

CLINICAL SCIENCE LETTERS

Allergic Contact Dermatitis and Systemic Contact Dermatitis in a Patient With Polysensitization to Topical Corticosteroids

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To the Editor:

Although allergic contact dermatitis (ACD) due to corticosteroids is a well-known and relatively common phenomenon, the systemic administration of corticosteroids only rarely produces skin reactions (systemic contact dermatitis [SCD]). We present the case of a patient with ACD to various corticosteroids, and who subsequently developed SCD to multiple systemic corticosteroids.

A 47-year-old man was seen in our outpatient clinic for a plaque of alopecia areata on the scalp. A 0.1% methylprednisolone aceponate emulsion was prescribed. Four days later, pruritic, macular, desquamative, erythematous lesions developed on the eyelids, neck, and around the plaque of alopecia. With a suspected diagnosis of corticosteroid-related ACD, 1% pimecrolimus cream was prescribed and skin patch testing was performed with True Test, using a series of corticosteroids and steroid-containing products (Lexxema emulsion). Readings were made on days 2, 5, and 7, obtaining positive reactions to multiple corticosteroids (Table 1, Figure). Skin prick and intradermal reaction tests were performed with hydrocortisone, prednisone, methylprednisolone, prednisolone, dexamethasone, and deflazacort, giving negative results, and oral therapeutic doses were then administered. Pruriginous, erythematous lesions affecting the neck, axillas, groin, and perineum (baboon-like) developed in all cases after a period of 6 to 24 hours. The lesions did not recur on placebo challenge. The skin biopsy of one of the lesions showed spongiotic dermatitis with a superficial perivascular inflammatory infiltrate and dermal edema. A diagnosis was made of ACD and SCD due to corticosteroids, with polysensitization. A use test was performed with 0.1% mometasone furoate cream, which did not produce lesions after 10 days, and this was therefore indicated for treatment if topical corticosteroids were required.

Corticosteroid-related ACD must be suspected when there is a deterioration or prolongation of a previous dermatitis or when the expected improvement does not occur. Using patch tests, Gonul and Gul¹ demonstrated sensitization in 22% of patients diagnosed with ACD who did not respond to topical corticosteroids. The rates of positivity to corticosteroids in patch tests vary between 0.52% and 6%, which has led to these allergens being

included in a number of standard series.²⁻⁴ In Spain, the Spanish Contact Dermatitis Research Group (GEIDC) initially introduced 1% tixocortol pivalate in petroleum jelly, subsequently adding 0.1% budesonide in petroleum jelly. In 2007, hydrocortisone-17-butyrate was also added to the True Test. In the epidemiologic study of ACD in Spain published by the GEIDC in 2001, positivity to corticosteroids was only detected in 1.01%.⁵ We do not know the present levels with the new corticosteroids used for screening.

In a retrospective study of 1188 patients undergoing patch tests with a specific corticosteroid series, it was shown that if tixocortol pivalate alone had been used, less than 50% of the sensitizations would have been detected.⁶



Figure. Various positive patch tests after application of a corticosteroid series (48 hours).

Tabla 1. Tests Performed on the Patient and Their Results

<i>Corticosteroid</i>	<i>Concentration (Petroleum Jelly)</i>	<i>Corticosteroid Group</i>	<i>Patch Test</i>	<i>Challenge</i>
Tixocortol pivalate	1	A	–	
Budesonide	0.1	B	++	
Hydrocortisone acetate	25	A	–	
Hydrocortisone-17-butyrate	1	D2	++	
Triamcinolone acetonide	1	B	+	
Triamcinolone acetonide	5	B	++	
Prednisolone	5	A	–	++
Betamethasone-17-valerate	1	D1	++	
Clobetasol-17-dipropionate	1	D1	+	
Dexamethasone 21-phosphate disodium	1	C	++	
Dexamethasone valerate	1	C	++	
Dexamethasone base	1	C	+/- (D7)	++
Hydrocortisone base	12.5	A	–	++
Betamethasone base	1	C	–	
Betamethasone dipropionate	0.5	D1	++	
Betamethasone valerate	1	D1	+	
Fluocinolone acetonide	0.25	B	+(D7)	
Lexxema emulsion	As supplied	D2	+	
Mometasone furoate	1%	D1	–	
Methylprednisolone (Urbason)	As supplied	A	–	++
Prednisone (Dacortin)	As supplied	A	–	++
Deflazacort (Zamene)	As supplied	A	–	++

With the 3 corticosteroids currently used for screening in the True Test, 71% would be detected; however, a significant number would remain undiagnosed. For this reason, the North American Contact Dermatitis Group has added 2 further corticosteroids to their standard series: 1% triamcinolone acetonide in petroleum jelly and 1% clobetasol-17-propionate in petroleum jelly.³ If positive results are obtained or there is a suspicion of sensitization, skin patch testing must be performed using a corticosteroid series to detect possible cross reactions. These series must include the substances most commonly used in that country. However, corticosteroids as widely used as mometasone furoate, prednicarbate, or methylprednisolone aceponate, among others, are not included in the commercially available specific series. Because of this, it is important to patch test the specific products used by the patient in order to minimize the loss of cases.

A late reading should be performed on day 6 or 7. Some studies have shown losses of 30% if this late reading is not performed, whereas in others it is less than 1%.^{6,7}

Multiple sensitization (coreactions or cross-reactions) is relatively common. In 1989, Coopman et al⁸ classified the corticosteroids into 4 groups according to their chemical structure and to the skin reactions that were observed with patch tests (Table 2). But this is of limited value as cross reactions have been reported between all the groups. It is much less common to find sensitization to a large number of corticosteroids from all groups, as occurred in our case.⁹ The mechanism for this is not clear, as it may be due to sensitization to the basic corticosteroid structure or to a common metabolite.

