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Aseptic Osteomyelitis of the Hip, an Unexpected Complication of Zoledronic Acid Treatment: A Case Report

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Abstract

Osteoporosis is a diffuse skeletal disorder characterized by decreased bone strength and a resultant increased risk of fracture. Zoledronic acid is a biphosphonate that is prescribed to patients with osteoporosis and preserved kidney function (glomerular filtration rate > 30 ml/min). We are reporting the case of an 80-year-old female with poly osteoarthritis who developed an aseptic osteomyelitis of the right hip two days after receiving a perfusion of zoledronic acid administered for the management of her osteoporotic fracture (with vertebral collapse at L1). Although minor secondary effects such as flu symptoms are reported following perfusions of zoledronic acid, the occurrence of osteomyelitis in this context remains unexplained. Spontaneous resolution was noted a few weeks later and with the administration of nonsteroidal anti-inflammatory drugs.

Keywords

Zoledronic Acid, Osteomyelitis, Osteoporosis

1. Introduction

Osteoporosis is a diffuse skeletal disorder characterized by decreased bone strength and increased fracture risk. The measure of BMD (bone mineral density) is useful both in the diagnosis of the disorder and for the fracture risk assessment [1]. Nevertheless, this investigation alone is insufficient for making therapeutic decisions. Zoledronic acid is a biphosphonate that plays a role in inhibiting osteoclastic re-

sorption. This treatment is administered yearly through the intravenous route. Considering its toxic effect on the kidney, the treatment is selectively given to patients with a glomerular filtration rate (GFR) above 30 ml/min. Minor secondary effects such as flu symptoms and gastrointestinal upsets are reported. Some less reported effects include arrhythmias [2] [3].

1.1. Patients and Methods

We are reporting here the case of an aseptic osteomyelitis of the hip in a patient who received a perfusion of zoledronic acid

1.2. Clinical Case

An 85-year-old female whose only cardiovascular risk factor is her age. She has polyosteoarthritis (coxarthrosis, multileveled Lombarthrosis, bilateral gonarthrosis) with osteoporotic vertebral collapse at L1. She receives a 5 mg zoledronic acid perfusion for the management of her osteoporosis. Two days later, she presents with an acute non-traumatic right hip pain associated with a fever at 39˚. History reveals no recent underlying infection (dental abscess, urinary tract or pulmonary infection). On clinical evaluation, we have a good general state with stable hemodynamic parameters, pain at the right hip with a restricted range of motion and limping. Abduction and adduction are limited; there are no palpable sentinel lymphadenopathies nor clinically observable focus of infection. Paraclinical findings on biology, we have an inflammatory syndrome with an erythrocyte sedimentation rate (ESR) = 87 mm/h (N < 10 mm/h), a C-reactive protein (CRP) = 42 mg/dl (N < 0.5 mg/dl) with moderate leukocytosis WBC = 9500/uL. The ANA (antinuclear antibodies), rheumatoid factor (RF) and the anti-cyclic citrullinated peptide (CCP) antibodies are negative. Uric acid, kidney function tests and liver function tests are normal. Phosphate calcium levels are not disturbed. The various samples collected (blood culture, microscopic urinalysis) came back negative. Chest radiograph is normal. The MRI of the right hip showed a contrast enhanced foci of the bone marrow and synovium. An inflammatory type of effusion is equally seen at the level of the pectineus facing the adductors and equally at the level of the right gluteal muscle. A thin fluid collection is also present at the level of the intermuscular fascia coursing through the quadriceps (**Figure 1** and **Figure 2**). The ultrasound guided hip puncture was noncontributive due to synovial hypertrophy, nonetheless, puncture of the peritrochanteric bursa showed a pale yellow, aseptic and paucicellular (**Figure 3**) fluid. The patient will benefit from simple monitoring associated with analgesics (acetaminophen 1 g three times a day), anti-inflammatory drug (naproxen 550 mg twice a day), rest, cryotherapy and physiotherapy after the fever drops. Three days after, the CRP progressively decreased to become negative 7 days later. The ESR became stable at 40 mm/H and CRP became normal. A month following her admission, a control MRI shows a reduced but not a complete regression of the bone edema and muscle infiltration. (**Figure 4** and **Figure 5**)

