LETTERS TO THE EDITOR

Prevalence of Congenital Nevus in 1000 Live Births in Granada, Spain

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To the Editor:
Congenital nevi are benign tumors that are present at birth or that appear during the first few months of life. Their prevalence varies between 0.2% and 5.9% according to the population studied.1-5

They are classified as small (1.5 cm), medium (1.5 to 19.9 cm), or giant (≥20 cm). This classification is important in view of the cosmetic and psychological implications, as well as the risk of a malignancy, which is greater in larger nevi6; thus, small and medium nevi have a low risk of malignancy and large nevi are associated with a risk of between 1% and 31%.7-9

We undertook a study of newborn babies in the Hospital Clínico Universitario San Celicio, Granada, Spain, to investigate the prevalence of congenital nevi in live births in Granada. We analyzed 1000 babies at birth (between November 2005 and December 2006). Only term births and white babies were included. Premature births and black babies were excluded.

The skin surface was examined in the first 72 hours of life in search of nevi, defined as round or oval brown pigmented lesions, whatever the size and intensity of color, whether flat or elevated, and wherever they were located.

All babies were examined naked by the same physician (an investigator from the Skin Oncology Group of the University of Granada) in the perinatology department after consent had been obtained from the mother. For each examination, a data collection protocol was followed that included personal details, sex, presence or absence of nevi, site of nevi, and nevus characteristics such as size, color, and shape.

Overall, 53.2% of the babies were female and 46.8% were male. Fourteen babies had congenital nevi (7 boys and 7 girls), corresponding to a prevalence of 1.39%. The most common site was the limbs (10), followed by the chest (3), and the head and neck (1).

The sizes of the nevi ranged from 0.1×0.1 cm to 3.8×2.3 cm. Overall, 85.7% of the nevi were small and 28.5% were medium-sized; we did not encounter any giant nevi. Eleven of the 14 nevi were flat and 3 were raised. Of the 3 raised nevi, 1 was a compound blue nevus.

Although there have been few studies of nevi in newborn babies, we did find differences in the reported prevalences. In Iranian newborn babies, the prevalence of congenital nevi (0.7%) was half that found in our series, the nevi were located mainly on the trunk, and all corresponded to small nevi.2 The prevalence among Finnish neonates was 1.5%.5 Among Chinese babies, 1% had congenital nevi,4 and among babies born in Israel, the highest frequency was reported in Jewish children of European ancestry.3

In our series, we found a larger number of nevi among boys and almost all were small nevi, in contrast to the findings of other authors.2,5,9

The prevalence and preferred site (limbs) in our study differed from those published by other investigators in different populations at different latitudes. An important aspect of our study is the large sample of babies examined in the first few hours after birth, making our results reliable and free of recall bias. However, this approach excludes nevi that appear later, and so it is also important to carry out subsequent studies to follow-up these children during their first 2 years of life.

References
To the Editor:

Unlike Western medicine, traditional Chinese medicine treats invisible functional or physiological disturbances. This is a bioenergy medicine, which aims to achieve electromagnetic, nutritional, and emotional balance in the body, without the use of drugs or surgery. Its tools include acupuncture, Chinese herbs, manipulative massage (Tui Na), and relaxation exercises (Tai Chi, Qigong), among others. In Western countries Chinese medicine has traditionally been considered a popular and unscientific discipline, based on superstition, although, in fact, more than 4000 years of practice endorse its knowledge and applications. More than 5000 botanical species have been identified and classified on the basis of their medicinal actions and uses. Combinations of herbs are commonly prescribed, rather than individual species, in order to improve effectiveness and to reduce adverse effects.

We present the case of a 23-year-old man of Chinese origin who attended the emergency department with extensive skin lesions following the ingestion of Chinese herbs known as Huang Lian (Coptis chinensis, Rhizoma coptidis) to treat acne. The patient stated these herbs were widely used in his family and that he himself had taken them previously with no adverse effects. On this occasion the lesions appeared less than 12 hours after the ingestion of a single dose of the plant extract, with no signs of infection or herpes recurrence. According to the patient, he had not been vaccinated recently or taken any other drug or herb.

