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### Perforating folliculitis and hand-foot-skin reaction due to sorafenib

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## Case presentation

- A 62-year-old African American woman presented with a painful rash on the extremities and feet ongoing for 2 months
- Her past medical history was as follows:
  - Hepatitis C virus infection treated with harvoni in 2018
  - Liver cirrhosis
  - Hepatocellular carcinoma (HCC) diagnosed 7 months prior to presentation, currently on sorafenib
- Painful rough, dark bumps erupted about 3 months after beginning treatment for HCC with sorafenib 400 mg BID
- She also had painful, yellow calluses on the bilateral plantar feet that erupted around the same time as the rash on the extremities

## Physical Exam

- Scattered on the bilateral lower extremities and left upper extremity there were many small hyperpigmented papules with central keratotic plug and surrounding erythema (Figures 2 and 3)
- On the bilateral plantar feet there were thick hyperkeratotic, yellow and hyperpigmented plaques overlying the calcaneus and metatarsal phalangeal joints (Figure 4)
- The bilateral palms exhibited ill-defined erythematous patches

## Diagnostic workup

- CMP was within normal limits
- Skin biopsies from keratotic papules on the right hip and right leg demonstrated a dilated hair follicle containing orthokeratotic and parakeratotic keratin and basophilic debris, consistent with perforating folliculitis (Figure 1)

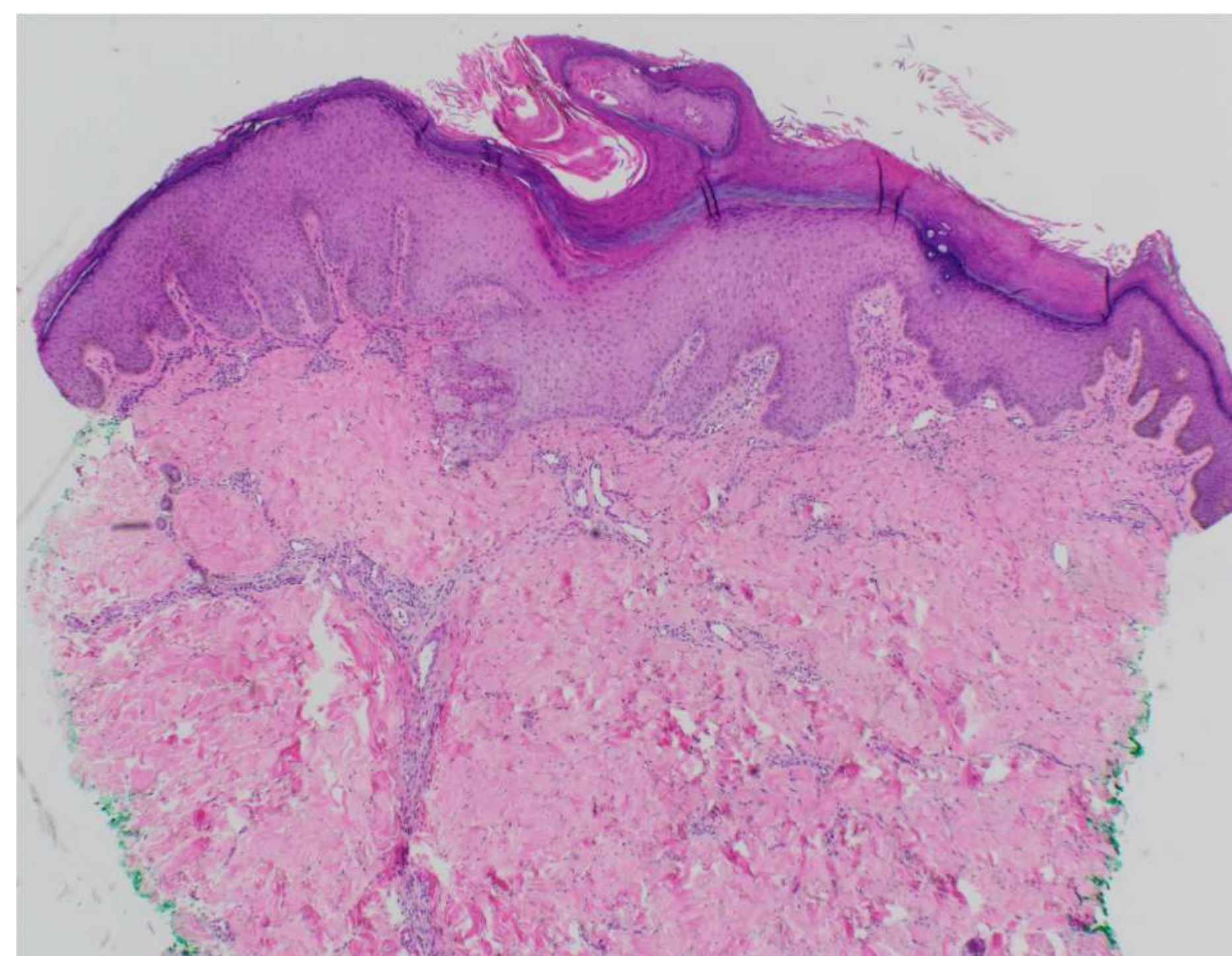


Figure 1: H&E demonstrating follicular plug and perforation

## Clinical Images



Figure 2. Hyperpigmented papules with central keratotic plug on the left leg

Figure 3. Close up of a keratotic papule on the right hip that was biopsied



Figure 4. Hyperkeratotic yellow and hyperpigmented plaques on the bilateral plantar feet overlying sites of pressure

## Diagnosis and Treatment

- Her palmar and plantar exam was consistent with hand-foot-skin reaction due to sorafenib
- She was started on clobetasol 0.05% ointment twice daily to the feet with improvement
- For the perforating folliculitis due to sorafenib she was started on doxycycline 100 mg BID and topical clobetasol 0.05% ointment BID to all affected areas on the body without improvement
- For her HCC she was maintained on the full dose of sorafenib 400 mg BID for 6 months before stopping and switching to nivolumab due to progression of her liver disease
- She was not able to follow up with dermatology due to worsening of her liver disease requiring hospitalization

## Discussion

- Sorafenib is an oral multikinase inhibitor approved for the treatment of renal cell carcinoma, HCC, and thyroid cancer
- Sorafenib and other multikinase inhibitors are known to cause various adverse cutaneous reactions including hand-foot-skin reaction, which is different from hand-foot-skin syndrome, as well as inflammatory eruptions and alopecia<sup>1</sup>
- Hand-foot-skin reaction is a painful complication characterized by hyperkeratotic plaques that develop over sites of pressure on the hands and feet, and are usually bilateral and symmetric<sup>1</sup>
- Treatment of mild cases includes use of emollients, keratolytic creams, and shoe inserts<sup>1</sup>
- Potent topical steroids may also be used, and severe cases necessitate dose reduction of the targeted therapy by at least 50%<sup>1</sup>
- Hand-foot-skin syndrome is a separate condition which is under the broader category of toxic erythema of chemotherapy, and is caused by a variety of chemotherapeutic agents and manifests as well-demarcated erythema of the palms and soles with edema and dysesthesia in severe cases
- Perforating folliculitis is a more rare complication of sorafenib that has only been reported in a few case reports<sup>2,3</sup>
- The pathogenesis is unknown
- Various treatments for perforating folliculitis have been tried including topical retinoids, topical steroids, and oral doxycycline with minimal efficacy<sup>2,3</sup>
- In one case, there was reported improvement with oral isotretinoin after five months<sup>3</sup>
- Perforating folliculitis usually improves after treatment cessation

## References

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