DOI: 10.4274/tod.galenos.2025.90922
Turk J Osteoporos

# *Arthritis Following Zoledronic Acid Infusion in a Knee Joint Affected by Paget's Disease*

## *Paget Hastalığından Etkilenen Bir Diz Ekleminde Zoledronik Asit İnfüzyonunu Takip Eden Artrit*

***Alper Mengi[1], Ensar Aydemir[2]***

[1]Sultan 1. Murat State Hospital, Clinic of Pain Management, Edirne, Türkiye
[2]Sultan 1. Murat State Hospital, Clinic of Endocrinology and Metabolism, Edirne, Türkiye

**Keywords:** Arthritis, zoledronic acid, Paget's disease, knee
**Anahtar kelimeler:** Artrit, zoledronik asit, Paget hastalığı, diz

**Dear Editor,**

A 69-year-old male patient presented to our outpatient pain management clinic with left knee pain. The pain had persisted for 2 weeks, exacerbating with movement but absent at rest. His numeric rating scale (NRS) score during motion was 6. The patient had a 10-year history of Paget's disease. Bone scintigraphy performed 6 months earlier revealed diffusely increased uptake in the thoracic vertebrae, left iliac crest, and bilateral proximal femurs. His alkaline phosphatase level was 1303 IU/L (normal range: 40-130 IU/L), and the glomerular filtration rate was 64 mL/min/1.73 $m^2$. Following the initial intravenous infusion of 5 mg zoledronic acid for the treatment of Paget's disease, the patient began to experience pain, increased warmth, and swelling in the left knee approximately 3 days later. He had no history of trauma to the left knee, no complaints of pain or swelling in any other joint, and no recent infections.

On physical examination, the patient's left knee had a flexion of 90° and an extension of -10°, with severe pain occurring at the end range of motion. The patellar tap test was positive, and increased local warmth was noted, although no instability was present. McMurray's test and both the anterior and posterior drawer test results were negative.

Although bone scintigraphy performed 6 months earlier did not show involvement around the knee, magnetic resonance imaging of the left knee revealed a lesion in the distal left femur consistent with Paget's disease. Radiographic imaging also revealed findings consistent with moderate osteoarthritis. Increased synovial fluid accumulation was observed in the knee joint space, lateral recess, and suprapatellar bursa (Figure 1).

Ultrasound-guided aspiration of the left knee yielded 25 mL of clear, slightly yellow fluid. Synovial fluid analysis revealed a leukocyte count of 3000 cells/$mm^3$ with a neutrophil ratio of 50%. No crystals were observed in the synovial fluid, and bacterial staining and culture yielded negative results. Subsequently, an ultrasound-guided intra-articular injection of 2 mL dexamethasone combined with 3 mL of 1% lidocaine was administered. At the 2-week follow-up, the patient's NRS score had decreased to 1. During approximately 4 months of follow-up, the patient remained free of knee pain.

Paget's disease is generally asymptomatic; however, when symptoms are present, bone pain is the most common complaint. Primary pain related to Paget's disease is considered to result from increased bone turnover and vascularity (1). This pain typically begins in the later stages of the disease, persists throughout the day and at rest, and worsens at night (2). In addition, pain may arise from complications associated with Paget's disease, such as osteoarthritis or joint deformity. This type of pain is classified as secondary pain and occurs more frequently than primary Paget's-related pain (1). In patients with periarticular involvement of Paget's disease, both primary and secondary Paget's-related pain may exacerbate with mechanical loading of the knee. Consequently, distinguishing whether the pain originates from Paget's disease or results from osteoarthritis can be challenging. A positive response to an intra-articular injection indicates that the pain has an intra-articular origin (2,3).

**Corresponding Author/Sorumlu Yazar:** Assoc. Prof. Alper Mengi, Sultan 1. Murat State Hospital, Clinic of Pain Management, Edirne, Türkiye
**E-mail:** a_mengi22@hotmail.com **ORCID ID:** orcid.org/0000-0003-0898-764X
**Received/Geliş Tarihi:** 04.09.2025 **Accepted/Kabul Tarihi:** 03.10.2025 **Epub:** 06.10.2025

**Cite this article as/Atıf:** Mengi A, Aydemir E. Arthritis following zoledronic acid infusion in a knee joint affected by Paget's disease. Turk J Osteoporos. [Epub Ahead of Print]