The lesions consisted of erythematous macules and papules, some “target-like” lesions, with a central vesicle-pustule and a more violaceous periphery. These initially appeared on the face and neck, and later spread down from the head and coalesced (Figure 1). The lesions were mildly pruritic, leaving slight residual pigmentation on healing.

Laboratory tests including blood count and biochemical analysis with renal and hepatic profile, autoantibodies (antinuclear antibodies, extractable nuclear antigen, and antineutrophil cytoplasmic autoantibodies), viral serology (Epstein Barr, hepatitis B and C, and human immunodeficiency virus [HIV]), and urine sediment only revealed leukocytosis of 1.2 × 10^{9}/L (82.4% neutrophils, 10.2% lymphocytes) and proteinuria of 30 mg/dL.

A skin biopsy was taken which showed slight epidermal acanthosis with atypical keratinocytic maturation and basal layer vacuolization, along with a predominantly lymphocytic perivascular inflammatory infiltrate in the superficial dermis (Figure 2).

The condition was treated with a tapering course of oral corticoids, oral anti-histamines, and topical corticoids. The lesions healed in 8 days leaving some post-inflammatory hyperpigmentation.

To date, no cases of toxicoderma after ingestion of Chinese herbs have been reported in the medical literature, although Chinese herbs—and Rhizoma coptidis in particular—have been known to produce allergic rash or anaphylactic reactions, along with other side effects, such as dizziness, tinnitus, nausea, vomiting, diarrhea, palpitations, and anemia. These polyvalent herbs, traditionally described as “bitter, cold, and drying,” are attributed with pharmacological properties including antimicrobial activity (fundamentally antibiotic, but also antiviral and antifungal), antiinflammatory, antiarrhythmic, vasodilatory, antipyretic, cholagogic, antiulcer, antiadrenergic, and local anesthetic properties. They also reduce cholesterol and prevent hemorrhagic cystitis induced by cyclophosphamide. The herb can be administered systemically or topically, and is generally used in combination with other Chinese herbs to improve its effectiveness and safety profile. The most important chemical component is berberine, but the plant also contains coptisine, worenine, palmatine, jatrorrhizine, magnoflorine, columbamine, and, curiously, colchicine. Therapeutic dosage ranges from 2 g to 10 g of dry weight, with a maximum dose of 15 g. Warnings state the herb should be used with care in “cold” patients, those with “a yin or yang deficiency,” or those who...
have undergone gastrectomy or splenectomy, and it should not be used at all in patients with glucose-6-phosphate dehydrogenase deficit.

*Rhizoma coptidis* and its main alkaloid component, berberine, inhibit the proinflammatory activity induced by tumor necrosis factor-alpha (TNF-α) in a dose-dependent manner. Recent studies have investigated the antiaemic properties of various groups of Chinese herbs—some containing *Rhizoma coptidis*—showing their antilipogenic and antibacterial action against *Propionibacterium acnes*. Higaki et al even suggest these are more effective than antibiotics such as minocycline or erythromycin because, unlike these, the Chinese herbs do not produce an increase in minimum inhibitory concentration.

The fact that the patient had previously ingested this extract without reaction suggests a hypersensitivity mechanism. Another hypothesis would be that the excess from the dose ingested could have produced an imbalance between the formation of reactive metabolites and enzymatic hepatic detoxification, leading to an accumulation of reactive oxidants, which acted as haptenes and provoked an immune response.

In conclusion, we wish to stress the power of Chinese herbs to produce both therapeutic benefit and side effects, including dermatological ones, whilst pointing out that the extensive use of such treatments in the growing Chinese population implies greater consideration must be given to the possibility of their ingestion in cases of toxicoderma.

