To the Editor:

The fat embolism syndrome was described by Zenker in 1861, although the triad of confusional state, dyspnea, and petechiae had already been mentioned in the German literature by Von Bergman. Despite being described more than 100 years ago, the diagnosis and specific treatment of this syndrome are still a subject of debate. With the 2 cases presented here, we aim to draw attention to a dermatological disorder which is widely discussed in the medical and surgical literature but which is unfamiliar to the dermatologist.

The first patient was an 18-year-old man who had suffered a motorbike accident and presented a major lung contusion and multiple long-bone fractures (Figure 1). The fractures were immobilized with plaster casts and the patient was admitted to hospital for routine surgery. He was asymptomatic for 48 hours, but before the surgical intervention, small papules a few millimeters in diameter appeared; they were of reddish color, did not blanch on pressure, and were distributed over the anterior aspect of the thorax, base of the neck, and conjunctivae, and in the axillas (Figure 2). This was followed by a rapid onset of neurological signs, consisting of temporospatial disorientation and clouding of consciousness, and acute respiratory failure. The chest radiograph showed bilateral opacities in both lung fields that were not present at the time of admission. No relevant findings except for mild thrombocytopenia were reported in the additional studies performed—complete blood count, biochemistry, coagulation, urinary sediment, and cerebral computed tomography (CT). Despite intensive supportive measures, the patient died a few hours later.

The second patient was a 27-year-old man, also victim of a motorcycle accident. He presented fractures of the right femur and left radius and ulna, and underwent surgical osteosynthesis. After being asymptomatic for 48 hours, he developed fever of up to 39°C associated with psychomotor agitation, severe acute respiratory failure, and pinpoint petechial lesions in the axillas and around the base of the neck.

The complete blood count revealed anemia of 9.5 g/dL and thrombocytopenia of $98 \times 10^9/L$; biochemistry and coagulation were normal. Lipiduria was observed in the urinary sediment. Cerebral CT was normal and the chest radiograph showed multiple, peripheral, focal opacities in both lung fields.

The clinical course was favorable and the patient was discharged from intensive care after 10 days and from the hospital 2 weeks later.

Fat embolism occurs in patients with long-bone fractures. The 2 cases presented here illustrate the complexity of this syndrome and the need for early diagnosis and prompt treatment.
Fractures or during orthopedic procedures. Fat present in the bone marrow is released, causing embolization of the capillary vessels in the lung parenchyma and in the peripheral circulation. Fat embolism can also occur in other nontraumatic disorders such as pancreatitis and sickle cell anemia, though this is rare. The presence of a fat embolism is a relatively common finding and is usually asymptomatic. However, a small number of patients develop serious signs and symptoms as a result of organ dysfunction that typically involves the skin, central nervous system, and lungs; the term fat embolism syndrome is reserved for these cases. The incidence of this syndrome is estimated at 0.5% of long bone fractures, although the majority of cases are not reported, and remain undetected in the context of a complex clinical situation. Usually, after being asymptomatic for a period of 2 or 3 days (lucid interval), the patient develops the typical clinical triad of respiratory failure, cerebral dysfunction, and petechiae. The petechiae appear in crops and with a typical distribution in the axillae and over the base of the neck, shoulders, anterior chest wall, and conjunctivae, following the path of the arterial branches of the arch of the aorta. They almost never affect the face or posterior aspect of the body. Disseminated petechiae may be associated with more severe cerebral and pulmonary dysfunction. These patients can also develop fever, anemia, thrombocytopenia, renal failure, jaundice, and tachycardia.

The diagnosis is clinical and requires a high degree of suspicion. Gurd, in 1970, proposed a series of diagnostic criteria (Table). This disorder often passes unnoticed due to its transitory nature and the lack of specificity of some signs.

The fat embolism syndrome is a serious condition that can sometimes follow a fulminant course. An early diagnosis of the condition and the initiation of appropriate therapeutic measures can reduce the number of complications and improve the prognosis. Mortality is currently around 5%-10%.

The skin lesions can sometimes appear before other clinical manifestations. The presence of petechiae with a characteristic distribution, in an appropriate clinical context, should therefore make us think of this disorder.

