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The nail flag sign in heart transplant recipients: case reports and review of the patients with the flag sign of the nail

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Abstract

The nail plate flag sign is a distinctive nail plate change that appears as white, red, white, and red sequential transverse bands beginning at the proximal nail fold. This distinctive nail change was initially described in patients with diabetes mellitus and leprosy; indeed, it was considered to be characteristic, but not diagnostic of leprosy. Subsequently, the flag sign was observed in patients with vitiligo. The flag sign has recently been noted in two men following heart transplantation. In summary, the flag sign is a unique nail change that has occurred in patients with autoimmune disorders, infection, and post transplantation surgery associated with immunosuppressive therapy to prevent organ rejection.

Keywords: cardiac, diabetes, heart, horizontal, flag, leprosy, nail, sign, transplant, vitiligo

Introduction

Nail changes can prompt the observer to evaluate the patient for potentially associated conditions. The flag sign is a distinctive nail change that presents as alternating white and red transverse bands on the nail plate [1, 2]. Two men who developed the flag sign following heart transplant are reported and the associated conditions of patients in whom the nail flag sign have been observed are discussed.

Case Synopsis

Case 1. A 54-year-old man presented for a total body skin check. His past medical history was significant

for an orthotopic heart transplant two years prior to presentation. His heart failure was preceded by an acute myocardial infarction. His postoperative course was acutely complicated by systemic *Candida* infection and acute renal failure. He subsequently developed disseminated cryptococcosis 6 months after surgery and an inferior vena cava thrombus one year after surgery. He also had hypothyroidism. His daily medications included amlodipine, apixaban, levothyroxine, posaconazole, sirolimus, and tacrolimus. He did not have alternating horizontal white and red bands on his fingernails or toenails prior to his heart transplant.

Cutaneous examination showed four keratotic plaques on his face and scalp (actinic keratoses) and hyperpigmentation on the sun exposed areas of his face, arms, and central chest (posaconazole photosensitivity). The nails of his thumbs and all fingers showed the flag sign: alternating white and red horizontal bands from his proximal nail fold to the distal tip of the nail plate (**Figure 1**). All his toenails had the similar finding of Terry nails; the proximal 90% to 95% of the nail plate was white and the distal 5% to 10% of the nail plate was red (**Figure 2**).

Case 2. A 70-year-old man presented for a total body skin check. His past medical history was significant for an orthotopic heart transplant three years prior. He had congestive heart failure with recurrent episodes of ventricular tachycardia that had not improved following three prior endocardial ablation treatments and oral antiarrhythmic therapy. He developed deep vein thrombosis of both the left common femoral vein and right popliteal vein four

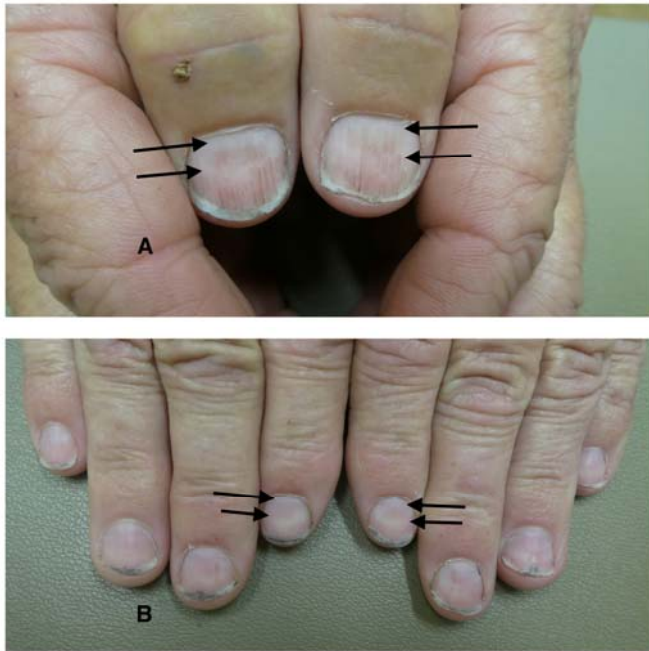


Figure 1. The nails of the **A)** thumbs and **B)** fingers of a 54-year-old heart transplant patient demonstrate the nail flag sign. There are alternating white (arrows) and red horizontal bands on the nail plates. The dyschromia begins as a white band just distal to the proximal nail fold; subsequently, there is a red, a white, and another red transverse band on the nail plate. The black discoloration on his thumbnails is exogenous pigment acquired by working on his automobile prior to his dermatology appointment.

months after surgery. He also had gout. His daily medications included allopurinol, bumetanide, lisinopril, rivaroxaban, sirolimus, tacrolimus, and tamsulosin. He did not have alternating horizontal white and red bands on his fingernails or toenails prior to his heart transplant.

Cutaneous examination showed 10 keratotic plaques on his face scalp and back (actinic keratoses). The nails of his thumbs showed the flag sign: from his proximal nail fold to the distal tip of the nail plate there were alternating white and red horizontal bands (**Figure 3**). The fingernails on both hands demonstrated Terry nails: the proximal 90% to 95% of the nail plate was white and the distal 5% to 10% of the nail plate was red. In addition, several of the fingernails showed single or multiple, thin or broad, red bands that extended from the proximal nail fold to the distal tip to the nail (idiopathic polydactylous longitudinal erythronychia). His toenails did not display any white or red dyschromia.



Figure 2. The **A)** right and **B)** left foot of a 54-year-old heart transplant recipient show Terry nails. The proximal 90% to 95% of the nail plate is white with a small rim of red that composes the distal 5% to 10% of the nail plate.

