

Mimicking Multiple Myeloma: Voriconazole-Induced Hyperfluorosis and Bone Lesions

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A 70-year-old man was found to have diffuse lytic and sclerotic bone lesions during a work-up to rule out malignancy after sustaining an unprovoked pulmonary embolus (Fig. 1). The patient reported several months of deep “bone pain” and debilitating weakness. Past medical history was significant for a history of disseminated coccidioidomycosis for which he was being treated with voriconazole. An extensive work-up, including biopsy of a bone lesion, bone marrow biopsy, and protein electrophoresis, was unrevealing. Due to an elevated alkaline phosphatase level in the setting of chronic voriconazole use, a fluoride level was checked and found to be markedly elevated at 16 mmol/L (normal 1–4 mmol/L).



Figure 1 Radiograph of the left humerus showing diffuse lytic lesions (a) and extensive endosteal scalloping (b).

Voriconazole is one of the triazoles, which are the mainstay of therapy for disseminated coccidioidomycosis infections. Chronic voriconazole use has been associated with elevated serum levels of fluoride and skeletal disease. Bony changes resemble periostitis deformans, a condition associated with drinking excessively fluoridated water^{1–3}. Additionally, voriconazole is believed to cause bony changes in a non-fluoride mediated pathway via osteoblast activation and stimulation of cytokine release⁴. In our patient, voriconazole was replaced with posaconazole and he experienced significant improvement within weeks of this change.

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REFERENCES

1. **Thompson GR, 3rd, Bays D, Cohen SH, Pappagianis D.** Fluoride excess in coccidioidomycosis patients receiving long-term antifungal therapy: an assessment of currently available triazoles. *Antimicrob Agents Chemother* 2012;56(1):563–4 doi: <https://doi.org/10.1128/AAC.05275-11>.
2. **Moon WJ, Scheller EL, Suneja A, Livermore JA, Malani AN, Moudgal V, Kerr LE, Ferguson E, Vandenberg DM.** Plasma fluoride level as a predictor of voriconazole-induced periostitis in patients with skeletal pain. *Clin Infect Dis* 2014;59(9):1237–45 doi: <https://doi.org/10.1093/cid/ciu513>.
3. **Adwan MH.** Voriconazole-induced periostitis: a new rheumatic disorder. *Clin Rheumatol* 2017;36(3):609–15 doi: <https://doi.org/10.1007/s10067-016-3341-7>.
4. **Allen KC, Sanchez CJ, Jr., Niece KL, Wenke JC, Akers KS.** Voriconazole Enhances the Osteogenic Activity of Human Osteoblasts In Vitro through a Fluoride-Independent Mechanism. *Antimicrob Agents Chemother* 2015;59(12):7205–13 doi: <https://doi.org/10.1128/AAC.00872-15>.

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