Given the sensitization to multiple corticosteroids and the possibility of a reaction after their systemic administration, it was decided to perform a controlled

Table 2. Corticosteroid Classes

Group	Structure	Component	Typical Cross-reactions
A	Without methyl substitution at C16, no side chain at C17. Possible short side chain at C21	Tixocortol pivalate	With D2
		Hydrocortisone	
		Prednisolone	
		Methylprednisolone	
		Prednisone	
B	cis-ketal or cis-diol structure at C16 and C17; possible side chain at C21	Budesonide	Budesonide with D2
		Triamcinolone	
		Triamcinolone acetonide	
		Fluocinolone acetonide	
		Fluocinonide	
C	Methyl substitution at C16, no side chain at C17, possible side chain at C21	Betamethasone	
		Dexamethasone	
		Desoximetasone	
		Fluocortolone	
D1	Methyl substitution at C16, side chain ester at C17/C21	Clobetasol propionate	
		Betamethasone dipropionate	
		Betametasone-17 valerate	
		Mometasone furoate	
		Diflucortolone valerate	
D2	No methyl or halogen substitution at C16, side chain ester at C17, possible side chain at C21	Hydrocortisone 17-butyrate	With A and with budesonide
		Hydrocortisone 17-aceponate	
		Methylprednisolone aceponate	
		Prednicarbate	

The molecule used for screening is in bold text

challenge test. A baboon-like pruriginous skin reaction, which is a recognized clinical pattern of SCD, occurred with all the corticosteroids tested. Although the patient can use pimecrolimus/tacrolimus or mometasone furoate topically, we have not been able to find a safe systemic corticosteroid in case the patient needs it in the future, and the risk-benefit relationship will have to be carefully evaluated. This is an exceptional situation, and although cases of ACD to multiple corticosteroids have been reported, we have only found one case in the literature similar to the patient presented in this article.¹⁰

We would like to draw attention to the importance of suspecting an ACD in those cases that do not respond adequately to corticosteroid treatment, and they should

be studied in specific contact units, both to confirm the diagnosis and to offer safe therapeutic alternatives.

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Conflicts of Interest

The authors declare no conflicts of interest.

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Neurofibromatosis Type 1 and Arnold-Chiari Malformation

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To the Editor:

Neurofibromatosis type 1 (NF-1) or von Recklinghausen disease is the most common neurocutaneous syndrome. It is characterized by the appearance of various cutaneous stigmata, neurological manifestations, and an increased susceptibility to develop tumors.¹ Although it is frequently

associated with a wide variety of central nervous system (CNS) dysplasias, the association with Arnold-Chiari malformation type I is unusual.

A 60-year-old woman with a past history of systemic hypertension, hiatus hernia, and iron-deficiency anemia, was seen in our outpatient clinic for lesions on her neck that had been present the years and that caused discomfort due to friction. On physical examination of the skin, multiple soft fibromas were observed in the cervical region; however, a large number of hyperpigmented macules with a homogeneous, light brown color and well-defined borders were also observed, mainly on the trunk, though also at the root of the limbs, and 9 of them were over 15 mm in diameter, and there were also groups of hyperchromic macules between 2 and 10 mm in diameter in both axillas, clinically consistent with lentigo simplex (Crowe sign). The patient stated that those lesions had been present since birth, and that her father had similar spots. Based on these findings, the patient was diagnosed with NF-1 and was referred to the neurology and ophthalmology departments to exclude CNS and optic nerve involvement. Ophthalmologic examination was normal, with no evidence of Lisch nodules. The patient had no neurological symptoms and neurological examination revealed generalized, symmetrical muscle hyperreflexia but no other alterations. Cerebral magnetic resonance imaging (MRI) showed herniation of the cerebellar tonsils into the upper cervical canal, below the level of the

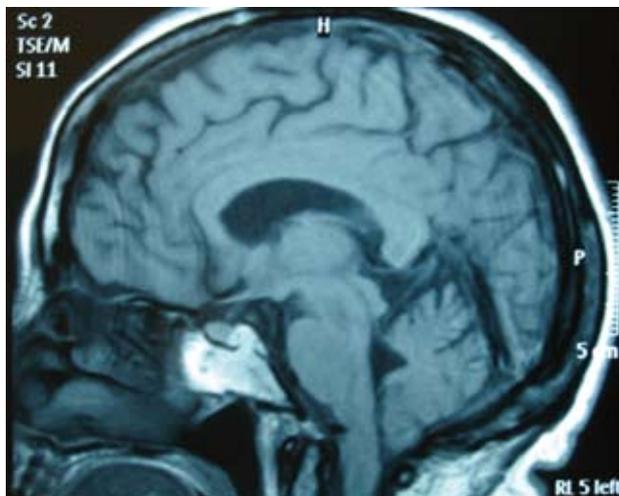


Figure 1. Sagittal cerebral magnetic resonance image: the T1-weighted image shows herniation of the cerebellar tonsils into the upper cervical canal, below the level of the occipital foramen, consistent with Arnold-Chiari malformation type I.

foramen magnum (Figure), consistent with an Arnold-Chiari malformation type I. Blood tests, abdominal ultrasound, and a bone scan were also performed, with normal results. As the Arnold-Chiari malformation type I was an incidental finding, and as the patient had no symptoms, no treatment was required.

Numerous neurological abnormalities related to NF-1 have been reported, including macrocephaly, unilateral sphenoidal dysplasia, glioma of the optic chiasm, optic nerve, diencephalon, or brainstem, meningiomas, cranial nerve schwannomas, plexiform or intraspinal neurofibromas, hamartomas, stenoses of the cerebral aqueduct, heterotopias, and hyperintense lesions in the basal ganglia, internal capsule, and cerebellum on T2-weighted MRI.² Vascular malformations or dysplasias have also been reported, some of which have been related to other neurocutaneous syndromes, such as Sturge-Weber syndrome.³

On the other hand, the association of Arnold-Chiari malformation type 1 and NF-1 is rare.^{1,2,4-10} We present the case of a patient with NF-1 and with an asymptomatic Arnold-Chiari malformation type I diagnosed as an incidental finding on performing cerebral MRI. The diagnosis of NF-1 was made in accordance with current criteria.¹¹ Although the Arnold-Chiari malformation type 1 is usually associated with other abnormalities such as basilar impression, occipitalization of the atlas, scoliosis, or spina bifida, in our case the patient only presented herniation of the cerebellar tonsils and of the medial part of the inferior lobe of the cerebellum into the cervical canal.