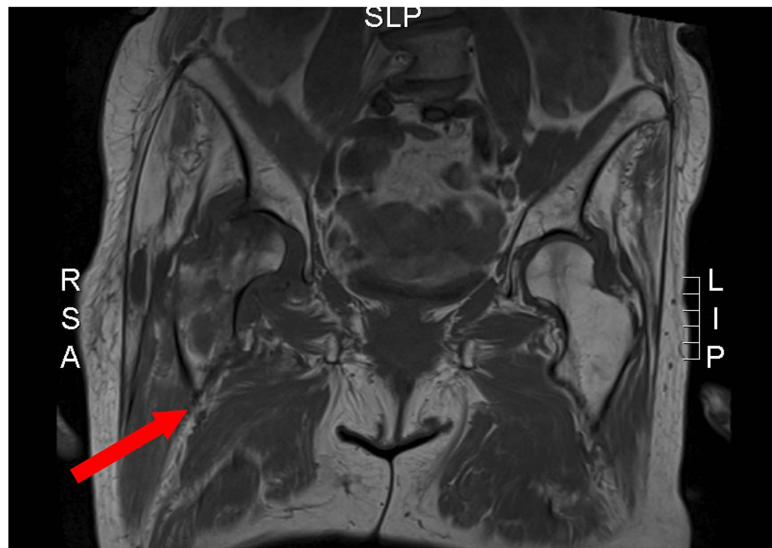

Figure 1. MRI of the hip, T1 images.

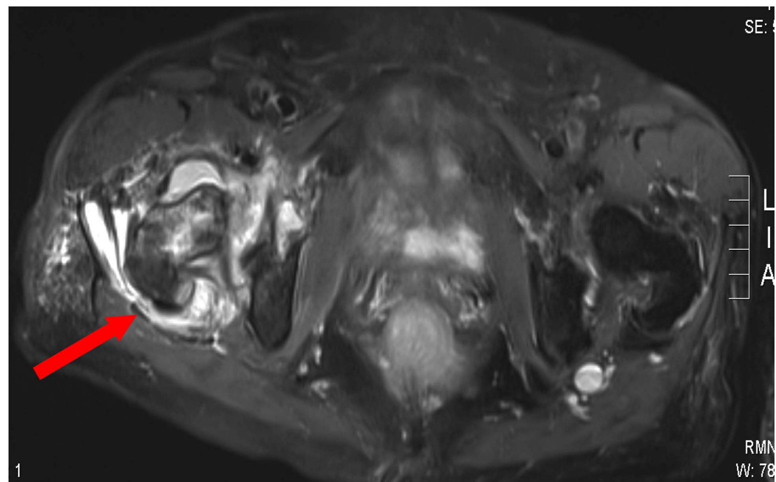

Figure 2. MRI of the hip, T2 images.

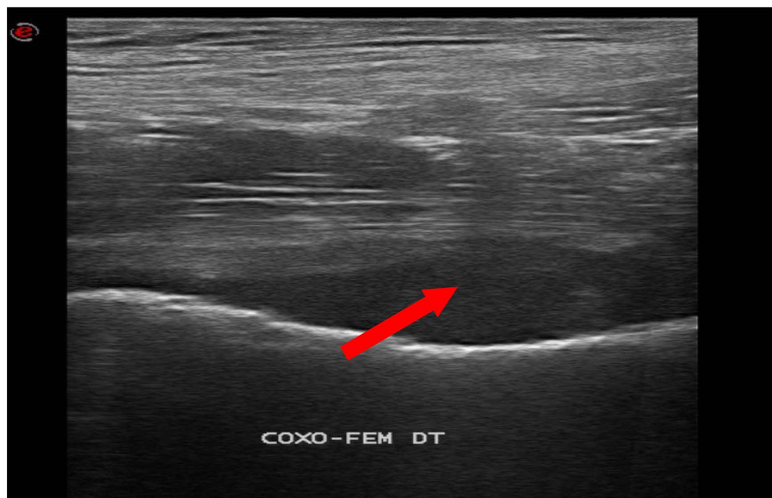

Figure 3. Ultrasound scan of the right hip.