Case Discussion

The flag sign is a unique dyschromia of the nail plate. It appears as alternating white and red horizontal streaks across the nail plate. A white band begins distal to the proximal nail fold and obscures the lunula; subsequent red, white, and red transverse bands can be observed as the nail plate progresses distally.

The flag sign of the nail was originally described by El Darouti et al. in 2011 [1]. The investigators commented that this nail finding had not been reported before [1]. Including the patients in this report, the nail flag sign has been observed in patients with diabetes mellitus, heart transplantation, leprosy, and vitiligo [1, 2].

El Darouti et al. considered the flag sign to be characteristic, but not diagnostic, of leprosy. In a study of 115 leprosy patients, 24 individuals had either fingernails (19 patients) or toenails (5 patients) that showed alternating transverse bands of white and red discoloration of the nail plate. The researchers noted that the flag sign occurred more frequently in patients with multibacillary leprosy

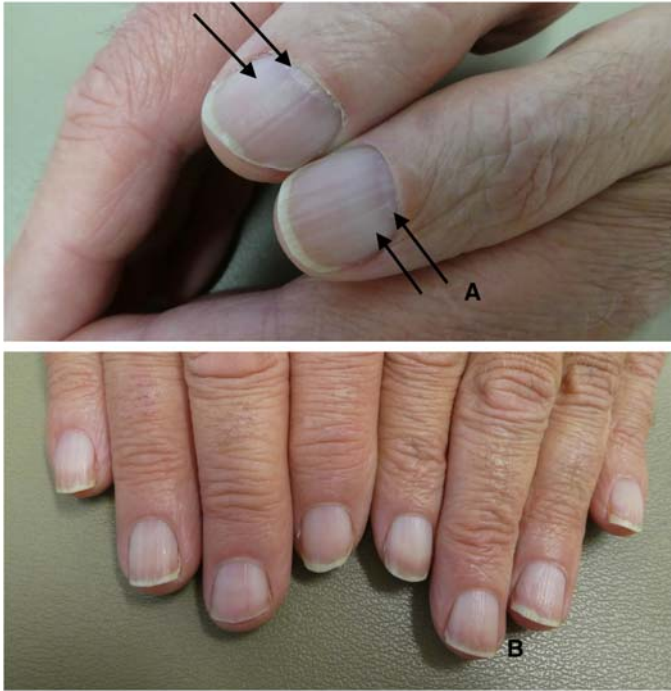


Figure 3. The nails of the **A)** thumbs, and **B)** fingers of a 70-year-old heart transplant patient. The nail flag sign is present on the thumbs (**A**). There are white (arrows), red, white, and red horizontal bands present on the nail plate from the proximal nail fold to the distal tip of the nail. The fingernails of both hands (**B**) show Terry nails and idiopathic polydactylous longitudinal erythronychia. The nail plates are white proximally (90% to 95%) with a red distal rim and there are single or multiple, narrow or broad, red linear streaks that extend from the proximal nail fold to the distal tip of the fingernails.

(23%, 17 of 81 individuals) than in paucibacillary leprosy patients (14%, 5 of 34 individuals). They postulated that more extensive vasculopathy in multibacillary leprosy patients contributed to the higher incidence of the flag sign in the nails of these individuals [1].

The same investigators evaluated the fingernails and toenails in 60 diabetic patients. In these individuals, the most common nail changes included longitudinal ridging (41.6%, fingernails in 17 individuals and toenails in 8 individuals), dystrophy (31.7%, fingernails in 16 individuals and toenails in three individuals), and increased curvature (13.3%, fingernails in 5 individuals and toenails in three individuals). However, the flag sign was observed on the fingernails in 5% of the patients (3 of 60 individuals) with diabetes mellitus [1].

Anabar et al., two years later in 2013, evaluated the nail changes in 91 patients with vitiligo. They also included a control group of 91 normal healthy age-matched and sex-matched individuals. Longitudinal striation (43.9%, 40 individuals) was the most common and significant nail abnormality in the vitiligo patients; absent lunula (16.5%, 15 individuals) was the second most significant observation. The flag sign was observed in 5 of the vitiligo patients (5.5%) and none of the control subjects [2].

Both men in this report who developed the nail flag sign had been recipients of a heart transplant and postoperative immunosuppressive therapy. A prospective study evaluating the fingernails and toenails of heart transplant patients prior to surgery and periodically following transplant of their new heart could be useful to evaluate the incidence of the nail flag sign in this patient population. In addition, a larger investigation evaluating not only heart transplant recipients but also patients undergoing other solid organ transplants and their immunosuppressive therapy might be helpful in elucidating additional etiologic features of the nail flag sign in these individuals.

In this report, the flag sign of the nails on the digits of the heart transplant patient's hands appeared after their heart transplant surgery. Both men also had Terry nails — an apparent leukonychia that represent an alteration of the nail bed with normal nail matrix and nail plate that has been observed in patients with congestive heart failure and characterized by the distal non-white nail plate being less than 20 percent of the nail [3]. In addition, one of the men had idiopathic polydactylous longitudinal erythronychia [4, 5]

Conclusion

The nail plate flag sign presents as sequential white, red, white, and red transverse bands; it is similar to the stripes on the flags of several nations, including the United States of America. This distinctive nail change was initially considered to be highly characteristic in leprosy patients; however, it has also been noted in patients with diabetes mellitus

and vitiligo. The current report extends this observation to postoperative patients who have received a heart transplantation.

Potential conflicts of interest

The author declares no conflicts of interests.

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