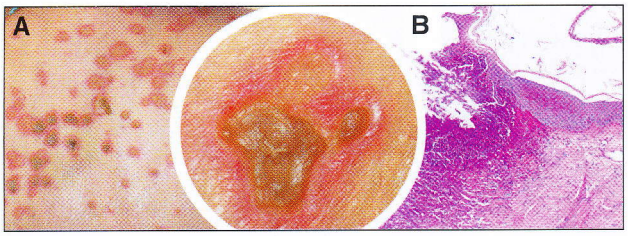

Figure 1. A) Upper back of the patient showing multiple disseminated 5-10 mm ecthymatous ulcers. Inset: Close-up of a single ecthymatous ulcer. **B)** Dermatopathology (H&E stain) showing ulceration of the epidermis and necrosis of the upper dermis with a mixed inflammatory infiltrate on the base of the ulceration.

lymphocytes and histiocytes. Cultures revealed *S. aureus* and *Enterobacter cloacae (figure 1B)*. Anti-BP180/230 and antinuclear antibodies were within normal ranges, ruling out the clinically suggestive differential diagnosis of ecthymatous bullous pemphigoid [1]. The diagnosis of an ecthymatous rash concomitant with a cetuximab therapy was made. We continued weekly infusions with cetuximab, but also treated with oral ciprofloxacine and topical sulfadiazine and hyaluronic acid, which resulted in a rapid but scarring resolution of the eruption.

Biological drugs acting directly on cellular receptors have clearer and better defined effects compared to classical systemic agents. However, clinical experience reveals that they nevertheless often lead to still unexplained effects. Cetuximab and other EGFR inhibitors can induce acneiform eruptions and paronychia among other cutaneous side effects [2]. Acne-like eruptions, predominantly on the seborrheic areas such as the face, neck, retroauricular area, shoulders and upper trunk are considered to be associated with improved disease response, time to progression and survival time [3]. It remains unclear whether our single observation of an even more severe skin reaction a) has a causal relationsship with the parallel intake of cetuximab, and b) corresponding to acne-like eruptions, signifies an increased antitumoral effect of cetuximab. Further observations will be necessary to establish these potential correlations. EGFR inhibition leads to dysregulation of basal membrane homeostasis and induces expression of the transcription factor p27kip1 in keratinocytes. This results in increased differentiation and apoptosis of keratinocytes [4]. In addition, together with cisplatin, immunosuppressive effects such as neutropenia can occur, facilitating bacterial superinfections [5]. Both the effects on keratinocyte differentiation and immunosuppression could have contributed to development of ecthymatous lesions. The goal of managing EGFR inhibitor-associated skin toxicity is to minimize the detrimental effects of the rash on patients' quality of life and treatment course without antagonizing the clinical efficacy of EGFR inhibitors [6]. Drugs completely inhibiting the rash could theoretically negate the detrimental effect of EGFR antagonists on the tumor. Preclinical data suggest topical application of a potent phosphatase inhibitor medione (Vit. K3) to rescue the inhibition of EGFR and downstream signaling molecules in the skin of mice receiving systemic EGFR inhibitor erolitinib or cetuximab [3].

In summary, the ecthymatous rash observed here during treatment with cetuximab might have developed due to smear infection of a subclinical acneiform eruption; the use of antibiotics covering the gram-negative spectrum, such as ciprofloxacine, should be considered in patients with therapy-refractory acneiform eruptions within an EGFR inhibitor regime. Our therapeutic agents are getting more specific as we progress towards fully understanding molecular pathogenetic mechanisms. However, during this process, unexpected and new potential side effects may challenge us. ■

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Adverse effect of a nutritional supplement for hair loss

The rationale for considering nutritional supplements as a complementary treatment for hair loss is based on the fact that selective nutrients can improve hair and scalp health. For hair loss, a wide range of different supplements, with diverse compositions, have been placed on the market. Like other nutritional supplements, their consumption has been increasing worldwide, mostly without clinical supervision. We report a case of disseminated *angioma rubi*, an adverse effect after a nutritional supplement therapy for hair loss.

A 73-year-old female was observed in our Dermatology Department because of hair rarefaction. Her clinical history revealed a breast node at the age of 30 and menopause at the age of 53, without substitution hormonal therapy. She had a family history of breast and colon cancers. She had

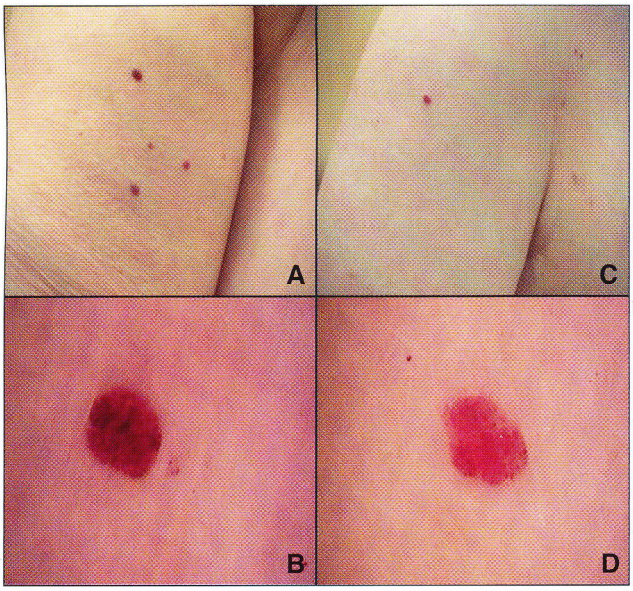

Figure 1. A) Increased number and enlarged *angioma rubi,* widely distributed over the trunk and arms three weeks after the introduction of vitamins with isoflavones. **B)** Dermoscopy of enlarged angioma. **C)** Reduced number and size, two months after discontinuation of the treatment. **D)** Dermoscopic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

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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-