The table summarizes the cases of Arnold-Chiari malformation type 1 associated with NF-1 reported in the literature. The prevalence of the Arnold-Chiari malformation type 1 is of 1 in 3700² and that of NF-1 is 1 in 4500 to 1 in 6700,¹¹ and the probability of having both conditions is therefore very low (1:16 650 000 to 1:24 790 000).² However, it must be remembered that Arnold-Chiari malformation type 1 can be asymptomatic, being detected as an incidental finding in neuroimaging studies, as in the case described here; the routine use of cranial-cervical magnetic resonance imaging in all patients with NF-1, even in the absence of symptoms or signs of neurological disease, will therefore probably reveal a higher frequency of this association. On this subject, Tubbs et al¹² demonstrated that up to 8.6% of patients with NF-1 (17 of a series of 198 patients) presented an asymptomatic Arnold-Chiari malformation type I.

The frequent detection of lesions affecting the CNS in patients with NF-1, including spina bifida, hydrocephalus, and meningocele, as well as the frequent presence of bone lesions such as scoliosis, macrocephaly, or sphenoidal dysplasia, suggests that this association is actually more than incidental. The gene mutation (17q11.2) found in NF-1 facilitates the abnormal proliferation of tissues and

Table. Cases or Case Series of Arnold-Chiari Malformation Type I Associated With Neurofibromatosis Type 1 Reported in the Literature

Authors	Year	Cases	Symptoms
Herrero A et al ¹⁰	2007	Woman, 23 y	Headache
Hara M and Arakawa M ¹	2005	Woman, 29 y	Gait disorder, sensory and urinary disturbances
Tubbs RS et al ¹²	2004	Series of 198 cases of Chiari I	8.6% of cases with asymptomatic NF-1
Chakravarty A et al ⁹	2002	Woman, 22 y	Optic nerve glioma, scoliosis, syringomyelia
Guistini S. et al ⁸	2002	2 cases	Asymptomatic (case 1) and hydrocephalus (case 2)
Batissela PA et al ²	1996	Boy, 11 y	Headache
Dooley J et al ⁷	1993	Boy, 16 y	Asymptomatic
Tominga T et al ⁶	1991	1 case	Headache, hydrocephalus
Affifi AK et al ⁵	1988	2 cases	Hydrocephalus (both)
Parkinson D and Hay R ⁴	1986	1 case	Rhinorrhoea, fistula

the subsequent appearance of ectodermal and mesodermal dysplasias and various tumors. The pathogenesis of Arnold-Chiari malformation type 1 appears to be related to hypoplasia of the posterior fossa, leading to herniation of the cerebellum through the foramen magnum. In this context, congenital central nervous system dysgenesis could represent a common pathogenic mechanism for both conditions.¹³

In summary, and in view of what has been discussed, we consider that Arnold-Chiari malformation type 1 should probably be considered as one of the CNS dysplasias to be excluded in all patients with NF-1. In our opinion, cerebral MRI should therefore be performed in all patients with NF-1.

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Conflicts of Interest

The authors declare no conflicts of interest.

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Hair Follicle Nevus: A Case Report and Review of the Literature

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To the Editor:

The hair follicle nevus is a very rare hamartoma that is usually congenital or appears in the first years of life, and presents as a papule, plaque, or nodule on the face.¹⁻⁶



Figure 1. Clinical image of the lesion. Velvety plaque on the lower eyelid of the right eye.

We present the case of a 16-year-old girl with no past history of interest, who was seen for a lesion on the lower eyelid of the right eye and that had been present since birth. The lesion was a homogeneous, skin-colored, velvety plaque of approximately 1 cm × 0.5 cm, with poorly defined borders, and with no orifices or comedones on its surface (Figure 1). The lesion was asymptomatic and had always been stable, with no sudden changes in size, shape, or appearance. A 4-mm punch-biopsy was taken from the center of the lesion, revealing a tumor with follicular differentiation. Serial sections were performed of the whole biopsy, observing a proliferation of mature hair follicles in similar stages of differentiation in the upper regions of the reticular dermis, surrounded by a highly cellular stroma (Figure 2). The connective tissue sheath of all the follicles presented marked fibrous thickening (Figure 3). No central cystic cavity was found in any part of the sample. The diagnosis of hair follicle nevus was made on the basis of the clinical features and the histological findings. As the lesion was asymptomatic and did not trouble the patient from a cosmetic point of

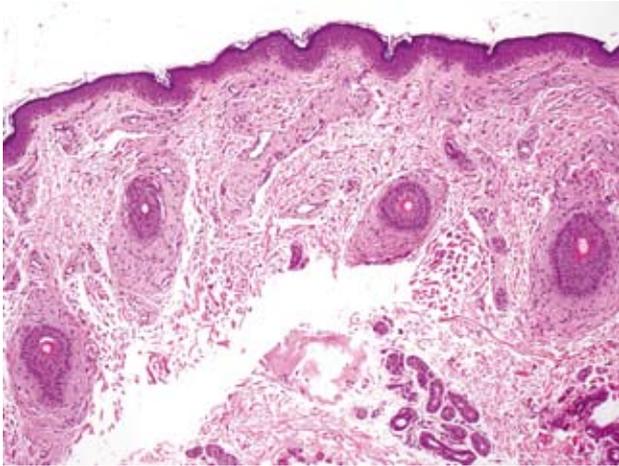


Figure 2. Hair follicles in the superficial dermis, with a cellular stroma. Hematoxylin-eosin, $\times 10$.

