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CASE REPORT

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Atypical osteomalacia mimicking radiological features of spondyloarthritis: Never judge a book by its cover

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Abstract

Longstanding osteomalacia, by its proliferative enthesopathic changes, may mimic the advanced features of SpA. Despite the typical radiological findings, the lack of response to anti-TNF should encourage clinicians to reconsider the diagnosis.

KEYWORDS

diagnosis, osteomalacia, sacroiliac joints, spine, spondyloarthritis

1 | INTRODUCTION

We report a case of hypophosphatemic vitamin D-resistant osteomalacia. What makes this case special is its radiological features and enthesopathic changes which mimic spondyloarthritis in its advanced stages. Its intriguing properties include a main pelvic radiographic manifestation (mimicking advanced stages of sacroiliitis) and extrapelvic features (syndesmophytes and dagger sign).

Osteomalacia (OM) is a metabolic bone disorder characterized by decreased mineralization of the bone matrix.[1] It can manifest with symptoms such as diffuse bone pain, muscular weakness, difficulty in walking, and restriction of spinal mobility and polyarthralgia. Because these symptoms are common, the diagnosis of OM may easily be missed or confused with several other conditions, such as spondyloarthritis (SpA), polymyalgia rheumatica, polymyositis, fibromyalgia, diffuse idiopathic skeletal hyperostosis, thyroid disease, overuse, metastatic bone disease, multiple myeloma, and osteoporosis.[2] In addition, increased osteoclastic activity and bone resorption, occurring at different sites of the skeleton, may lead to sacroiliac joints (SIJ) lesions mimicking sacroiliitis.[3]

Here, we report a case of OM in a Tunisian female misdiagnosed and treated as SpA, because of "misleading" radiological findings.

2 | CASE

A 46-year-old woman patient who had previously been diagnosed as hypophosphatemic vitamin D-resistant OM was admitted to our department in February 2014. She complained of fatigue, diffuse lower back pain, and polyarthralgia since she was 25. Her family history revealed that her sister had also been diagnosed with OM. When referred to an internist in 1999, laboratory findings revealed low serum phosphorus, normal calcium, low 25-hydroxy vitamin D3, and elevated alkaline phosphatase (ALP) levels. The diagnosis of OM was confirmed by an iliac crest bone biopsy, and she was kept on vitamin D and dietary phosphorus supplementation. Despite an initial relative relief, back pain recurred. She was admitted to our department of rheumatology with severe back and neck pain, walking difficulty, and polyarthralgia. The patient said she had not

experienced any SpA symptoms in the past (eye redness or pain, sexually transmitted infections, chronic diarrhea, psoriasis, or enthesitis).

2.1 | Physical examination

Joint examination revealed no synovitis, enthesitis, or dactylitis. Range of motion of the cervical and lumbar spine was limited. Fingertip-to-floor distance was estimated at 30 cm, Schober index at 0 cm, chest expansion at 2 cm, and chin-to-manubrium distance at 5 cm. Sacroiliac joints (SIJ) compression test, FABER (Patrick's) test, and sacral thrust test were positive. The hips had a reduced range of motion in all directions. Neurological examination revealed no sensory deficits, normal motor strength, and normal deep-tendon reflexes.

2.2 | Laboratory findings

Inflammatory markers, liver transaminases, and creatinine values were normal. ALP was 655 IU/L (30-120 IU/L). Phosphorus level was low at 0.54 mmol/L (1.1-1.45 mmol/L) while the level of calcium was normal (2.34 mmol/L). Parathyroid hormone (PTH) level was at 9.56 pmol/L (1.6-6.9 pmol/L) and 25-hydroxy vitamin D level was at 22.2 ng/mL (30-100 ng/mL). Human leukocyte antigen (HLA) B27 was negative.

2.3 | Radiological findings

Pelvic radiograph showed bilateral sacroiliitis (near complete fusion of the SIJ) and bilateral hip arthritis (erosions and subchondral sclerosis) (Figure 1). Cervical spine radiograph revealed anterior syndesmophytes and posterior inter apophyseal arthritis between C2, C5, C6, and C7 (Figure 2). Dorsal spine radiograph demonstrated anterior syndesmophytes and calcifications of the interspinous ligament, leading to "dagger sign" (Figure 3). The humerus radiograph showed marked bilateral enlargement of deltoid tuberosity (Figure 4). We ran further tests: musculoskeletal ultrasound detected subclinical small joint synovitis; whereas, parathyroid ultrasound was normal. We performed a computed tomography (CT) and confirmed radiographic evidence of ankylosis of SIJ and fusion of spinal joints (Figure 5). The patient's bone mineral density revealed a total L1-L4 T score of −2.6.