### Table. Gurd Diagnostic Criteria

<table>
<thead>
<tr>
<th>Major</th>
<th>Minor</th>
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<tr>
<td>Hypoxia</td>
<td>Tachycardia (&gt;120 beats per minute)</td>
</tr>
<tr>
<td>Central nervous system depression</td>
<td>Fever (temperature &gt; 39°C)</td>
</tr>
<tr>
<td>Petechiae</td>
<td>Unexplained anemia</td>
</tr>
<tr>
<td></td>
<td>Thrombocytopenia (platelet count &gt;15 × 10⁹/L)</td>
</tr>
</tbody>
</table>

### References

To the Editor:

Giant cell arteritis or temporal arteritis (TA) is the most common systemic vasculitis in adults.1 Histologically there is a lymphocytic-monocytic panarteritis with the formation of granulomas and giant cells. There is patchy involvement of medium and large arteries, particularly the extracranial branches of the carotid artery and, more specifically, the temporal artery.

The clinical presentation of TA is variable, with multiple, nonspecific symptoms in elderly patients, particularly women, who initially present fever, asthenia, weight loss, headache, unpredictable joint and muscle pain, stiffness, and polymyalgia rheumatica.1-7 Up to a third of patients develop visual symptoms. Loss of vision, sometimes bilateral and irreversible, is the main complication of this condition and it can sometimes be the first symptom. The alterations in the blood tests in TA can also be relatively nonspecific, with normocytic-normochromic anemia, elevated alkaline phosphatase, and a raised erythrocyte sedimentation rate (ESR).1-7 Up to 40% of patients develop atypical clinical manifestations such as respiratory symptoms, pyrexia of unknown origin, aortic aneurysms, or digestive tract, neurological, or skin disorders.1

We present the case of a 91-year-old woman with a past history of systemic hypertension, congestive cardiac failure, and atrioventricular block for which a pacemaker had been implanted. She came to the emergency department with a 48-hour history of bilateral loss of vision, with no accompanying symptoms.

On physical examination there was asymmetric, unreactive, bilateral mydriasis with changes suggestive of ischemic optic neuritis on funduscopv.

The blood test performed in the emergency department revealed a normocytic anemia (hemoglobin, 10.7 g/dL) and an ESR of 23 mm/h. Cerebral computed tomography showed no relevant abnormalities. On a suspicion of TA, biopsy of the temporal artery was performed and treatment was started with intravenous methylprednisolone at a dose of 250 mg every 6 hours.

Histological study of the artery showed a thickened wall with a moderate chronic inflammatory infiltrate in the media and adventitia of the vessel, composed of lymphocytes, histiocytes, occasional eosinophils, and occasional images suggestive of giant cells (Figure 1).

Two days after starting the treatment, the patient presented intense pain in the tongue, leading to difficulty moving the tongue, swallowing, and speaking. On examination, there was a large, well-defined, deep, excavated ulcer with a clean base and that was not infiltrated on palpation (Figure 2); it was very painful.

On a repeat blood test, the ESR had risen to 88 mm/h, with no other abnormalities.

Biopsy of the tongue lesion showed a deep ulcer that reached the skeletal muscle tissue, with fibrosis and images of myocyte necrosis, suggestive of ischemia (Figure 3).
severity, and it occurs in a subgroup of older patients with a higher incidence of loss of vision and a mortality of up to 40%. Still less common is involvement of the tongue, in the form of pain, stiffness, ulceration, or extensive necrosis.6,7

When the diagnosis is suspected, TA must be treated rapidly to avoid irreversible complications, particularly complete loss of vision. TA usually responds well to high doses of corticosteroids. The ischemic disorders, including those of the skin, can appear at any time in the course of the disease, particularly during the tapering of steroid treatment;6 these patients must therefore remain on treatment for long periods, sometimes for years or even for life.

TA must be included in the differential diagnosis of tongue disorders in elderly patients with heterogeneous clinical presentations with multiple, nonspecific symptoms with no other apparent cause.

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Conflicts of interest
The authors declare no conflict of interest

References
To the Editor:

Extramammary Paget disease (EPD), first described by Crocker in 1889, is a rare intraepithelial neoplasia of regions of the skin rich in apocrine glands. The lesions present clinically as erythematous scaly or slightly pruriginous plaques, and histological studies show cells with large cytoplasm and prominent nucleoli throughout the epidermis. In immunohistochemical studies they test positive for carcinoembryonic antigen (CEA), epithelial membrane antigen (EMA), and high molecular weight cytokeratins—findings that allow differential diagnosis from Bowen disease or pagetoid melanoma. The histogenesis of EPD is the subject of debate, with suggestions that it could arise from pluripotent epidermal cells with subsequent glandular differentiation. The lesions have traditionally been described in 3 subtypes: exclusively cutaneous; with an associated adnexal carcinoma; or with a visceral neoplasia. The prognosis varies according to the subgroup.