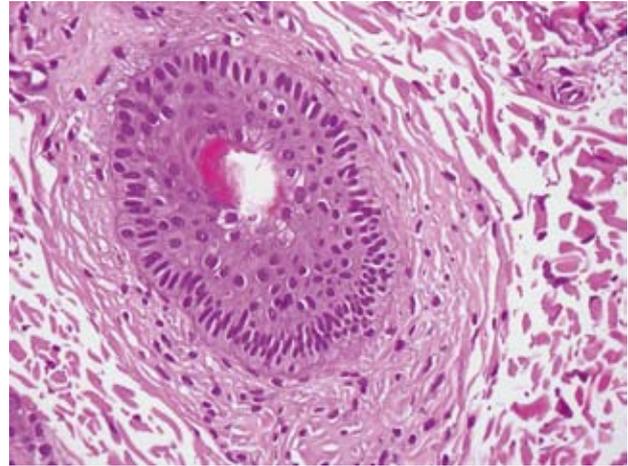


Figure 3. Detail of the fibrous perifollicular thickening. Hematoxylin-eosin, $\times 40$.

view, it was decided not to perform excision and she was advised to return if she noticed any change.

Hair follicle nevus is a rare follicular hamartoma. It presents as a skin-colored or erythematous papule, plaque, or nodule situated on the face. It may arise in the early years of life or be present from birth and is usually asymptomatic.^{1,3-5}

From a histological point of view, it is characterized by a proliferation of hair follicles, usually of small size, in the upper part of the dermis, with perifollicular fibrous thickening surrounded by a highly cellular stroma. Sebaceous or eccrine glands and muscle fibers may sometimes be seen, leading to the hair follicle nevus being considered as a true hamartoma.^{1,3}

Until the description by Pippione et al⁶ in 1984, the exact significance of the hair follicle nevus was unclear. Many of the cases reported as hair follicle nevus were clearly trichofolliculomas.⁷ There were also those who considered these 2 terms to be synonyms for the same neoplasm, as in the review by Labandeira et al.³ In 1993, Ackerman et al⁸ even went as far as to insist that the hair follicle nevus was really a trichofolliculoma sampled from its periphery and, for this reason, the central cystic cavity of that lesion was not seen. In agreement with Pippione, other authors considered the hair follicle nevus to be a lesion with sufficient individual features to be differentiated from trichofolliculoma.³⁻⁶ They suggest that, in order to reach a correct diagnosis of hair follicle nevus, it is necessary to perform serial sections of the specimen in order to exclude the presence of a cystic structure specific to trichofolliculoma. In any case, as stated by Requena,⁹ “although the 2 lesions are different, trichofolliculoma and hair follicle nevus probably represent 2 closely related follicular hamartomas, as the hair follicle nevus is formed

of minute hair follicles surrounded by a stroma similar to that of the trichofolliculoma.”

There have also been authors who associate the hair follicle nevus with accessory tragi, as they can have common histological features, with the exception of the presence of cartilage in the tragi.¹⁰

What does appear to be true is that it is an extremely rare lesion. Davis and Cohen² performed a review of the 20 cases published up to 1996; between then and the latest description by Okada et al,⁵ 7 more cases have been published.

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Conflicts of Interest

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Actinomyces of the Lip: an Exceptional Site

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To the Editor:

Actinomyces is a chronic bacterial infection that is becoming less common due to the widespread use of antibiotics and the improvement in oral hygiene.

There are 4 main clinical forms, differentiated according to the site affected: cervicofacial, thoracic, ileocecal, and pelvic. However, many other sites have been reported.

Actinomyces of the lip is very rare. In an extensive review, we only found 3 cases published in the past 30 years.¹⁻³

We present the case of a 69-year-old man with no past history of interest, who was seen for a tender, nodular

lesion on the lip that had been present for 1 year. The patient reported no suppuration; the mouth showed signs of sepsis, and on the mucosal surface of the lower lip there was a round, violaceous, well-delimited, very hard nodule with a diameter of 2 cm (Figure 1). There were no palpable regional lymph nodes.

On the suspicion of a tumor of the minor salivary glands, the lesion was excised under local anesthesia; the nodule proved very adherent to the adjacent tissues and significant bleeding occurred during the excision. Culture was not performed.

Histological study showed an abscess surrounded by a fibrous capsule. Within the abscess there were granulomatous areas with abundant macrophages and plasma cells and other areas with a predominance of multinuclear cells (Figure 2).

Some of these latter areas contained irregular, amorphous basophilic masses that had peripheral, radial, pear-shaped, eosinophilic projections (Figure 3). These masses did not stain with Ziehl-Neelsen stain, and the Gomori silver metenamine stain demonstrated that they were formed of aggregates of filamentous bacilli.

With the diagnosis of actinomyces of the lower lip, general blood tests with serology for human immunodeficiency virus, otorhinolaryngological examination, chest radiograph, and abdominal ultrasound were performed, with normal results. Complementary treatment was prescribed with oral amoxicillin 500 mg every 6 hours for 3 months. Two years later, the patient had suffered no recurrence.

Actinomyces is produced by various species of the genus *Actinomyces*, particularly *Actinomyces israelii*. These are branching, pleomorphic, filamentous, gram-positive bacilli that are obligate or facultative anaerobes and are not acid or alcohol fast. They form part of the normal flora of the mouth, gastrointestinal tract, and female genital



Figure 1. Violaceous nodule with a diameter of 2 cm, located in the mucosa of the lower lip.

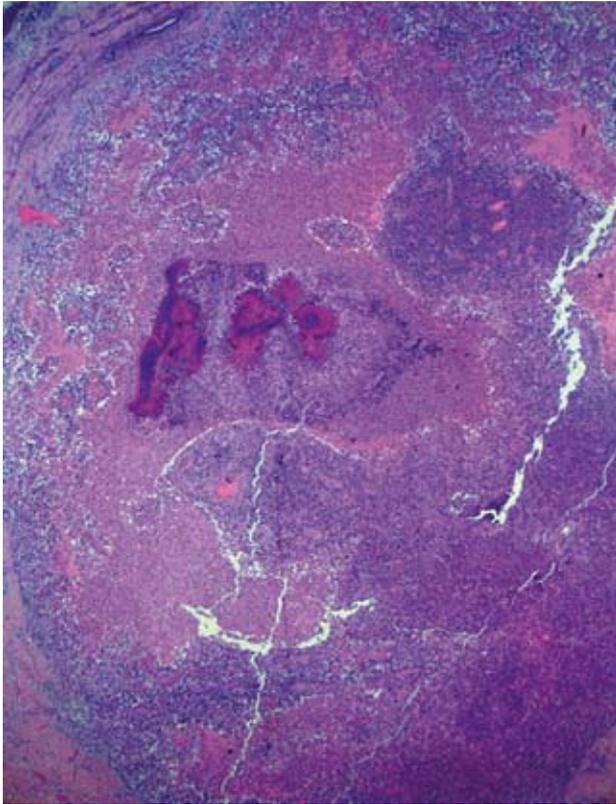


Figure 2. Well-defined abscess with granulomatous areas and others with a predominance of multinuclear cells and that contain sulfur granules (hematoxylin-eosin, $\times 10$).

