

Acne Inversa-like Lesions Induced by a Low Dose of Sorafenib

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Introduction

Sorafenib is an oral multikinase inhibitor approved for the treatment of unresectable hepatocellular carcinoma, differentiated thyroid cancer, and advanced renal-cell carcinoma. This drug blocks tumor cell proliferation and angiogenesis by inhibiting the Raf serine/threonine kinases (*RAF1* and *BRAF*) as well as multiple receptor tyrosine kinases [1]. Adverse skin reactions occur in up to 90% of patients. Although acneiform eruptions have been widely reported in association with epidermal growth factor receptor (EGFR) inhibition, ranging from 24%-91% of patients, those induced by sorafenib are rare. They usually appear in the first 6 weeks after drug onset and are located on the face. Regarding clinical-pathological characteristics, acneiform eruptions induced by sorafenib are classified into 3 groups: papulopustular eruptions without associated retention lesions, nodular-cystic eruptions, and perforating folliculitis [2]. Of these groups, papulopustular facial eruptions have been the most frequently observed. Here we report a case of acne inversa-like lesions induced by a low

dose of sorafenib in a 62-year-old man with hepatocellular carcinoma.

Case Presentation

A 62-year-old man was referred to us for evaluation of 2 exudative lesions on his lower extremities of 1-month duration. His medical history included sorafenib 400 mg/day for 4 months for diffuse hepatocellular carcinoma. The patient denied a history of similar lesions prior to the onset of sorafenib. Physical examination revealed 2 indurated erythematous plaques on both thighs that were 2 to 6 cm in diameter (Figure 1, A and B). The lesions had small oozing cavities, fistulous tracts, and depressed scar areas. No involvement of other locations was observed.

Skin swabs for viral and bacterial cultures were negative. A skin biopsy showed perifollicular and perivascular lymphohistiocytic infiltration (Figure 2A). Dilated follicular infundibula were filled with compact parakeratotic cornified cells and neutrophils (Figure 2B). A diagnosis of acne inversa-like lesions induced by sorafenib was made, and topic



Figure 1. (A, B) Two indurated erythematous plaques with fistulous tracts and depressed scar areas on both legs.

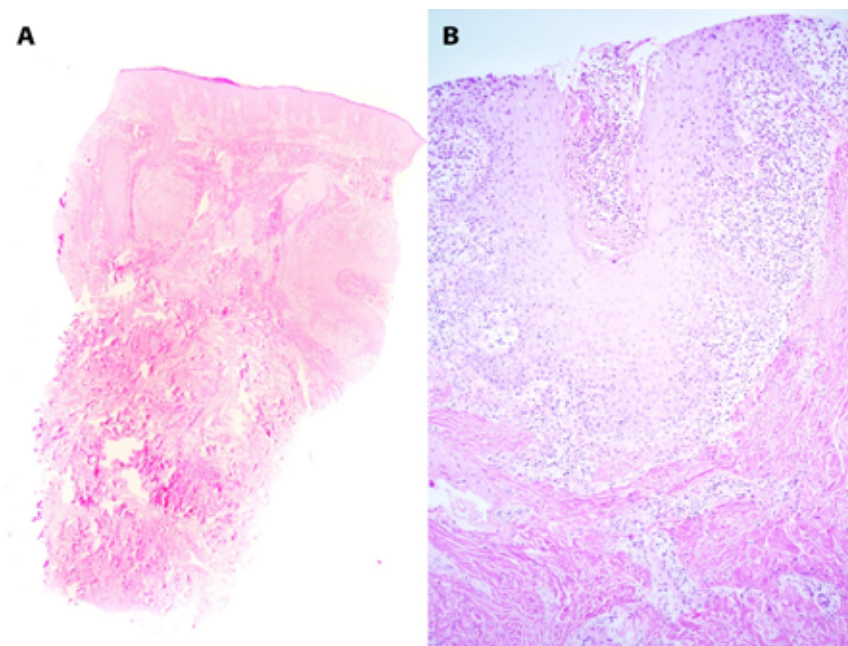


Figure 2. (A) Perifollicular and perivascular lymphohistiocytic infiltration (H&E, $\times 20$). (B) Dilated follicular infundibula filled with compact parakeratotic cornified cells and neutrophils (H&E, $\times 100$).

fusidic acid was prescribed twice a day. The oncologist temporarily discontinued treatment with sorafenib due to liver decompensation. After 1 month of sorafenib interruption, there was complete resolution of the eruption with mild scarring.

Conclusions

Five cases of acne inversa-like lesions associated with sorafenib have been reported, all of them in males [1,2]. Clinical features of 4 of these patients were similar to the case presented here, and except for 1 case of classic hidradenitis suppurativa located in the bilateral axillae and inguinal region, the localization was atypical in affecting the legs, abdomen, or buttocks. Histopathological analysis showed comedone-like follicular dilatation with perifollicular lymphohistiocytic infiltration. There appears to be a dose-dependent relationship between sorafenib and acneiform reaction. Except in 1 case in which an acne inversa-like eruption resolved spontaneously, lesions only improved with dose reduction or treatment interruption in combination with topical retinoids, antibiotics, or benzoyl peroxide [1,2].

If we apply the Naranjo drug reaction assessment tool to this case, the result would be “probable.” Unlike previously reported cases, our patient developed acneiform lesions while on a low dose of 200 mg twice a day. Further studies are needed to elucidate the pathogenic explanation and dose relationship between sorafenib and acne inversa-like lesions.

References

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