### References


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### Sweet Syndrome as a Possible Initial Manifestation of Human Immunodeficiency Virus Infection

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To the Editor:

Acute febrile neutrophilic dermatosis was initially described by Sweet in 1964 as reactive dermatoses in middle-aged women following upper respiratory tract infections. These dermatoses had 4 characteristic clinical elements: fever; leukocytosis; eruption of erythematous and edematous plaques on the extremities, face, and neck; and a dense predominantly neutrophilic inflammatory infiltrate in the dermis, with no sign of vasculitis. The reactive nature of this condition is noted for its frequent association with infectious, inflammatory, or neoplastic processes. We present a new case of Sweet syndrome as the initial manifestation of infection with the human immunodeficiency virus (HIV).

A 35-year-old male, with no relevant medical history, was examined for fluid-filled erythematous and edematous lesions that had presented 4 days earlier. These were painful to pressure and were found on the upper lip (Figure 1), outer ears, scalp, knees and elbows (Figure 2), and finger pads, with no associated fever or malaise. The patient had no previous catarrhal symptoms, and had taken no medication in the previous month. Test results showed a white cell count of 10.6 x 10^3/uL with a differential showing 57% neutrophils, 26% lymphocytes, 4% monocytes, and 13% eosinophils.

![Figure 1. Violaceous erythematous and edematous plaques painful to pressure, on the upper lip.](image)

![Figure 2. Violaceous erythematous and edematous plaque on the left elbow.](image)
Letters to the Editor

Benign Lymphangiomatosus Papules and Plaques After Radiotherapy

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To the Editor:

Lymphangiomas are tumors that normally appear at birth. They are formed from dilated lymph vessels that may extend to the subcutaneous cellular tissue. A number of causes of acquired lymphangiomas such as radiotherapy and surgery have been reported. The area irradiated during radiotherapy may develop benign vascular proliferations such as acquired progressive lymphangioma or malignant processes such as high-grade angiosarcoma, even when low doses of radiation are used.1,2 Within what are considered acquired blood cell count of 8200 cells/mL, 70% neutrophils, and left shift (7% band forms). Globular sedimentation rate was 25 mm/h and the chest x-ray revealed no significant abnormalities. Histology of a biopsy sample taken from a lesion on the forearm showed the presence of a subepidermal blister with intense neutrophilic inflammatory infiltrate, but no signs of leukocytoclastic vasculitis. Serology was negative for syphilis, herpes simplex, and hepatitis B and C, but positive for HIV-1 in an enzyme-linked immunosorbent assay. This finding was confirmed in a second test. The skin lesions improved after initiating treatment with a tapering course of oral prednisone (beginning at 50 mg/d) for 6 weeks, with no subsequent relapse. The patient was referred to the infectious diseases department of the hospital, with initial analysis showing a low CD4+ T-cell count (285 cells/mL) and a viral load of 100,000 copies/mL.

The association of Sweet syndrome with HIV infection has rarely been described in the literature,2,7 and only twice has Sweet syndrome been reported as the first manifestation of HIV infection.2,4 The CD4+ T-cell count in the cases described varied between 368 cells/mL5 and less than 50 cells/mL.3 suggesting that immunological status is not the only factor involved in the pathogenesis of the process. Some authors have suggested that the immunological changes induced by HIV could play an important role in triggering dermatoses, through the formation of immunocomplexes, with activation of polymorphonuclear neutrophils.2 Also, certain HIV proteins, such as transactivating protein, have been reported to be an important factor for inducing neutrophil chemotaxis.7

Other suggested pathogenic factors include photosensitivity,2 reactions to antiretroviral therapies,2 or those related to phenomena of sudden immune restoration in patients in whom antiretroviral therapy has been recently initiated.4 Cofactors may have played a role in some of the cases reported, for example the treatment of drug-induced aplasia in HIV-positive patients with granulocyte colony-stimulating factor (G-CSF).3

The presence of blister-like lesions in Sweet Syndrome is described relatively frequently4 as the clinical outcome of intense edema and inflammatory infiltrate in the dermis, which leads to subepidermal detachment.

