Cutaneous Vasculitis Induced by Osimertinib

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A 65-year-old female with T2aN3M1c stage IVB adenocarcinoma of the lung commenced osimertinib monotherapy 80 mg/day. Six weeks after the initiation of osimertinib, multiple palpable purpura with neither pain nor pruritus appeared on her legs (Fig. 1). She presented without fever, arthralgia, fatigue, or other symptoms associated with systemic vasculitis. She had no signs of connective tissue disease. Laboratory testing revealed a platelet count of 158,000/μL and serum immunoglobulin A was within the normal range. Antinuclear antibody, rheumatoid factor, cryoglobulin, proteinase-3

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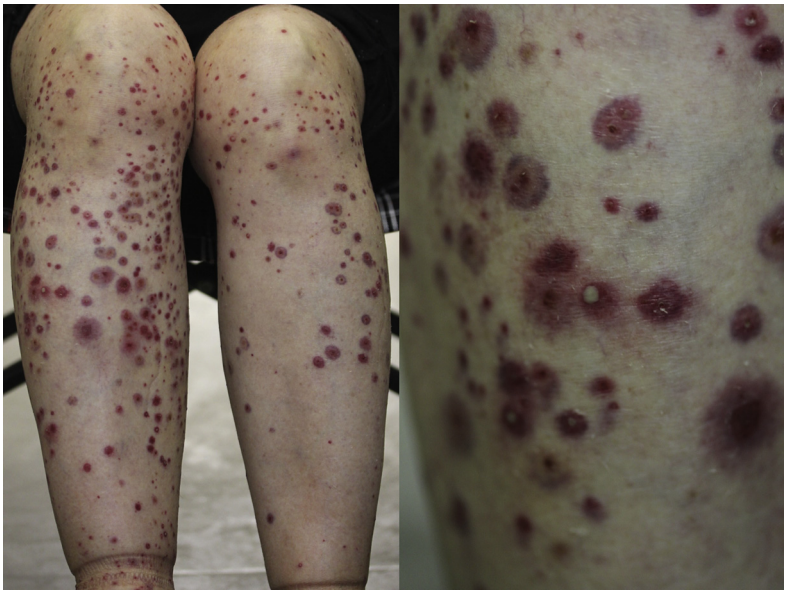

Figure 1. Multiple palpable purpura appeared on her legs.

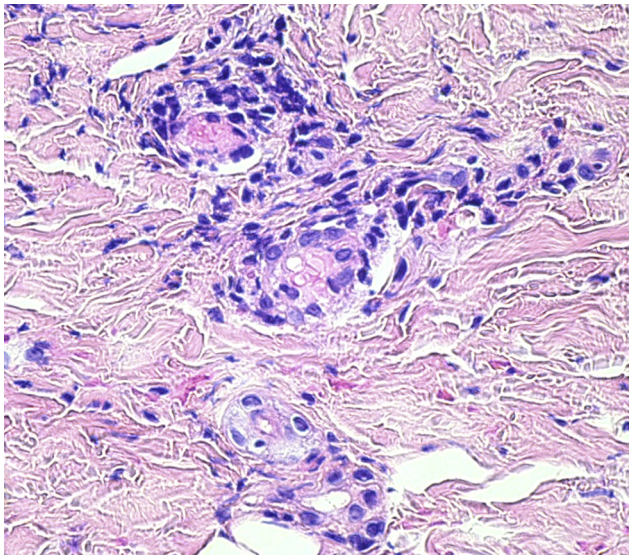

Figure 2. A skin biopsy revealed perivascular infiltrates of neutrophils with karyorrhexis and swelling of the vessel walls (hematoxylin-eosin stain; original magnification x 200).

antineutrophil cytoplasmic antibody (ANCA) and myeloperoxidase-ANCA were all negative. Urinalysis was normal. Histopathology of a skin biopsy revealed perivascular infiltrates of neutrophils with karyorrhexis and swelling of the vessel walls (Fig. 2). Fibrinoid necrosis and the deposit of immunoglobulin A were not detected. After discontinuation of osimertinib, the skin lesions disappeared. From these findings, she was diagnosed with cutaneous vasculitis induced by osimertinib. However, she desired to receive osimertinib again for treatment of her lung cancer. To rechallenge osimertinib, she received oral prednisolone (started with 25 mg/d and subsequently reduced to 7.5 mg/d). Multiple purpura disappeared with prednisolone, and she has continued with osimertinib (80 mg/d) at present.

To our knowledge, the present case is the first case in which osimertinib induced cutaneous vasculitis. Osimertinib is an oral third-generation tyrosine kinase inhibitor (TKI) of EGFR.[1] The other EGFR TKIs, gefitinib and erlotinib, were reported to induce cutaneous vasculitis.[2-4] Cutaneous vasculitis induced by EGFR TKI is a rare adverse effect and the mechanism is unknown. Clinicians should be aware of cutaneous vasculitis during osimertinib treatment because drug-induced cutaneous vasculitis can lead to systemic vasculitis resulting in dysfunction of internal organs and sometimes death.[5] Oral corticosteroids might enable the continued use of EGFR TKI for cases in which cutaneous vasculitis is induced by EGFR TKI, and might contribute to a better prognosis.

Acknowledgments

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