

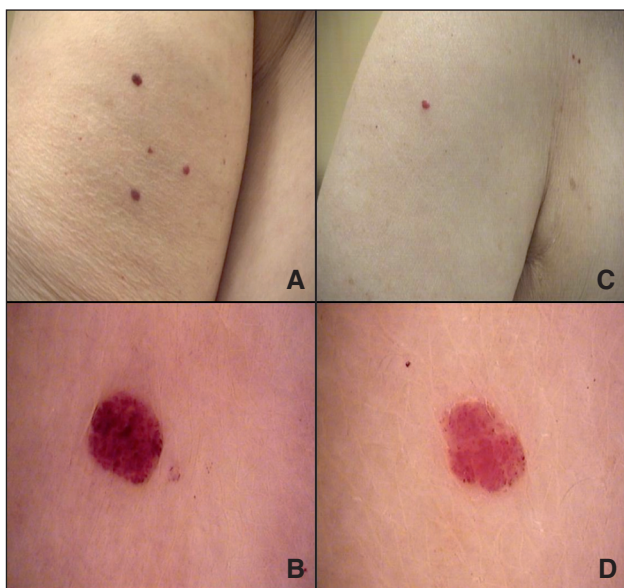


Figure 1. A) Increased number and enlarged *angioma rubi*, widely distributed over the trunk and arms three weeks after the introduction of vitamins with isoflavones. B) Dermoscopy of enlarged angioma. C) Reduced number and size, two months after discontinuation of the treatment. D) Dermoscopic view two months after discontinuation of the treatment.

been taking, for the last three months, a nutritional supplement for hair loss (composed of hydrolyzed wheat and sesame, magnesium and zinc citrates, vitamins B5, B6, B8, PP and spirulin). An additional supplement composed of *Primula* oil, methionine, cystine, yellow beeswax (emulsifier), zinc sulphate, soya extracts, and PP, E, B5, B6, B8 vitamins, was then prescribed. Three weeks later, she noticed a significant increase in the number and size of *angioma rubi*, widely distributed over the trunk and arms (figure 1A, B). For this reason she was advised to stop this last medication and continue all the other treatments she was using before. The *angioma rubi* lesions reduced in size two months after discontinuation of this treatment (figure 1C–D). We hypothesized that this adverse effect could be related to a nutritional supplement interaction, possibly due to soy isoflavones, that were introduced three weeks before. All other medication had been taken since several weeks before.

Hair loss in postmenopausal women seems to be multifactorial, with senile changes in physiology and immunity probably involved in its onset [1]. The role of diet supplements in hair loss is still not well understood. Soy extracts have been recognized as providing a wide range of health benefits, such as lowering rates of heart attack, reducing blood cholesterol levels, relieving menopausal symptoms in postmenopausal women, and in the general enhancement of the immune system [2]. Additionally, soy isoflavones have been indicated to be relevant in reducing hair loss and male pattern baldness [3].

Adverse effects of soy isoflavone consumption are still poorly described. However, there is evidence that soy isoflavone-containing foods exert lipid-independent effects on vascular walls [2]. The results of studies have been controversial and it seems that divergent effects may be in part related to the different isoflavone supplements used

[4, 5]. In fact, it has been suggested that, like estrogens, isoflavones can affect specific adhesion molecules (sICAM, sVCAM-1, E- and P-selectins) expressed on vascular endothelia [2, 4, 6]. However, the effect of lowering these adhesion molecules may be limited to subjects with a specific estrogen receptor β phenotype [6]. Additionally, one study demonstrated that soy isoflavones increase the pro-inflammatory cytokine IL-6 [6]. As soy isoflavones act on estrogen receptors, it is possible that when introduced later in life as supplements, they may affect vascular wall integrity in a pro-inflammatory way. This process may be involved in the disseminated increase in number and size of the *angioma rubi* observed in our case.

To our knowledge, this is the first report of a skin adverse effect due to a nutritional supplement for hair loss, containing isoflavones. In spite of the interest of nutritional soy isoflavone supplements in hair loss therapy, clinicians should consider that they might not be indicated for everyone. Further studies are needed to confirm our clinical report. ■

Disclosure. Financial support: none. Conflict of interest: none.