2.4 | Diagnosis and therapeutic management

Upon these findings, we diagnosed axial and peripheral SpA associated with hypophosphatemic vitamin D-resistant OM.

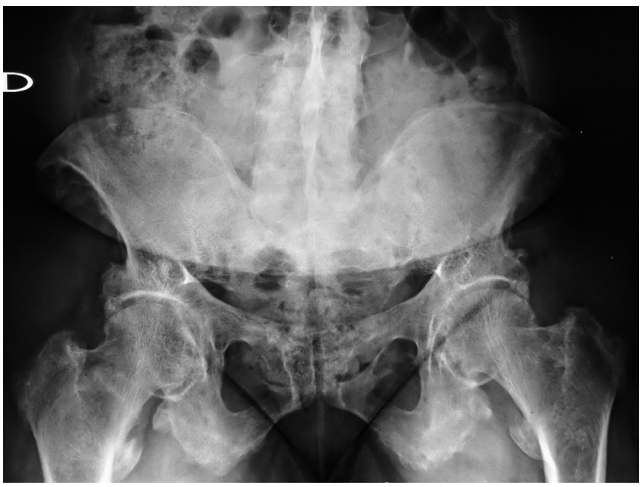

FIGURE 1 Pelvic radiograph showing apparent ankylosis of sacroiliac joints, erosions, and subchondral sclerosis of coxo-femoral joints and bony proliferation of iliac crest and hips

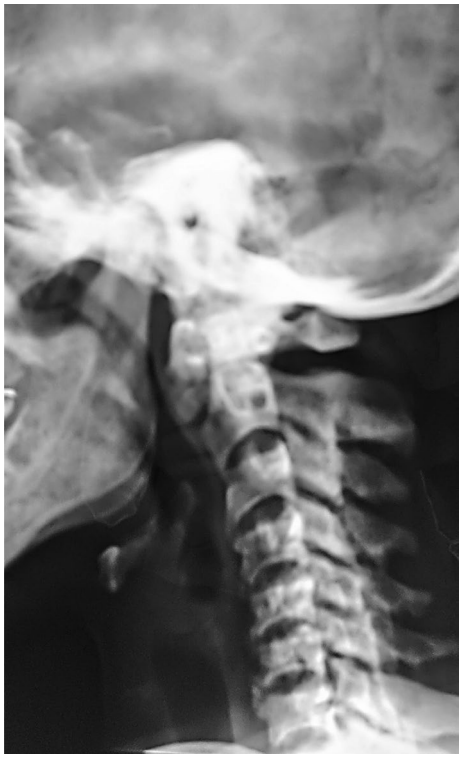

FIGURE 2 Lateral cervical spine radiograph showing large, nonbridging anterior osteophytes at C2, C5, C6, and C7 vertebral bodies

In addition to vitamin D, calcium, and phosphorus supplementation, the patient was initially treated with indomethacin 150 mg/day and methotrexate 15 mg/week. Because of gastrointestinal side effects, both were discontinued and replaced with etanercept. However, the pain did not subside, but rather worsened. Etanercept was changed to adalimumab, but without improvement. Given the lack of response to multiple lines of treatment, and as we were aware of numerous

