Toenails melanonychia induced by hydroxyurea

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A 74-year-old Caucasian female patient was referred for the suspicion of multiple onychomycosis of the toes and plantar dermatophytosis. Her past medical history was notable for overweight (body mass index: 34 kg/m²) and essential thrombocythemia treated with hydroxyurea (HU), 300 mg twice a day for the past 3 years with an excellent biological efficacy on circulating platelets count. Nail pigmentation appeared progressively 5 months ago, extending from the nail matrix to its distal part and affected the 10 toenails (figure 1). Nails of the hands were unaffected. Besides, she disclosed localized xerosis of the feet. Physical examination was otherwise unremarkable. Multiple mycologic tests (direct examination and culture) performed on all the pigmented toenails yield negative results.

A diagnosis of drug-induced melanonychia was made, but efficacy of HU prompted to maintain the treatment. HU is a chemotherapeutic agent frequently used in the management of sickle cell anaemia and myeloproliferative disorders such as chronic leukaemia, polycythemia vera and essential thrombocythemia. HU may be responsible for a wide range of cutaneous

Figure 1
Melanonychia of toenails and toes xerosis
and mucosal adverse events such as xerosis, cutaneous, mucosal and nail hyperpigmentation, skin atrophy, lichenoid reactions, plantar and palmar keratoderma, alopecia, vasculitis, dermatomyositis like eruption, oral ulcerations, stomatitis, leg ulcers and squamous cell carcinomas [1,2]. Incidence of these side effects taken altogether may concern up to 95% of the patients [2]. A wide range of nail changes has been described with HU such as onycholysis, onychodystrophy, brittle atrophic nails, onychoschizia, blue lunula and melanonychia [3-5]. Finger and toenails nail pigmentation (melanonychia) occur in less than 5% of the patients, mostly women, within an average range of 11 months of treatment [4], but delays between 2 months [6] to 5 years [7] have been observed. The time interval between therapy initiation and the first signs of pigmentation might be related to nail growth rate [4]. Aste et al. observed that fingernails were always affected and sometimes toenails [4], but all 20 nails may be affected [6,8] and toenails may be predominant as formerly reported [7]. Nails pigmentation display various pattern: longitudinal bands, transverse bands and diffuse pigmentation [4,6,8,9]. The nails are not thickened or atrophic and surrounding skin is normal, but other cutaneous complications associated with HU can be observed in a patient [10]. HU is a cytostatic drug inhibiting DNA synthesis but the physiopathogenesis of such pigmentation is not known: genetic predisposition, direct toxic effect on the nail bed and matrix, photosensibilization and focal stimulation of ungual matrix melanocytes are suspected [4]. In our case, the later hypothesis can be considered as the patient displayed only toenails involvement and chronic rubbing of the toes in tight shoes worsened by overweight may explain such pigmentation.

HU-induced melanonychia may be an underestimated asymptomatic side effect that does not imply treatment withdrawal.

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References