The present patient presented with true leukonychia in association with Crohn disease as well as selenium deficiency. Although there have been some reports about associations of leukonychia, Crohn disease, and selenium deficiency, all 3 conditions have not been discussed together. An association of Crohn disease with half-and-half nails has been reported in at least 1 case,2 but the serum selenium levels were not estimated in that case. Furthermore, Crohn disease has been associated with selenium deficiency,3 but the nail conditions were not described in detail in those reports. Therefore, we believe this case to be the first providing evidence that true leukonychia is caused in part, if not wholly, by selenium deficiency in Crohn disease and is curable with selenium substitution. However, care must be taken with adverse effects,4 and selenium levels must be carefully monitored to avoid toxic effects.

Leukonychia is caused by the abnormality of either nail bed or nail plate. In half-and-half nails, Lindsay5 has suggested that the whitish part of the nails stayed at the same portion and remained unchanged while the nail grew toward the distal portion, implying that the cause of color change begins in the nail bed rather than the nail plate. On the other hand, our true leukonychia case showed an interesting clinical course during the improvement of nail color in which the whitish part moved toward the distal portion during the nail growth after selenium substitution, suggesting that the primary pathologic site was not in the nail bed but in the nail plate.

In addition, little is known about specific physiological roles of selenium in the formation and/or maintenance of the nail apparatus. Selenium is a component of the antioxidant en-
zymes such as glutathione peroxidase and thioredoxin reductase as well as 3 deiodinase enzymes, which convert one thyroid hormone to another. Accordingly, it would be interesting to identify the level of selenium inside the nail matrix and to check also the thyroid profile and the activity of the antioxidant enzymes before and after the selenium substitution. Further study is needed to elucidate the pathogenic mechanisms of leukonychia due to deficiency of selenium.

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Hydroxyurea-Induced Leg Ulceration in a Patient With a Homozygous MTHFR Polymorphism Misdiagnosed as Pyoderma Gangrenosum

Both hydroxyurea, an antimitabolite used to treat chronic myeloproliferative diseases, and methylene tetrahydrofolate reductase (MTHFR) polymorphisms have been associated with cutaneous ulceration.1-3 We present a case of a severe leg ulcer that likely occurred from hydroxyurea use in a patient with a MTHFR polymorphism.

Report of a Case | A woman in her 70s with a history of myelodysplastic syndrome, well controlled with hydroxyurea for 14 years, presented with an extensive right leg ulcer of 10 months’ duration. The ulcer began after cryotherapy and enlarged despite oral antibiotic treatment for Staphylococcus aureus infection and local wound care. A wedge biopsy showed papillary dermal fibrinoid necrosis of vessel walls with mild leukocytoclasia, and tissue culture findings were negative. The patient was then treated with clobetasol ointment for presumed pyoderma gangrenosum. Hydroxyurea treatment was discontinued owing to concern for impaired wound healing but was restarted 2 months later when her thrombocytosis significantly worsened.

With the addition of prednisone and azathioprine to her treatment regimen, the ulcer continued to progress. When the patient was seen in our office, her ulcer measured 20 × 12 cm with exposed muscle and tendons (Figure, A). She was admitted to the hospital, and hydroxyurea, prednisone, and azathioprine were permanently removed from her drug regimen. Vascular assessment failed to reveal significantly reduced arterial flow. After undergoing extensive surgical debridement and receiving intravenous antibiotics, she was discharged with a wound vacuum-assisted closure (VAC) device. Three months later, she underwent a split-thickness skin graft closure of the ulcer leading to complete resolution (Figure, B).

A full coagulopathy workup was later performed to investigate impaired wound healing. The patient was found to be homozygous for the C677T polymorphism of the MTHFR gene. She was treated with a vitamin B complex–vitamin C–biotin–folic acid supplement, which led to cessation of new ulcer development.

Discussion | The prevalence of hydroxyurea-induced cutaneous ulceration is approximately 8%.1-3 These ulcers commonly occur on the legs and may take months to develop. In most cases, ulcers attributed to hydroxyurea slowly heal after discontinuation of the drug treatment, although it can take

Figure. Clinical Images From the Present Case

A, Large ulceration on the right distal leg with exposed muscle and tendons.
B, The ulcer completely healed after discontinuation of hydroxyurea and full-thickness skin graft closure.