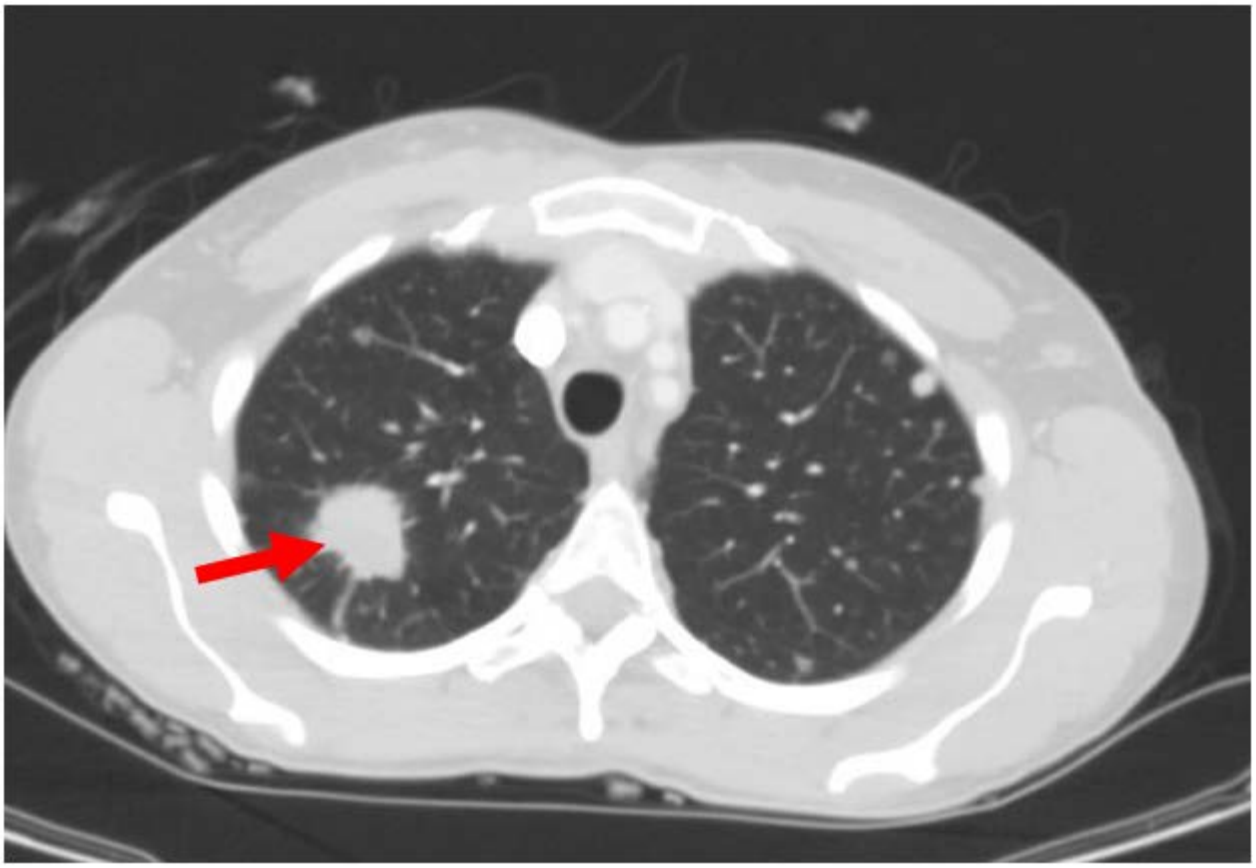

Figure 5. CT of the chest demonstrating a spiculated lung mass in the right upper lobe on axial view

