

Clinical Image

Reactive Histiocytic Dermatitis from Ponatinib

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A 54-year-old male had *BCR::ABL1 p190, TP53, IKZF1*-mutated acute lymphoblastic leukemia with extramedullary disease of the clivus and ribs. He received alkylating chemotherapy and ponatinib, followed by blinatumomab and ponatinib, achieving complete remission but with minimal residual disease. He then attained complete molecular remission after undergoing myeloablative haploidentical-related stem cell transplantation conditioned with cyclophosphamide and total body irradiation with posttransplant cyclophosphamide, mycophenolate mofetil, and tacrolimus graft-versus-host disease prophylaxis. On day 60 post-transplant, he began a daily maintenance dose of 15 mg of ponatinib. He had no graft-versus-host disease, and immunosuppression with tacrolimus was tapered off by day 90 post-transplant. The patient tolerated ponatinib well without any side effects.

On day 385 post-transplant, he suddenly developed severe pain in his left leg, accompanied by a 6 cm indurated, tender, erythematous plaque (Figure 1A). Bacterial and fungal blood cultures were unrevealing. The skin lesion was unresponsive to topical steroids or intravenous vancomycin and piperacillin-tazobactam antibiotics. A skin biopsy revealed scattered eosinophils with interstitial and perivascular histiocytic dermatitis (Figure 1B, x400, hematoxylin, and eosin stain

and Figure 1C, CD163 histiocyte stain) without atypia, vasculitis, leukemia cutis, or graft-versus-host disease. Stains and tissue cultures for *Nocardia*, mycobacteria, and fungi were unremarkable. Ponatinib was discontinued, and the rash resolved within a month.

Ponatinib has moved to earlier lines of therapy for acute lymphoblastic leukemia and is now used in the frontline setting. Reactive dermatitis can occur with ponatinib in a dose-dependent manner, usually within 6 months but even 2 years later. Rashes have been reported in 27% of patients on ponatinib 45 mg versus 2.6% at the lowest dose of 15 mg. This case highlights the importance of recognizing cutaneous adverse reactions associated with ponatinib, even after long-term use and even at low doses. In our patient, the painful rash abated only after stopping ponatinib.

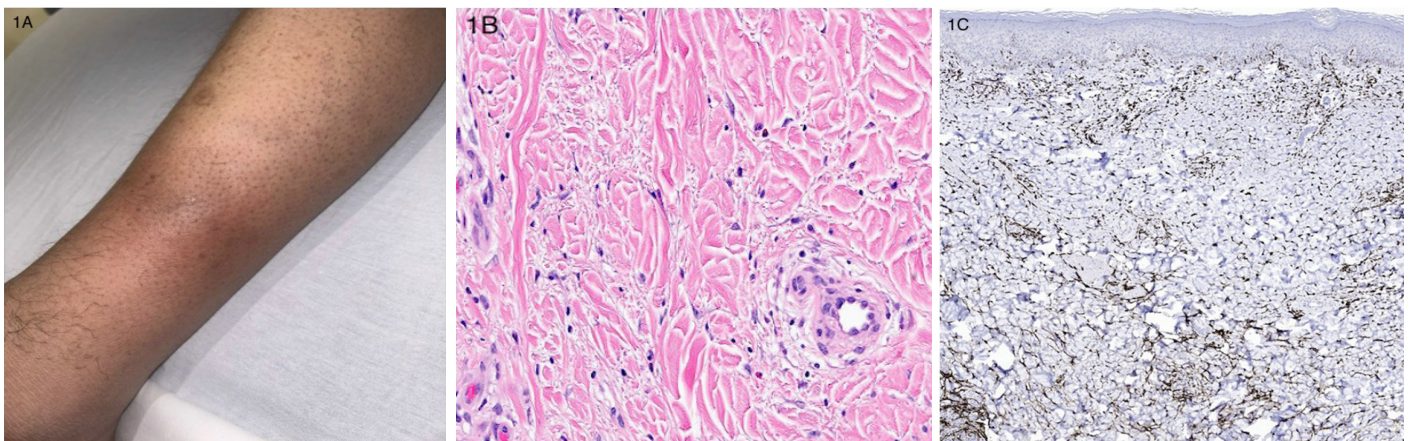
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