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doi:10.1684/ejd.2010.1249

Antecubital allergic contact dermatitis from intravenous iron infusion: a possible etiological role of nickel

A 37-year-old woman receiving treatment with daily intravenous infusions of 5 mL sodium ferric gluconate com-

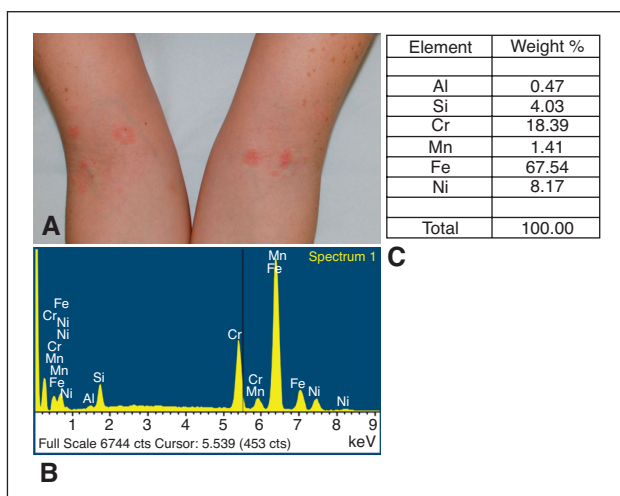


Figure 1. A) Eczematous patches developed around the infusion sites on patient's antecubital areas. X-Ray microanalysis report. B) EDS spectrum of the sample, containing Al, Si, Cr, Mn, Fe Ni. C) Table of quantitative results.

plex (Ferlixit[®], Sanofi-Aventis, Milano, Italia) for anemia, presented with bilateral itchy erythematous scaly and vesicular eruptions around the infusion sites on her forearms (figure 1A), which developed after about 10 intravenous therapies. During each infusion, the needle (Icofly[®] 23G, KD Medical GmbH Hospital Products, Berlin, Germany) remained inserted in the skin for about 15 minutes. While topical treatment with corticosteroids had no effect, the dermatitis spontaneously cleared within 15 days after the infusion treatment was discontinued. Patch tests were performed with the Italian baseline SIDAPA series (Società Italiana di Dermatologia Allergologica Professionale e Ambientale); a strong positive reaction was observed only to nickel sulfate 5% pet. (+D2/+++D3). Nickel was supposed as a possible contact allergen responsible for the dermatitis; therefore the nickel content was measured both in the sodium ferric gluconate complex preparation and in the butterfly needle.

Quantitative analysis of nickel in the Ferlixit[®] samples, processed by acid digestion with concentrated nitric acid in microwave oven (Milestone ETHOS 900, USA), was carried out with a model Analyst 800 Atomic Absorption Spectrometer (Perkin-Elmer, USA) equipped with a Zeeman background correction system and an electrothermal atomizer with a transversely heated graphite tube. The mean concentration of nickel in the Ferlixit[®] sodium ferric gluconate complex, obtained with a calibration curve ($y = 0.0041x + 0.0003$; $r^2 = 0.9997$), was 141 µg/L ($\sigma = 24$, three ampoules investigated); the standard addition method was also employed on one of the three samples ($y = 0.0037x + 0.0434$) giving a concentration of 146 µg/L.

The elemental composition of 4 Icofly[®] 23G needle samples was determined by Scanning Electron Microscopy analysis (SEM) with an EVO 40 Zeiss equipped with an energy dispersive X-ray spectrometer. The needles were found to contain 8% nickel (figure 1B).

Allergic contact dermatitis from nickel in acupuncture needles, multi-injectors and other invasive medical tools has

been reported [1-3]. It is well known that nickel may also be released by needles into the fluid passing through intravenous catheters, eliciting systemic allergic dermatitis in sensitized patients [4, 5]. Systemic exposure to nickel usually induces specific cutaneous reactions, like symmetrical widespread dermatitis, flare-up reactions in previously positive patch tests, dyshidrotic hand eczema, flexural dermatitis, urticarial reactions or maculopapular rash. In our case, the clinical features did not fit with the diagnosis of a systemic allergic dermatitis, thus a relevant systemic exposure to nickel released by the needles during intravenous infusions seemed unlikely.

To our knowledge, no cases of systemic contact dermatitis from nickel contained in sodium ferric gluconate complex preparations have been reported. Indeed, the concentration of nickel we detected in the Ferlixit[®] samples is much lower than the permitted daily parenteral exposure established by the European Medicine Agency (EMA) [6]. Therefore, the low content of nickel infused might not reach the elicitation threshold in serum of exposed individuals.

In our case, based on the spectrometric demonstration of 8% nickel in the needle, it may be supposed that it could produce a localized allergic contact dermatitis at the sites of needle insertion. Furthermore, consistent with nickel determination in the analyzed sodium ferric gluconate complex samples, skin contamination by extravasated small amounts of nickel contained in the parenteral iron preparation must be considered as well. Intradermic traces of nickel might elicit an allergic contact dermatitis.

In conclusion, although both the more widely used stainless steel needles and the sodium ferric gluconate complex preparations are usually safe, in the case of prolonged and repeated intravenous infusions, allergic contact dermatitis can occur in persons with strong nickel sensitization. ■

Disclosure. Financial support: none. Conflict of interest: none.