In this case, factors associated with Sweet syndrome other than infection by HIV were not observed, given that the patient reported none of the traditional indicators (catarrh, new medication). Even if the exact mechanism of the association is uncertain, we must stress the significance of considering infection with HIV in patients with Sweet syndrome, especially in young patients exhibiting associated risk behaviors.

References

lymphangiomatous lesions, benign lymphangiomatous papules after radiotherapy have specific characteristics.

Our patient was a 54-year-old woman with a history of stage T2 N1b M0 infiltrating ductal carcinoma in the right breast, diagnosed in 1998, and treated by tumorectomy and right axillary lymphadenectomy, chemotherapy, hormone therapy, and external radiotherapy of the entire chest wall and right breast at a dose of 50 Gy. She attended our clinic for the evaluation of progressive asymptomatic lesions on the irradiated skin of the right breast. The lesions had appeared approximately 1 year earlier (6 years after receiving radiotherapy).

Physical examination of the right breast showed yellowish skin coloring. This skin was covered with multiple erythematous papules that coalesced in places to form small vesicular plaques and lesions filled with clear or occasionally bloody fluid (Figure 1). There was no associated lymphedema.

Biopsy of one of the vesicles revealed marked vascular dilation in the papillary dermis that extended into the epidermis (Figure 2). As the vessels penetrated deeper into the dermis, they got narrower and more irregular and tortuous, and took on a lymphatic appearance (Figure 3).

The vascular spaces were covered by a single discontinuous strand of endothelial cells with oval hyperchromatic nuclei that protruded towards the lumen and that showed no prominent nucleoli, with no signs of atypical or mitotic cells. Typically, the vascular lumen was empty, as is the case for lymphatic vessels, although at times a proteinaceous material and some red blood cells could be found, as well as endothelium-lined papillary projections. The endothelial cells were strongly positive for CD31 and CD34, as well as for D2-40, a marker specific to lymphatic vessels. In accordance with these clinical and histologic findings, we diagnosed lymphangiomatous papules and plaques after radiotherapy.

In 1994, Finenberg and Rosen described benign vascular proliferations in the skin of the breast and chest wall after postoperative radiotherapy for breast cancer. Over the last 20 years, a range of terms have been used to describe these lesions, such as atypical vascular lesions, acquired lymphangiectasis, progressive acquired lymphangioma, circumscribed lymphangioma, and benign lymphangiomatous papules. Diaz-Cascajo et al proposed the term benign lymphangiomatous papules following radiotherapy for benign skin lesions that show a predominance of lymphatic vessels and that present clinically as erythematous papules related to radiotherapy treatment.

In recent years, new cases of this condition have been described. All patients have been women aged between 33 and 72 years, and the most common primary tumor has been breast cancer. In all cases of breast cancer, the primary tumor was removed by partial or radical mastectomy, and all patients received external postoperative radiotherapy at doses between 46 and 50 Gy.

The lesions present as erythematous papules measuring less than 1 cm in diameter and that coalesce to form small plaques. Sometimes, as was the case in our patient, vesicles may be present. The latency period between radiotherapy and the onset of the first lesions is long, between 3 and 20 years. Characteristically, the patients do not report associated symptoms or present lymphedema.

Histology reveals marked vascular dilation in the papillary dermis that may extend into the epidermis, thereby giving the lesion a tuberous appearance. The vascular lesion is relatively well circumscribed, although not encapsulated, and may reach the deep dermis and occasionally extend to the subcutaneous cellular tissue, although this happens more often with malignant tumors such as angiosarcomas.

The vascular spaces are covered by a single discontinuous thread of endothelial cells that may have flat or large, oval nuclei that are hyperchromatic and that protrude towards the lumen. Occasionally, small nucleoli may be present. Mitotic and atypical cells are not present.

In summary, we believe that, in agreement with Diaz-Cascajo et al, lymphangiomatous papules and plaques after radiotherapy are a variant of acquired lymphangioma. Likewise, the term benign lymphangiomatous papules...
or plaques after radiotherapy is the most appropriate because it makes reference to the clinical presentation of the lesions, their nature, and their relationship with radiotherapy.

References