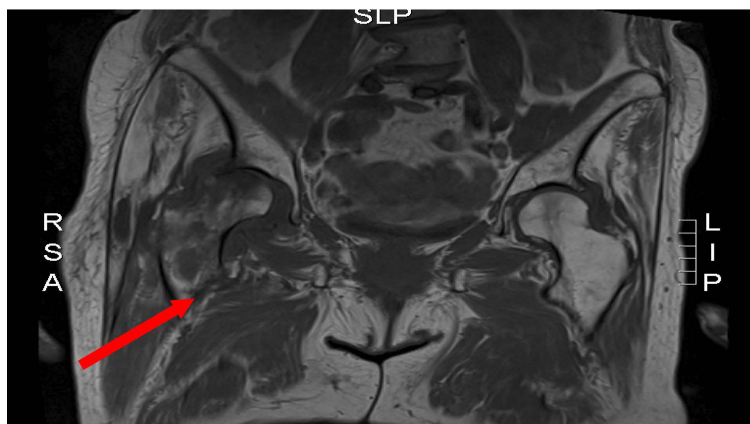

Figure 4. MRI, one month later.

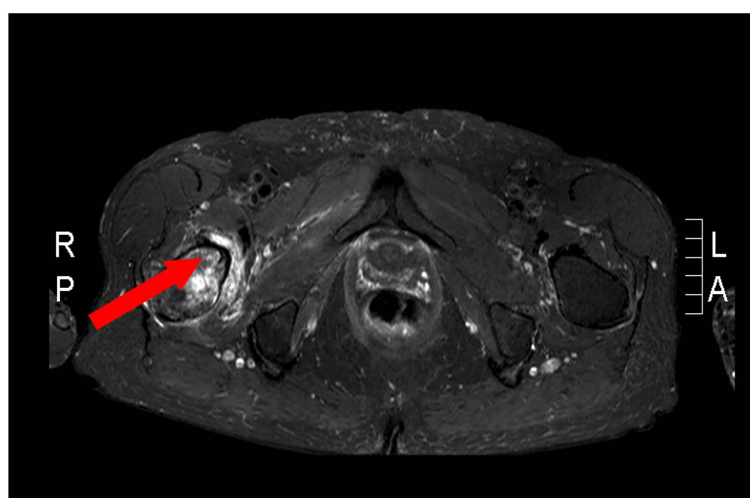

Figure 5. Follow-up MRI, one month later, T2 sequence.

2. Discussion

Osteomyelitis following zoledronic acid perfusion is not reported in the literature. A series of 3889 patients receiving zoledronic acid perfusion yearly for three years, no case of arthritis was reported. The most frequent side effects were fever, myalgias, flu symptoms, and headache. Nevertheless, we had a significant number of cases with cardiovascular events such as atrial fibrillation, and impaired kidney function [3]. These symptoms generally regress over three days. Febrile reactions were more significant in patients with unexplained raised levels of PTH [4]. Although fever in patients receiving zoledronic acid was explained by elevated CRP and some cytokines like IL6 and TNF alpha, the mechanism of osteomyelitis still remains unexplained [5] [6]. The absence of crystals, inflammatory liquid and medullary contrast-enhanced foci on MRI contradicts the possibility of a microcrystalline arthritis. By isolating, for example, the osteoblasts present in osteophytes of the arthrosic knee, and those of the subchondral non-arthrosic joints, Sako et al. showed that the osteoblasts of osteophytes play a role in the degradation process by significantly producing more IL6, IL8 and MMP-13 than non-arthrosic

osteoblasts [7]. The amplification mechanism of a degenerative coxopathy thus remains the most feasible in our patient. If this is the case, the local release by inflammatory tissues of inflammatory mediators would have been done by all surrounding tissues: synovitis, bursitis, muscle fascia and bone marrow. This hypothesis is more likely as it has been shown in vivo that IL1-beta is a pivot in joint destruction mechanisms and the principal mediator in enzymatic activation in synergy with TNF alpha in osteoarthritis [8]-[10]. Zoledronic acid could potentiate the macrophagic process that causes the amplification of the inflammatory cascade by acting at all levels of the degenerative process of the bone marrow and the peritendinous bursa?