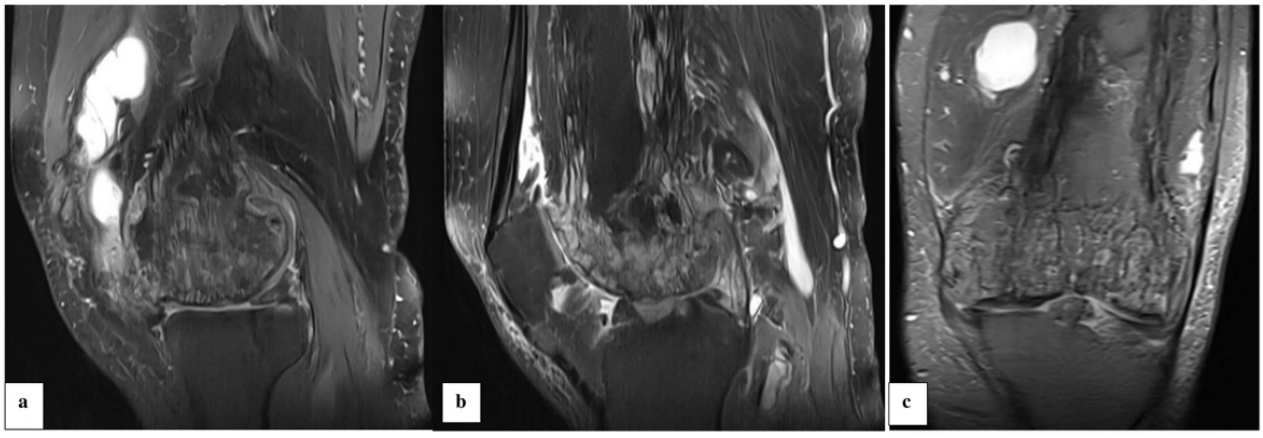


**Figure 1.** Increased fluid in the knee joint space, lateral recess and suprapatellar bursa, a and b: Fat suppressed proton density sequence of sagittal view of the knee, c: Fat suppressed proton density sequence of coronal view of the knee

Bisphosphonates are recommended for the treatment of Paget's disease, with zoledronic acid being the bisphosphonate most likely to elicit a favorable therapeutic response (4). Common side effects following zoledronic acid infusion include transient fever, fatigue, joint pain, muscle pain, nausea, and bone pain. However, the development of arthritis after zoledronic acid infusion is a rare side effect. In the few reported cases, the joints affected by arthritis included the knee, wrist, fingers, ankle, and toe joints. In most of these cases, clinical or radiographic evidence of pre-existing osteoarthritis was documented, and the resulting arthritis was interpreted as an exacerbation of osteoarthritis (5). In our patient, the knee that developed arthritis exhibited moderate degenerative changes. The radiographic findings and joint aspiration results, similar to other reported cases, suggest that the arthritis observed in our patient was a zoledronic acid-induced exacerbation of osteoarthritis. What distinguishes our case from previous reports is that this exacerbation occurred in a patient receiving zoledronic acid for the treatment of Paget's disease rather than for osteoporosis, and notably, the joint that developed arthritis also exhibited Paget's disease involvement.

To the best of our knowledge, no other case in the literature describes a patient with Paget's disease who developed arthritis attributable to zoledronic acid infusion. Through this report, we aim to highlight that in addition to its common side effects, zoledronic acid—frequently used in the treatment of Paget's disease—may rarely induce arthritis, and this possibility should be considered in the differential diagnosis.

## Footnotes

### Authorship Contributions

Surgical and Medical Practices: A.M., Concept: A.M., E.A., Design: A.M., Data Collection or Processing: A.M., E.A., Analysis or Interpretation: A.M., Literature Search: A.M., E.A., Writing: A.M., E.A.

**Conflict of Interest:** No conflict of interest was declared by the authors.

**Financial Disclosure:** The authors declared that this study received no financial support.

## References

1. Cook SJ, Wall C. Paget's disease of bone: a clinical update. Aust J Gen Pract. 2021;50:23-9.
2. Whyte MP. Clinical practice. Paget's disease of bone. N Engl J Med. 2006;355:593-600.
3. Popat R, Tsitskaris K, Millington S, Dawson-Bowling S, Hanna SA. Total knee arthroplasty in patients with Paget's disease of bone: a systematic review. World J Orthop. 2018;9:229-34.
4. Ralston SH, Corral-Gudino L, Cooper C, Francis RM, Fraser WD, Gennari L, et al. Diagnosis and management of Paget's disease of bone in adults: a clinical guideline. J Bone Miner Res. 2019;34:579-604.
5. Wei J, Cho CSI. Bilateral knee effusions secondary to zoledronic acid infusion. JCEM Case Rep. 2024;2:luae199.