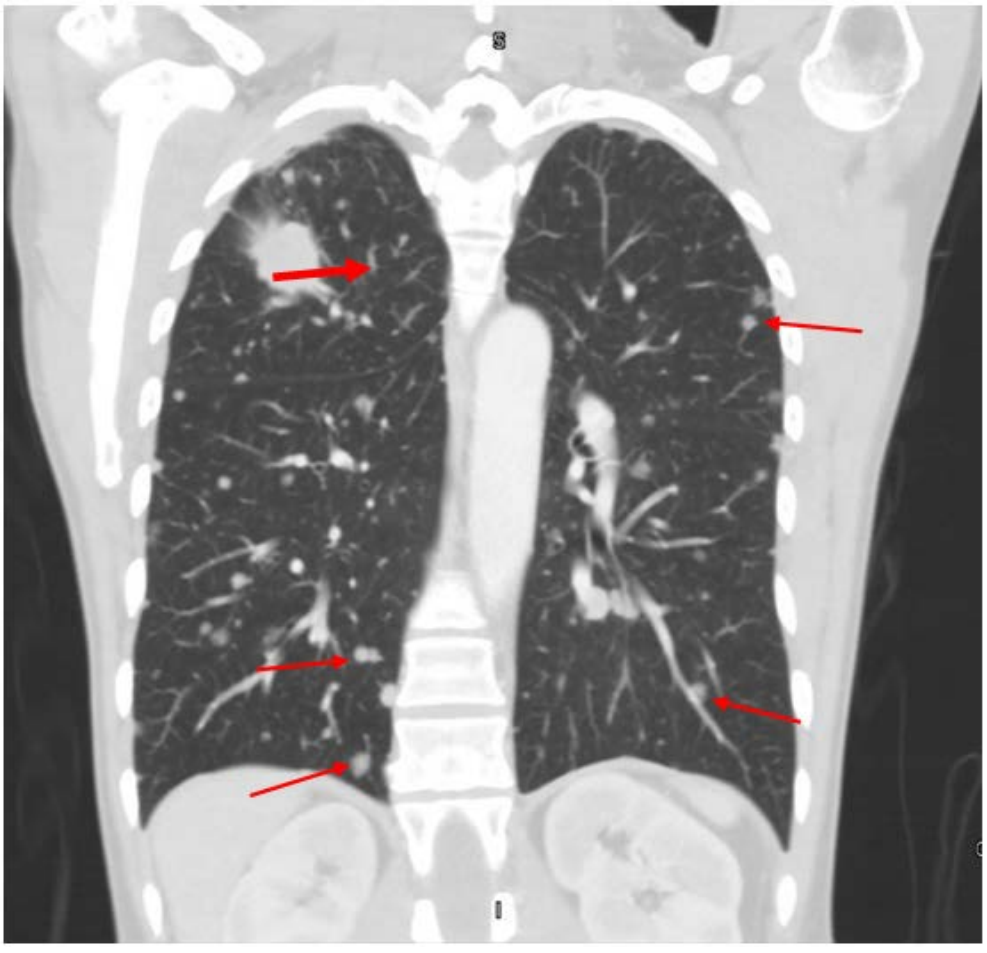

Figure 6. CT of the chest showing a malignant right upper lobe mass and bilateral pulmonary nodules on coronal view

The patient was diagnosed with hypertrophic osteoarthropathy secondary to non-small cell carcinoma of the lung. She was referred to oncology for definitive treatment of her underling malignancy. Her polyarthralgias were treated with topical diclofenac gel and naproxen 500 mg twice daily. She will follow up in rheumatology clinic for continued monitoring and treatment of her joint symptoms.

3. Discussion

Secondary hypertrophic osteoarthropathy is an uncommon presentation of joint pain and swelling that may first present itself to primary care clinics. Primary care physicians and rheumatologists should aware of the triad of digital clubbing, arthralgias, and periostosis because of the significant clinical implications they possess. Prompt investigation for the underlying cause should be performed in all cases with the focus towards chest pathology.

Diagnosing secondary HOA can be challenging in cases when digital clubbing is absent. Cases of secondary HOA that mimic inflammatory forms of arthritis such as reactive arthritis and rheumatoid arthritis have been reported in the literature [6,7]. Clinicians should pay close attention to clues that may raise suspicion for an underlying rheumatologic paraneoplastic syndrome including: age of onset, rapid and atypical progression of symptoms, systemic symptoms such as weight loss and fatigue, and associated risk factors for malignancy such as history of heavy smoking [8].