Otherwise, Suppressor of cytokine signaling-3 (SOCS3) inhibits the Janus kinase (Jaki) and regulates protein degradation and suppression of cytokine signaling. SOCS3 modulates the macrophage response and cytokines such as IL6 and leptin. Zoledronate is an inhibitor of SOCS3 and thus acts in increasing the local inflammatory phenomenon by inhibiting STAT3 and by increasing the local production of IL6 [11]. This matches our hypothesis. In our patient, no treatment was necessary, and the control MRI showed a spontaneous favourable evolution, the restoration of the hip mobility and regression of the inflammatory syndrome. The only intervening event was the administration of zoledronic acid, implying a cause-and-effect reaction.

3. Conclusion

Aseptic osteomyelitis that abruptly appeared following a zoledronic acid perfusion mimics a likely septic osteoarthritis in this elderly patient. The favourable spontaneous evolution of clinical and paraclinical parameters goes in favour of an isolated event. A cause-and-effect relation is thus drawn out.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy (2001) Osteoporosis Prevention, Diagnosis, and Therapy. *JAMA*, **285**, 785-795. https://doi.org/10.1001/jama.285.6.785

[2] Briot, K., Cortet, B., Thomas, T., Audran, M., Blain, H., Breuil, V., *et al*. (2012) Actualisation 2012 des recommandations françaises du traitement médicamenteux de l'ostéoporose post-ménopausique. *Revue du Rhumatisme*, **79**, 264-274. https://doi.org/10.1016/j.rhum.2012.02.006

[3] Black, D.M., Delmas, P.D., Eastell, R., Reid, I.R., Boonen, S., Cauley, J.A., *et al*. (2007) Once-yearly Zoledronic Acid for Treatment of Postmenopausal Osteoporosis. *New England Journal of Medicine*, **356**, 1809-1822. https://doi.org/10.1056/nejmoa067312

[4] Deng, H.O., Li, D.F., Zhang, W.J., Zhi, X.M., Xu, L. and Wu, W. (2011) Factors Associated with Acute Febrile Reaction in Elderly Patients Receiving Intravenous Zoledronic Acid for Osteo-Porosis. *Journal of Southern Medical University*, 31, 2076-2078.

[5] Sykiotis, A., Papaioannou, G., Mavropoulos, J., Triantaphyllopoulou, M., Papandroulaki, F., Ktena, V., *et al.* (2013) Markers of Inflammation after Zoledronic Acid Redosing. *Journal of Bone and Mineral Metabolism*, **32**, 72-77. https://doi.org/10.1007/s00774-013-0467-4

[6] Dicuonzo, G., Vincenzi, B., Santini, D., Avvisati, G., Rocci, L., Battistoni, F., *et al.* (2003) Fever after Zoledronic Acid Administration Is Due to Increase in TNF-α and IL-6. *Journal of Interferon & Cytokine Research*, **23**, 649-654. https://doi.org/10.1089/107999003322558782

[7] de Jaeger, C. and Cherin, P. (2011) L'arthrose: Une nouvelle maladie inflammatoire? Actualités fondamentales et thérapeutiques. *Médecine & Longévité*, **3**, 116-136. https://doi.org/10.1016/j.mlong.2011.04.001

[8] Munier, A., Gras, V., Andrejak, M., Bernard, N., Jean-Pastor, M., Gautier, S., *et al.* (2005) Zoledronic Acid and Renal Toxicity: Data from French Adverse Effect Reporting Database. *Annals of Pharmacotherapy*, **39**, 1194-1197. https://doi.org/10.1345/aph.1e589

[9] Martel-Pelletier, J. and Pelletier, J.P. (1989) Molecular Basis for the Action of Tiaprofenic Acid on Human Osteoarthritic Cartilage Degradation: Protective Effects of NSAID. *Seminars in Arthritis and Rheumatism*, **18**, 19-26. https://doi.org/10.1016/0049-0172(89)90080-2

[10] van den Berg, W.B. (2001) Uncoupling of Inflammatory and Destructive Mechanisms in Arthritis. *Seminars in Arthritis and Rheumatism*, **30**, 7-16. https://doi.org/10.1053/sarh.2001.23704

[11] Scheller, E.L., Hankenson, K.D., Reuben, J.S. and Krebsbach, P.H. (2011) Zoledronic Acid Inhibits Macrophage SOCS3 Expression and Enhances Cytokine Production. *Journal of Cellular Biochemistry*, **112**, 3364-3372. https://doi.org/10.1002/jcb.23267