tract. These organisms have a very low pathogenicity and therefore require a previous tissue lesion (surgery, trauma, foreign body, pre-existing inflammatory process, etc) and the presence of other cooperating microorganisms (copathogens) to cause infection.⁴ Although actinomycosis usually affects immunocompetent individuals, factors that reduce host defenses favor this infection.

Clinically it is characterized by slowly developing, localized tumors that tend to develop abscesses and fistulas; the presence of yellowish granules of 1 to 2 mm in diameter in the exudate (sulfur granules) is characteristic but not pathognomic. The infection provokes an intense

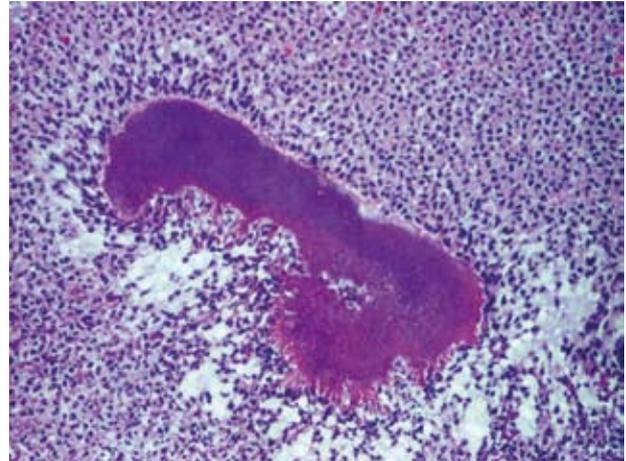


Figure 3. Characteristic sulfur granules of actinomycosis: basophilic with eosinophilic, pear-shaped extensions (hematoxylin-eosin, $\times 200$).

fibrotic reaction in the surrounding tissues, giving rise to a woody consistency, frequently mimicking a neoplasm.

Published cases of actinomycosis of the lip (Table) presented as isolated, small, hard abscesses that were not associated with deeper lesions or with immunosuppression, and the majority were confused with tumors of the minor salivary glands.

The diagnosis is made by anaerobic culture or by the histological demonstration of the presence of the characteristic sulfur granules within the abscesses. The histological differential diagnosis must include other conditions that produce sulfur granules. Although the size, morphology, and color of the granules is highly suggestive, it should be demonstrated that they are formed of aggregates of fine, filamentous bacilli using Gram or Gomori stains; these studies will detect granules formed of nonfilamentous bacilli (botryomycosis) or thick hyphae of fungi (eumycetomas) and those formed of nonfilamentous, acid and alcohol fast bacilli, which would exclude a diagnosis of actinomycetomas and nocardiosis.

The intense fibrosis that surrounds the abscesses in this condition impedes the penetration of antibiotics, and the ideal treatment is therefore a combination of surgical

Table. Clinical Features of Actinomycosis of the Lip

No.	Author	Year	Age, y	Sex	Site	Size, cm	Clinical Course	Clinical Diagnosis
1	Kikiewicz D ¹	1978	50	M	Upper lip	*	5 mo	Infected cyst
2	Appiah-Anane S and Tickle M ²	1995	32	F	Upper lip	2	2 mo	MSG tumor
3	Lan MC et al ³	2007	50	M	Lower lip	1	3 mo	MSG tumor
4	Sánchez Estella J et al	2009	69	M	Lower lip	2	1 y	MSG tumor

*Size of a cherry. Abbreviations: F, female; M, male; MSG, minor salivary gland.

excision and antibiotic therapy. The antibiotic of choice is penicillin, and prolonged treatment is recommended in order to prevent recurrences; the duration of treatment will vary according to the complexity of the condition (from 3 to 18 months). Due to a lack of previous experience in such cases, we decided to prescribe complementary treatment for 3 months after surgery, using an oral penicillin derivative, with a good outcome after follow-up.

An interesting issue is how the infection becomes established in cases of actinomycosis of the lip in which there is no recent history of predisposing factors. Infection of minimal self-injury would be favored by poor oral hygiene, as in our patient, or, more probably, infection occurs in a previous mucocele, as suggested in one of the cases published after the histological finding of a possible salivary retention cyst adjacent to the actinomycotic abscess.²

Dermatofibroma with Cholesterol Deposits in a Patient With HIV Infection

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To the Editor:

Dermatofibroma (DF), also called histiocytoma, cutaneous fibrous histiocytoma, nodular subepidermal fibrosis, or sclerosing hemangioma, is a very common, benign skin tumor of fibrohistiocytic origin. It presents as firm, single or multiple tumors that are usually hyperpigmented and less than 1 cm in diameter; they tend to appear on the lower limbs of young women. Histologically they are characterized by a poorly demarcated dermal nodule consisting of variable proportions of fibroblasts, young and mature collagen, capillaries, and histiocytes. Treatment is by surgical excision, although this is not usually necessary. The debate continues as to whether this is a neoplastic disorder or if it is actually a reactive proliferation of fibroblasts secondary to insect bites or minor trauma.¹

More than 40 clinical-pathologic variants of DF have been reported, classified according to their clinical presentation, structural and stromal features, or variations in their cellular make-up²; however, there are many other subvariants, given that 10% of all DFs are combined (simultaneous presence of 2 or more histopathological forms).³

The cholesterotic fibrous histiocytoma is a rare variant of DF described by Hunt et al⁴ in 1990. It consists of a lesion that is clinically identical to classic DF, but the diagnosis is based on the histopathological study,

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which reveals cholesterol deposits within the lesion. Its appearance should suggest the possibility of an underlying hyperlipoproteinemia. We report a new case of DF with deposits of cholesterol crystals seen in a patient with human immunodeficiency virus (HIV) infection, with no associated dyslipidemia.