Unfortunately, there are no useful serologic tests that can confirm the diagnosis. Markers of bone turnover such as alkaline phosphatase have been associated with disease activity in some cases, and it is hypothesized that they can be used to potentially monitor disease progression and treatment response [9]. Joint involvement is most often non-inflammatory and lacks the radiographic features of joint space narrowing, periarticular osteopenia, or erosions seen in inflammatory arthritis [9]. The use of bone scintigraphy has been reported and is considered sensitive in detecting early periosteal involvement of the tubular long bones [10].

As discussed in our case, secondary HOA as a paraneoplastic syndrome is most frequently associated with non-small cell lung cancer. In a review of over 2,600 patients with lung cancer in China, secondary HOA was found in less than 1% of patients with the median age being 63 years old [11]. It was most strongly associated with males, heavy smokers, adenocarcinoma, and advanced disease at time of diagnosis (stage III to IV disease) [11].

In our case, the patient happened to be a relatively young woman who presented with several weeks of worsening joint pains, lower extremity swelling, and symptoms of generalized fatigue. History was significant for years of heavy smoking. Her symptoms and clinical presentation were somewhat atypical given the rapid progression and severity. Her exam revealed clear digital clubbing without evidence of synovitis. X-rays demonstrated periostitis of the tubular long bones without joint space narrowing or articular erosions. The presence of periostitis completed the triad of secondary HOA and further raised suspicion of lung cancer prior to histologic confirmation days later.

4. Conclusion

Secondary hypertrophic osteoarthropathy represents a rare rheumatologic paraneoplastic syndrome characterized by digital clubbing, arthralgias, and periostosis. A thorough history and physical examination along with radiographic findings can help guide clinicians in identifying the diagnosis. Prompt recognition and evaluation is paramount due to the strong association with underlying pulmonary malignancy. Treatment is focused on addressing the underlying malignancy while NSAIDs are often used for pain relief.

References

[1] MATINEZ-LAVIN, M., et al. “Hypertrophic osteoarthropathy: consensus on its definition, classification, assessment and diagnostic criteria.” *Journal of rheumatology*. 20.8 (1993): 1386-1387.

[2] Zhang, Zeng, Changqing Zhang, and Zhenlin Zhang. “Primary hypertrophic osteoarthropathy: an update.” *Frontiers of medicine* 7.1 (2013): 60-64.

[3] Yap, Felix Y., et al. “Hypertrophic osteoarthropathy: clinical and imaging features.” *Radiographics*. 37.1 (2017): 157-195.

[4] Meyer, Hans-Jonas, et al. “Secondary hypertrophic osteoarthropathy caused by non-pleural or pulmonary tumors.” *Medicine*. 96.36 (2017).

[5] Harada, Shun-ichi, et al. “Induction of vascular endothelial growth factor expression by prostaglandin E2 and E1 in osteoblasts.” *The Journal of clinical investigation*. 93.6 (1994): 2490-2496.

[6] Bozzao, Francesco, et al. “Hypertrophic osteoarthropathy mimicking a reactive arthritis: a case report and review of the literature.” *BMC musculoskeletal disorders*. 19.1 (2018): 1-6.

[7] Ulutaş, Firdevs, et al. “Hypertrophic Osteoarthropathy Presenting as Rheumatoid Arthritis Mimicker: A Case Report.” *Cureus*. 12.7 (2020).

[8] Parada-Turska, Jolanta. “Paraneoplastic rheumatologic syndromes in the elderly.” *Wiadomosci Lekarskie (Warsaw, Poland: 1960)*. 72.9 cz 1 (2019): 1646-1654.

[9] Pineda, Carlos, and Manuel Martínez-Lavín. “Hypertrophic osteoarthropathy: what a rheumatologist should know about this uncommon condition.” *Rheumatic diseases clinics of North America*. 39.2 (2013): 383-400.

[10] Mudalsha, Ravina, et al. “Tc-99m MDP bone scintigraphy in a case of Touraine-Solente-Gole syndrome.” *Indian journal of nuclear medicine: IJNM: the official journal of the Society of Nuclear Medicine, India*. 26.1 (2011): 46.

[11] Ito, Takeo, et al. “Hypertrophic pulmonary osteoarthropathy as a paraneoplastic manifestation of lung cancer.” *Journal of thoracic oncology*. 5.7 (2010): 976-980.