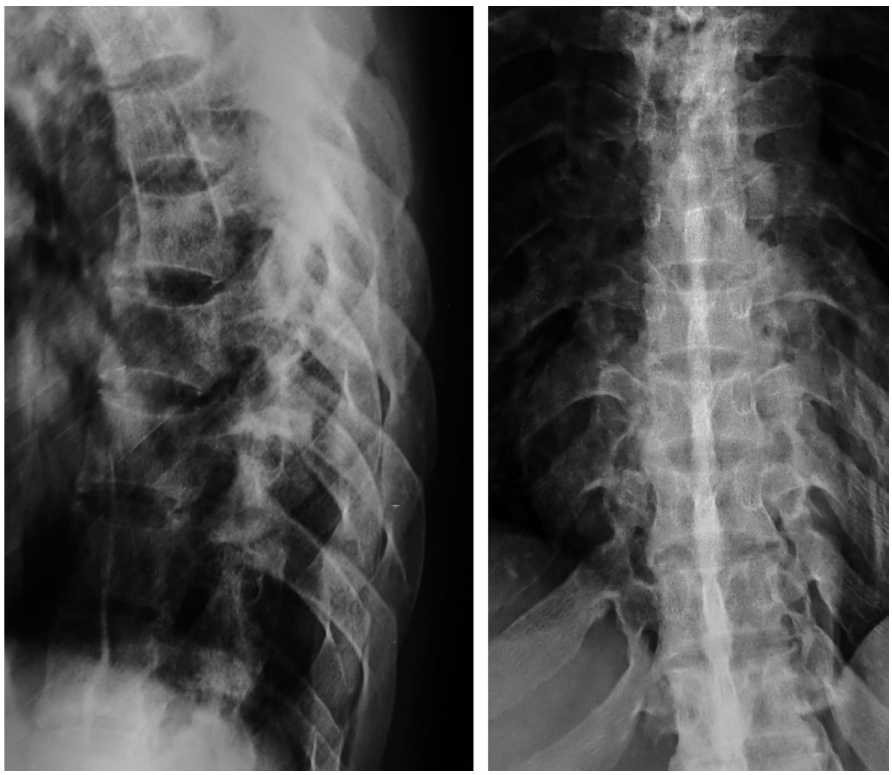

FIGURE 3 Dorsal spine radiograph showing syndesmophytes and calcification of interspinous ligament (dagger sign)

instances of OM mimicking SpA, we readmitted the patient in order to reevaluate the diagnosis. A musculoskeletal radiologist reviewed the radiographs and CT. The results were considered as compatible with proliferative enthesopathic changes induced by longstanding OM. The SpA diagnosis was excluded, and the patient was diagnosed with OM.

3 | DISCUSSION

OM occurs as a result of bone mineral imbalance.[2] The resulting secondary hyperparathyroidism may induce similar radiographic changes to those seen in SpA: symmetrical widening of the SIJ space and subchondral bone erosions surrounded by osteosclerosis.[3]

Several cases of OM misdiagnosed as SpA have been reported.[2,4-8] The largest study was conducted by Jin et al The study included 26 patients with hypophosphatemia osteomalacia misdiagnosed as SpA.[8] The reasons for misdiagnosis were the initial presentation with low back pain, the morning stiffness, positron emission tomography (PET-CT) or MRI, and the SIJ lesions not only in X-ray, but also in CT. Two critical factors were reported and may have been enough reason to reconsider the diagnosis of SpA: the poor efficacy of NSAIDs, glucocorticoids, DMARDs, and biologicals, and the predominance of radiological lesions in sacrum or ilium rather than in joints.

In the previous cases, the main puzzling symptom was the pelvic radiological appearance mimicking sacroiliitis. In our patient, the main question was whether the case was purely OM or presented together with SpA. In addition to the appearance of SIJ mimicking advanced stages of sacroiliitis (ankylosis), extrapelvic features (syndesmophytes and dagger sign) may also have led to misdiagnosis. In fact, it has been previously reported that, unlike sacroiliitis, neither joint space narrowing nor ankylosis is induced by hyperparathyroidism.[9] However, the lack of treatment response to TNF inhibitors, despite their well-known ability to reduce clinical symptoms in patients with SpA, encouraged us to reconsider the diagnosis.

When reviewing the literature, we found one report carried out in 1989 which confirms that longstanding hypophosphatemic osteomalacia may lead to proliferative enthesopathic changes.[10] These enthesopathies, which involve the axial and appendicular skeleton, have received little attention in the radiological literature. Radiological findings in the cervical and the thoracolumbar spine, as described by Burnstein et al, include hyperostosis, marginal symmetrical syndesmophytes, and calcification of interspinous, supraspinous, and anterior and posterior longitudinal ligaments.[10] The joint appearance of these symptoms may lead to "the dagger sign." SIJ changes mimicking sacroiliitis include not only widening of the joint space, bone erosions and osteosclerosis,[3] but also ankylosis with ossification of the anterior sacroiliac ligaments and true intraarticular bone formation.[10]