The patient was a 37-year-old man with a past history of hepatitis C virus and HIV infection; his most recent CD4 lymphocyte count was 600/ μ L, with an undetectable viral load. He was on combination antiretroviral therapy with didanosine, nelfinavir, and stavudine. There was no personal or family history of hypercholesterolemia or hypertriglyceridemia. He came to the dermatology department for evaluation of 3 lesions on the left foot, left lateral chest wall, and left elbow; the lesions had been present for less than a year. All were asymptomatic except for the one on the left elbow, which was tender to pressure. The patient reported no trauma or previous lesions in those areas.

On physical examination, 3 brownish tumors were observed on the left foot, left lateral chest wall, and left elbow. They had a smooth surface, were between 0.5 and 1 cm in diameter, were firm on palpation, and were not adherent to the deep planes (Figure 1). Lateral pressure produced a depression in the overlying skin (dimple sign).



Figure 1. Brownish tumor, 1 cm in diameter, situated on the left elbow.

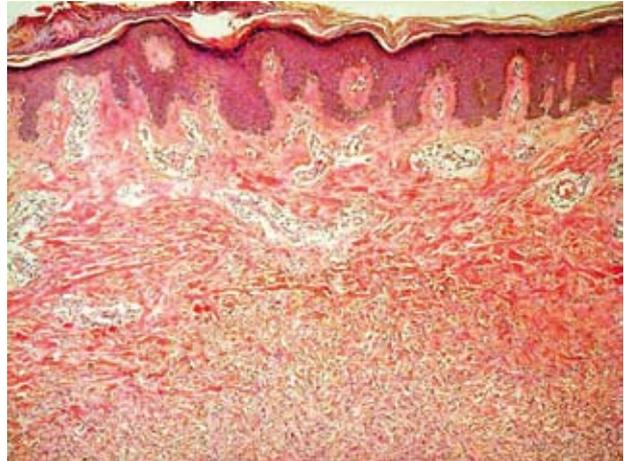


Figure 2. Histiocytes and abundant fibroblasts between thick bundles of collagen in the middle and deep dermis, respecting a thin superficial layer (hematoxylin-eosin, $\times 100$).

The patient also presented a lipodystrophic phenotype, with central adiposity and lipoatrophy of the face and limbs. There were no cutaneous manifestations of hyperlipoproteinemia.

With the clinical diagnosis of DF, the lesion on the left elbow was excised, and histopathological study revealed a poorly demarcated, symmetrical nodular proliferation formed of histiocytes and a marked proliferation of fibroblasts between thick bundles of collagen, which occupied the middle and deep dermis, respecting a thin superficial layer (Figure 2). Groups of biconvex, needle-shaped crystals of cholesterol were observed within the lesion (Figure 3). The overlying epidermis was acanthotic and papillomatous, with basal hyperpigmentation.

The other 2 lesions were excised later, and histopathological study confirmed their fibrohistiocytic origin, though deposits of cholesterol crystals were not seen. The complementary tests performed, including a complete blood count and biochemistry, only revealed hypertransaminasemia; the levels of cholesterol (214 mg/dL, reference range: 145–255 mg/dL) and triglycerides (115 mg/dL, reference range: 35–150 mg/dL) were normal.

The cholesterotic variant of DF is characterized by deposits of cholesterol crystals and is included among the DF with stromal peculiarities (together with those that present sclerosis, mucin, or hemosiderin). The first report was made by Hunt et al,⁴ who presented the case of a woman with a known history of hypercholesterolemia, with 2 lesions clinically suggestive of DF; histopathological study revealed cholesterol deposits within the lesions, surrounded by numerous histiocytes and foreign body-type giant cells. Those authors concluded that, as occurs with malignant fibrous histiocytoma,⁵ DFs are tumors

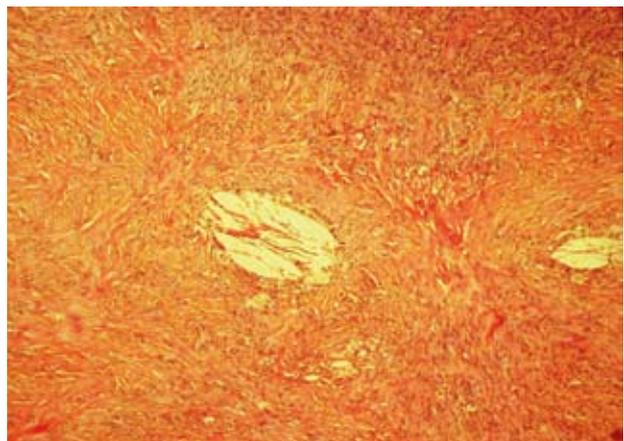


Figure 3. Deposits of groups of biconvex, needle-shaped cholesterol crystals can be seen in the middle and deep dermis, surrounded by histiocytes, with a proliferation of fibroblasts and thick bundles of collagen (hematoxylin-eosin, $\times 200$).

with histiocytic capacity, which may be expressed in the context of a hyperlipoproteinemia. This will give rise to xanthomatous changes and deposits of cholesterol similar those found in tuberous xanthomas and cholesterol granulomas. The finding of this variant of DF should alert doctors to the need to evaluate the patient's plasma lipid levels.⁴ The clinical and histological differential diagnosis includes dermatofibrosarcoma protuberans, tuberous xanthoma (including type II normolipemic cutaneous xanthomas, which are associated with lymphoproliferative disorders and with HIV infection),⁶ plexiform xanthomatous tumor,⁷ infectious diseases (atypical mycobacteriosis), erythema elevatum diutinum, Kaposi sarcoma, and lipidized dermatofibroma.⁸

