CLINICAL IMAGES

Voriconazole-induced periostitis

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Figure 1: Radiograph of the left shoulder of a 66-year-old woman showing smooth periosteal thickening in the distal third of the clavicle (arrow).

A 66-year-old woman with a two-year history of T-cell prolymphocytic leukemia presented with left shoulder pain of 10 months' duration. A month before the admission, the pain became severe, constant and disabling. She was taking voriconazole for invasive neurohistoplasmosis (300 mg twice daily for 10 months). The patient had painful restriction of the left shoulder's active range of motion and tenderness on palpation of the chest wall and left leg. Alkaline phosphatase levels were elevated (200 [normal 25–100] U/L) and creatinine levels were normal. Smooth periosteal thickening of the left clavicle was seen on radiography (Figure 1). A bone scan showed multiple areas of increased tracer activity (Figure 2A).

The differential diagnosis included a periosteal reaction secondary to leukemia, infection-related periosteal apposition and drug-induced periostitis. After ruling out a recurrence of leukemia and infection, we diagnosed voriconazole-induced periostitis.[1] Discontinuation of voriconazole led to the resolution of pain within 48 hours. At a three-month follow-up, the alkaline phosphatase level and bone scan were normal (Figure 2B). At nine months, there was no evidence of leukemic relapse or active infection.

Fluorosis (the integration of fluoride into bone structure) and promotion of bone formation by osteoblast stimulation is the proposed mechanism of voriconazole-related periostitis.[2,3] Risk factors for fluorosis include renal impairment, long-term use of voriconazole at therapeutic doses, slow drug metabolism and elevated fluoride levels.[2] Unlike voriconazole, other fluorinated triazoles (e.g., fluconazole and posaconazole) are not associated with periostitis.[2] Drug-induced reversible periostitis has also been described in connection with prostaglandin E1[4] and interleukin-11.[5]

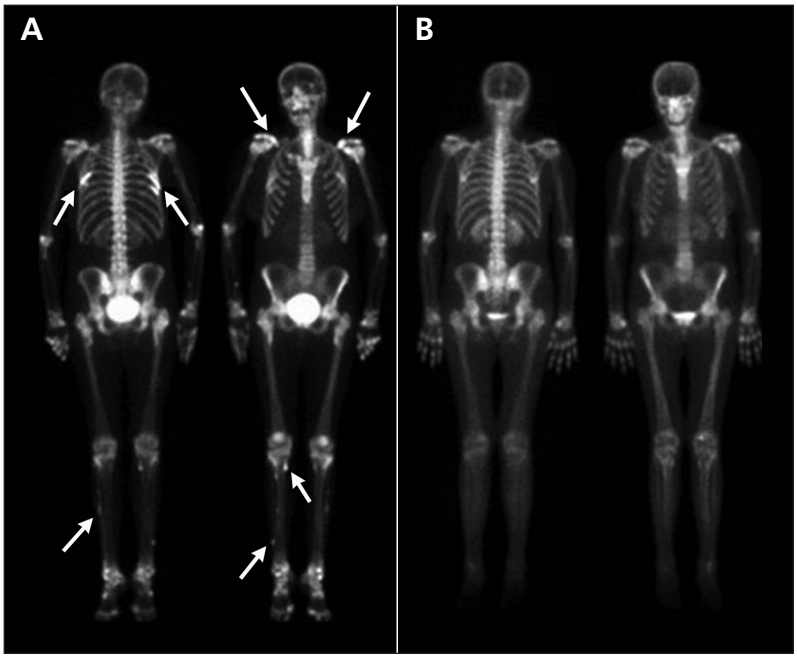

Figure 2: (A) Whole-body bone scan showing multiple areas of increased tracer activity involving the clavicles, ribs and long bones (arrows). (B) Follow-up bone scan showing resolution of the increased tracer activity.

References

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