In sum, radiographic sacroiliitis, usually known as the hallmark of SpA, can be observed in a variety of other

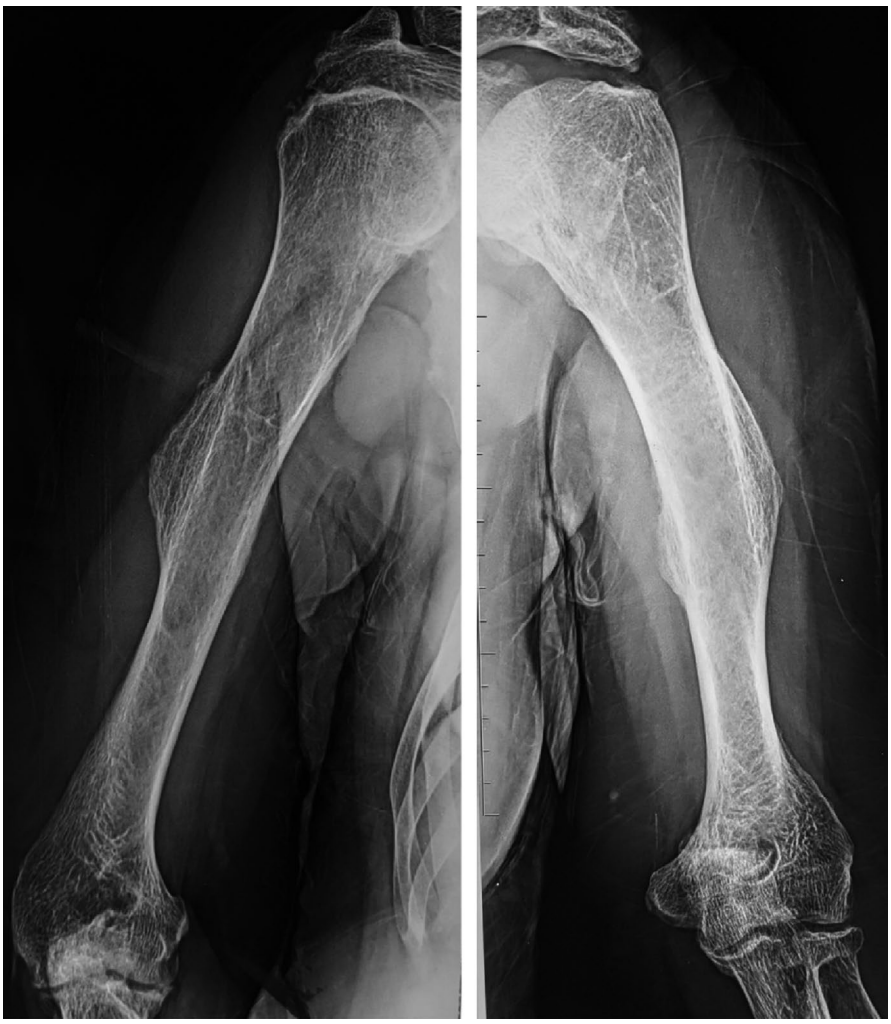

FIGURE 4 Humerus radiographs showing bilateral marked enlargement of deltoid tuberosity