We have not found reports of DF with cholesterol deposits in a patient with HIV infection in the literature. Interestingly, seropositive patients frequently present both DFs⁹ and dislipidemia,¹⁰ and we therefore consider that the association we describe here is not due to chance. The term multiple eruptive DF is used to define the appearance of 5 to 8 lesions within the space of 4 months. They usually occur in patients with autoimmune diseases, particularly systemic lupus erythematosus on treatment with immunosuppressant drugs, hematological tumors, organ transplant, immunodeficiencies (HIV), and patients with Down syndrome, but are also seen in healthy individuals. In some patients with HIV infection, the lesions develop after starting combination antiretroviral therapy.⁹ That treatment has been associated with a wide range of metabolic syndromes, such as peripheral lipodystrophy, dislipidemia, and insulin resistance. Dyslipidemias are common in the patients on antiretroviral treatment and present with different frequencies according to the drug used, and include isolated or combined elevations of the triglycerides and total cholesterol, with variable changes in the low and high density lipoproteins.^{6,10}

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Conflicts of Interest

The authors declare no conflicts of interest.

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Wedge Excision of the Pinna: How to Avoid a Notch in the Helical Border

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To the Editor:

The pinna is an anatomical structure with a high level of exposure to solar radiation; between 5% and 8% of all skin tumors occur here,¹ the most common being squamous cell carcinoma and basal cell carcinoma. Almost half of these tumors affect the helical rim.²

Although in a lateral location, the ears are prominent and symmetrical structures, so any defect is very visible from an esthetic point of view.³

Wedge excision is one of the most commonly used techniques to repair defects of up to a quarter of the circumference of the helix.¹ However, it is common for this type of surgical intervention to produce a notch in the free border of the auricle during the healing process.^{2,4}

In order to avoid this complication we propose a technique for reconstruction of the border of the auricle. Once the wedge shape of the area to be removed has been marked on to the ear (Figure 1), the free skin border on



Figure 1. Squamous cell carcinoma on the helical border. Initial marking of the modified wedge.

one side is advanced to a distance of about 0.5 cm, while the skin on the other side is resected by the same amount, allowing reconstruction to be performed with an overlap of the 2 borders (Figure 2). This reinforcement of the edge of the scar prevents a postsurgical notch from appearing (Figure 3). The wound is closed by tissue planes.

In conclusion, we describe a modification of the classic wedge that simply and effectively avoids the formation of an antiesthetic notch on the free border of the ear.

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Figure 2. Modified wedge resection. 1 of the 2 sides is extended to advance and overlap the other.



Figure 3. Final outcome one month after surgery. No deformity is visible on the helical border of the ear.

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Sildenafil in the Treatment of Digital Ulcers in Patients with Systemic Sclerosis

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To the Editor:

In systemic sclerosis, the collagen deposition, vasculopathy, and Raynaud phenomenon produce abnormalities in microcirculation that lead to ischemia, distal ulceration (DU) and, occasionally, necrosis of one or more phalanges.¹ We report 2 cases in which sildenafil was used as a treatment option.

The first case was a 46-year-old woman with a history of diffuse cutaneous systemic sclerosis diagnosed 4 years previously, who was receiving antiplatelet therapy and nifedipine. Four months earlier she presented DU with necrosis of the distal phalanx of the fifth finger on the right-hand, requiring amputation. The patient recently

attended presenting new DU on the third finger of the right-hand, with periungual hemorrhagic lesions but no signs of necrosis of the finger. On the fifth finger of the same hand, partial closure of the surgical scar could be observed on the amputation stump (Figure 1). The patient tested positive for antinuclear antibodies with a titer of 1:640 but negative for antiscleroderma (anti-Scl)-70 antibodies. Periungual capillaroscopy revealed enlarged capillaries, avascular areas and hemorrhages in the proximal nailfold. Given this situation, treatment was initiated with oral sildenafil 50 mg/d (in a single dose at night). A subjective improvement (reduction in number and intensity) of episodes of Raynaud phenomenon was