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doi:10.1684/ejd.2011.1254

Subungueal pigmented lesions: warning for dermoscopic melanoma diagnosis

A 45-year-old man presented to us for a persistent discoloration of a toenail on the right foot. He reported that an alteration of the nail pigmentation had appeared approximately two years previously, after a nail trauma. Initially, he had paid no attention to this lesion because it was neither painful nor symptomatic. Six months later his general physician referred him to a dermatologist, for the persistence of the pigmentation of the nail plate. The dermatologist made the diagnosis of subungueal hematoma from the clinical and dermoscopic examinations, which showed dermoscopic features of subungueal hematoma. A couple of months later, the patient presented to us for a second evaluation of the lesion.

Our physical examination revealed the presence of two pigmented bands of the nail plate, extending from the proximal nail fold up to its free edge, with irregular borders (figure 1A). Dermoscopic examination showed some round shaped structures of a pigment with a color range from reddish to black on the left side of the lesion, that resembled the dermoscopy features of a subungueal hematoma (figure 1B). On the contrary, within the right band, we observed brown-to-black lines with irregular spacing and thickness that resembled a melanoma of the nail plate (figure 1B). We made the clinical diagnosis of a suspected subungueal melanoma. We therefore decided to perform two incisional biopsies, one on the right band of the lesion and one on the left part in order to evaluate the exact extension of the entire lesion. The histopathological examination confirmed the diagnosis of subungueal melanoma on the right band and, in addition, the diagnosis of subungueal hematoma on the left side of the lesion. The final diagnosis, after the complete excision of the lesion was a malignant melanoma with Breslow thickness of 0.7 mm.

The differential diagnosis between melanoma of the nail plate from its simulators is, in the majority of cases, a hard challenge for physicians [1]. A number of different disorders, such as infections and inflammatory, trauma or neoplastic diseases, have an analogous clinical presentation of malignant melanoma [2]. Among the lesions that simulate a subungueal melanoma, the subungueal hematoma is the most common [3]. The current use of the dermatoscope in dermatological practice has shown that clinical examination alone of nail lesions is often inadequate in assessing suspect lesions, in particular in the early stages. Dermoscopic examination significantly improves diagnostic accuracy compared with naked eye examination [4, 5]. However, linear microhaemorrhages

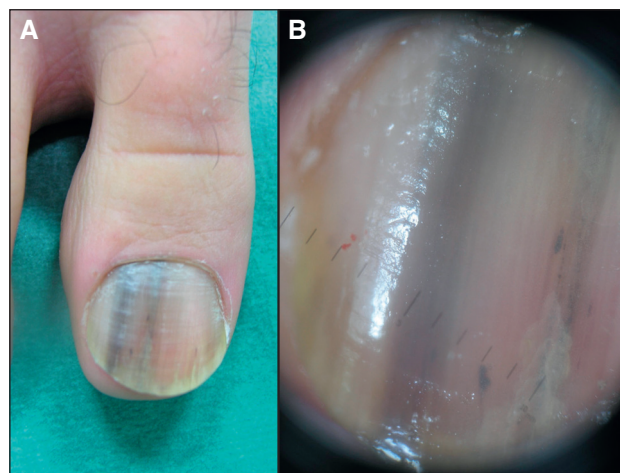


Figure 1. The toenail on the right foot of the patient revealed the presence of two pigmented bands, extending from the proximal nail fold up to its free edge, with irregular borders (A). Dermoscopic examination showed some round shaped structures of a pigment with a color range from reddish to black on the left side of the lesion, that resembled the dermoscopy features of a subungueal hematoma (B).

and reddish round shaped structures, typical of subungueal hematoma, have been described in 5% of subungueal melanoma [4].

We would like to underline that the presence of dermoscopic features of subungueal hematoma are not pathognomonic for the diagnosis of hematoma. In fact, the diagnosis of subungueal hematoma should be made merely after the exclusion of the presence of criteria typical of melanocytic lesions.

In addition, a history of trauma has been reported in 25 to 55% of melanomas of the nail plate [6] and therefore the presence of characteristics of subungueal hematoma in the context of a subungueal melanoma is not uncommon. Therefore, in many cases, dermoscopy does not improve the diagnostic accuracy of nail bed melanoma but on the contrary can be a confounding factor.

For the aforementioned reasons, the diagnosis of benign subungueal hemorrhage always requires careful exclusion of other suspicious features, including an irregular pigmented pattern and in the case of doubt, an incisional biopsy is mandatory. ■

Disclosure. Financial support: none. Conflict of interest: none.

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