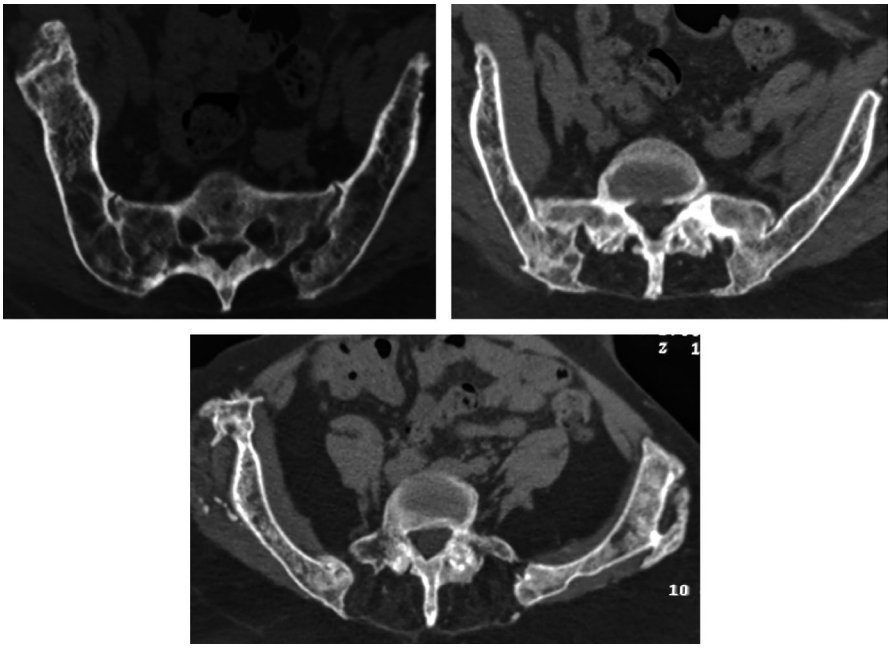

FIGURE 5 Computed tomography showing intraarticular bone formation of sacroiliac joints

diseases. The key message is that longstanding OM, by its proliferative enthesopathic changes, may mimic SpA with the typical advanced features such as syndesmophytes and complete fusion of the SIJ.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

KM: interpreted the data and assisted in the preparation of the manuscript. DBN: extracted patient history from the medical records and wrote the initial draft of the manuscript. HR: extracted and interpreted imaging data from the medical records. HF, OH, and DK: revised the manuscript. WH: revised the manuscript and approved the final version to be published.

ETHICAL APPROVAL

Ethical approval was obtained from the Scientific and Ethical Committees of the hospital.

DATA AVAILABILITY STATEMENT

The datasets used and/or analyzed are available from the corresponding author on reasonable request.

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REFERENCES

1. Emini-Sadiku M, Morina-Kuqi N. Concealing clothing leading to severe vitamin D deficiency, osteomalacia and muscle weakness. *Open Access Maced J Med Sci*. 2019;7(13):2146-2149. https://doi.org/10.3889/oamjms.2019.584
2. Sivas F, Yurdakul FG, Durak M, Hatipoğlu G, Önal ED, Bodur H. Hypophosphatemic osteomalacia: a case simulating ankylosing spondylitis treated with anti-TNF therapy. *Osteoporos Int*. 2016;27(12):3651-3654. https://doi.org/10.1007/s00198-016-3758-5
3. Jevtic V. Imaging of renal osteodystrophy. *Eur J Radiol*. 2003;46(2):85-95. https://doi.org/10.1016/s0720-048x(03)00072-x
4. Aslam F, Chivers FS, Doshi KB, Chang-Miller A. Positive HLA-B27 and sacroiliitis is not always spondyloarthritis. *Int J Rheum Dis*. 2019;22(12):2213-2217. https://doi.org/10.1111/1756-185X.13738
5. Akkus S, Tamer MN, Yorgancigil H. A case of osteomalacia mimicking ankylosing spondylitis. *Rheumatol Int*. 2001;20(6):239-242. https://doi.org/10.1007/s002960100120
6. Garip Y, Dedeoglu M, Bodur H. Osteomalacia mimicking spondyloarthropathy: a case report. *Osteoporos Int*. 2014;25(7):1983-1985. https://doi.org/10.1007/s00198-014-2716-3
7. Hoshino C, Satoh N, Sugawara S, Kuriyama C, Kikuchi A, Ohta M. Sporadic adult-onset hypophosphatemic osteomalacia caused by excessive action of fibroblast growth factor 23. *Intern Med*. 2008;47(5):453-457. https://doi.org/10.2169/internalmedicine.47.0665
8. Jin J, Sun F, Wang G, et al. The clinical characteristics of 26 cases of hypophosphatemia osteomalacia misdiagnosed as spondyloarthritis. *Zhonghua Nei Ke Za Zhi*. 2014;53(11):847-851.
9. Tuite MJ. Sacroiliac joint imaging. *Semin Musculoskelet Radiol*. 2008;12(1):72-82. https://doi.org/10.1055/s-2008-1067939
10. Burnstein MI, Lawson JP, Kottamasu SR, Ellis BI, Micho J. The enthesopathic changes of hypophosphatemic osteomalacia in adults: radiologic findings. *AJR Am J Roentgenol*. 1989;153(4):785-790. https://doi.org/10.2214/ajr.153.4.785

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