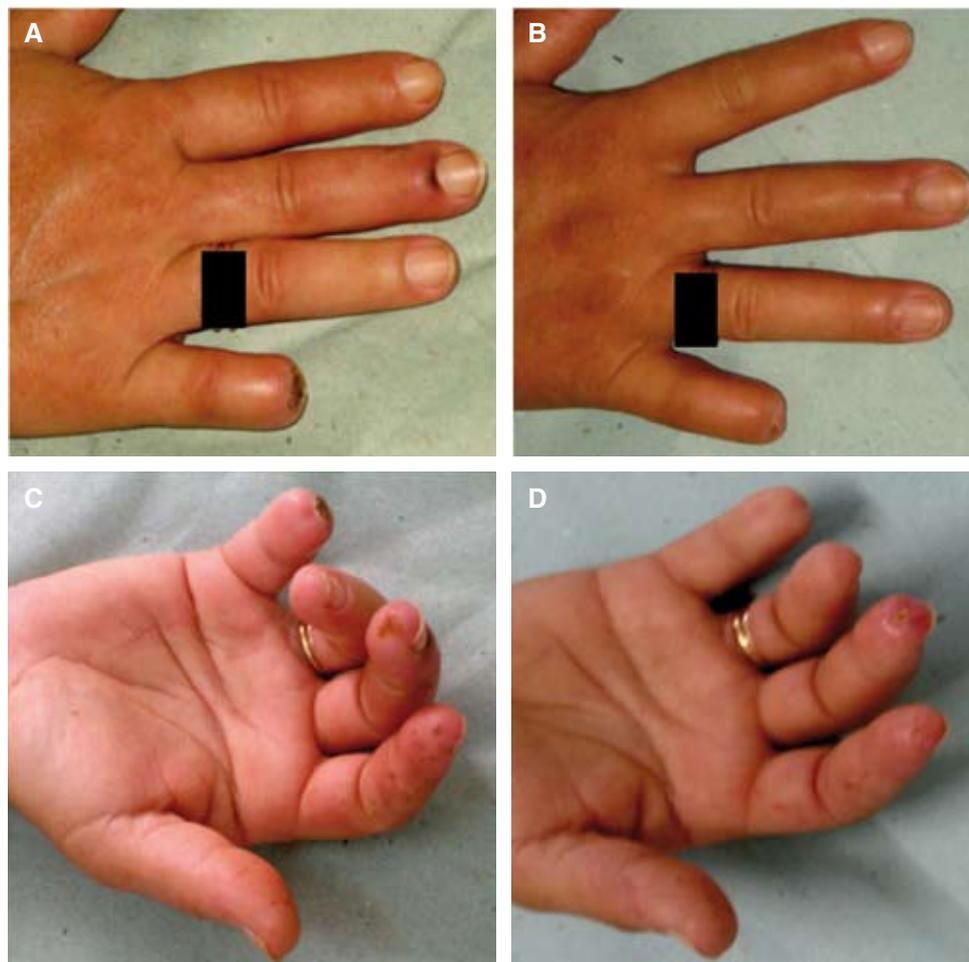


Figure 1. Appearance of the lesions (Case 1) before (A and C) and after (B and D) treatment with sildenafil.

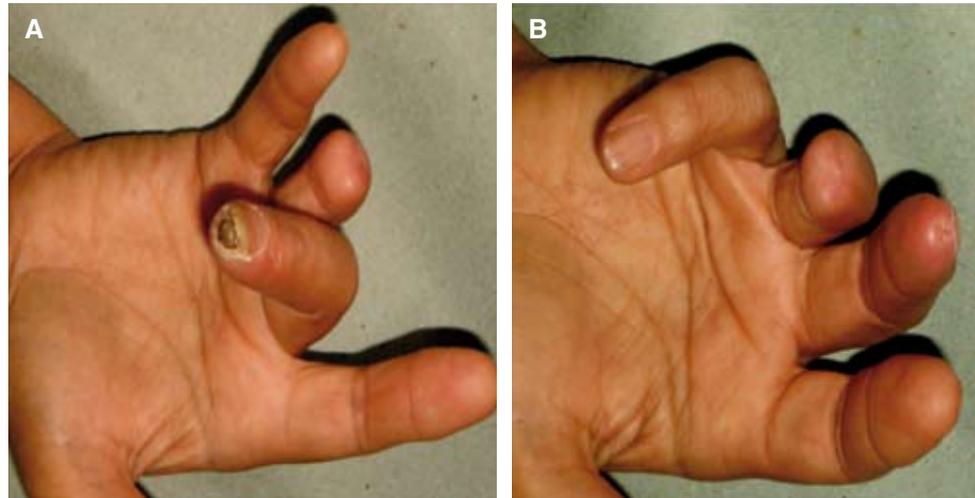


Figure 2. Appearance of the lesions (Case 2) before (A) and after (B) treatment with sildenafil.

achieved with complete recovery of the finger pad on the affected finger, disappearance of the ischemic and hemorrhagic lesions, and complete closure of the surgical wound 60 days after treatment was started (Figure 1). A year later the patient presented serious renal insufficiency, and was admitted to the intensive care unit where she later died.

The second case was a 63-year-old woman diagnosed 2 years ago with limited cutaneous systemic sclerosis and a recent history of gastroesophageal reflux. Treatment was initiated with antiplatelet drugs, ranitidine, and calcium channel blockers, which exacerbated the digestive symptoms and were therefore replaced with pentoxifylline. A year previously she had developed necrosis of the distal phalanx of the ring finger, requiring amputation. The patient consulted for DU on the finger pad of the third finger of the right-hand, with signs of ischemia and necrosis, associated with subungual hemorrhage, edema, and erythema on the distal phalanx of the same finger (Figure 2).

She tested positive for antinuclear antibodies with a titer of 1:320 with positive anticentromere antibodies. Periungual capillaroscopy revealed megacapillaries and avascular areas. Treatment was initiated with oral sildenafil 50 mg/d (in a single dose at night), obtaining subjective improvement in the episodes of Raynaud phenomenon and complete healing of the lesion in 60 days (Figure 2). Twenty months later she began to experience dyspnea, and an echocardiograph showed indirect signs of moderate pulmonary hypertension.

Raynaud phenomenon and DU are common in patients with systemic sclerosis.^{1,2} Treatment includes local and general measures: the application of antiseptics and debridement of wounds; and avoidance of exposure to cold and drugs that induce vasospasm, giving up smoking, and adequate use of analgesia, respectively.^{2,3} Where there

are serious lesions, vasodilator treatment should be started with calcium channel blockers, associated with antiplatelet treatment and heparin at anticoagulant doses.^{2,3} In serious and persistent digital ischemia, benefits have been seen in the use of prostacycline analogs such as intravenous alprostadil, iloprost, or epoprostenol.³ Bosentan (an endothelin-receptor antagonist) has proven effective in the prevention of further DU.⁴

Recently improvements in DU have been reported when using sildenafil in patients with primary and secondary Raynaud syndrome.⁵⁻⁹ As drugs such as iloprost and epoprostenol are not available in our hospital, we used sildenafil in both cases. We followed the therapeutic regimen first outlined by Lichtenstein⁵ for the treatment of Raynaud syndrome and DU. In both cases the DU resolved rapidly, with good tolerance and no adverse effects. An increase of oxidative stress associated with a deficit in nitric oxide is one of the factors involved in the pathogenesis of microvascular abnormalities and in wound-healing mechanisms.^{1,10} The inhibition of 5-phosphodiesterase mediated by sildenafil results in the accumulation of cyclic guanosine monophosphate (cGMP), leading to a reduction in intracellular calcium that produces relaxation of the vascular smooth muscle and therefore vasodilation.³ This type of inhibition prevents the breakdown of cGMP, increasing the effects of nitric oxide on the endothelium—a phenomenon that constitutes an attractive proposal in the treatment of DU in systemic sclerosis.⁹ Early intervention of this type could provide benefits without producing major adverse effects when used with caution in patients with arterial hypertension; it is contraindicated in patients on treatment with nitrates. In terms of dosage, the duration of treatment with sildenafil has varied, though it is usually given for at least 4 weeks, and doses of 50 mg/d or every 12 hours are used.⁷⁻⁹

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Conflicts of Interest

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