We present 2 new cases of EPD treated by Mohs micrographic surgery (MMS).

The patients were 2 men aged 74 and 80 years old, both consulting for plaques, one in the axillary region and the other in the pubic area, present for 5 months and 2 years respectively, and refractory to treatment with topical corticosteroids (Figures 1 and 2). Clinically these were asymptomatic, noninfiltrated erythematous plaques of a pearly appearance. Full examination produced no evidence of other suspicious skin lesions or local swollen lymph nodes, and no further spread was detected. The results of skin biopsies were consistent with EPD (Figure 3) with positive immunostaining for cytokeratins 8 and 18, cell adhesion molecule 5.2, CEA, and EMA. They tested negative for S-100 and human melanoma black 45. Surgery was undertaken by deferred CMM in 2 and 3 stages, respectively (margins of 2 cm of perilesional tissue in the first stage). Both patients underwent reconstruction of the postexcisional defect with advancement plasty and direct closure in layers, and there were no signs of local recurrence 14 and 10 months later, respectively.

EPD is a rare disease where 98% of cases occur in the genital or anoperineal region, with the axillary region as the most common extragenital site. Association with internal neoplasia (12%-20%) is most common in perianal EPD, with rates of between 15% and 45%.

There are no clearly established guidelines for treatment (as is also the case for diagnosis and follow-up), but surgical excision with wide margins or MMS are the techniques of choice when there is no association with underlying neoplasia. MMS is a treatment option for skin tumors that includes histological monitoring of the surgical margins of the tumor prior to reconstruction. There are 2 modes: conventional MMS where tissue is frozen and subjected to histological evaluation immediately following surgery, and deferred MMS, where the tissue is embedded in paraffin for later study.
The most extensive series to date was published in 2004, and involved a retrospective cohort study of 27 cases of EPD treated with MMS. The study examined 19 patients with primary EPD and 8 with recurrent EPD following initial surgery. The recurrence rate was 16% after 58 months of postoperative follow-up for primary tumors, compared with 50% after 28 months of follow-up in patients with recurrent EPD. This suggested that EPD are more aggressive, probably due to the multicentric location of these recurrent tumors.

The more extensive second series of EPD treated with MMS included 95 patients—80 treated with wide surgical excision and 15 with MMS. Statistically significant results were obtained after a period of follow-up of between 24 and 65 months, with recurrence of 22% for conventional surgery compared with 8% for MMS.

According to published data, recurrence with MMS ranges from 8% to 26%, compared with 33% to 60% for wide surgical excision (3-5 cm margins of healthy perilesional tissue). However, recurrence with MMS may be higher than 50% when dealing with a recurrent tumor.

Adjuvant lymphadenectomy in not routinely recommended unless there are palpable lymph nodes as increased overall survival has not been demonstrated.

When MMS cannot be used, various other techniques have been tried in an effort to determine the tumor margins preoperatively, including multiple scouting biopsies, photodynamic mapping, and fluorescein-aided visualization. When complete excision is not possible other alternatives are described in the literature, including radiotherapy, topical or oral chemotherapy, CO2 laser therapy, or topical imiquimod.

In conclusion, despite the uncommon nature of this disease, it must be considered in all patients presenting slow-developing erythematous scaly plaques in areas rich in apocrine glands. MMS has achieved good results in the treatment of EPD with a lower rate of recurrence than wide surgical excision, and so can be considered the treatment of choice at the present time.

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Conflicts of Interest
The authors declare no conflicts of interest.

References
To the Editor:

Doxorubicin is a chemotherapy agent of the anthracycline group. It is effective in many solid and hematological tumors, although use is limited by adverse effects—above all cardiotoxicity and myelosuppression. Use of pegylated liposomal doxorubicin (PLD) has recently become more common as it is effective against Kaposi sarcoma and ovarian cancer. This form of the drug has fewer adverse effects, but marked cutaneous toxicity still limits the dosage prescribed. Common cutaneous reactions include palmoplantar erythrodysesthesia (“hand-foot” syndrome) and stomatitis, and a diffuse follicular eruption or intertriginous rash is also highly characteristic of PLD use.

We present a new case of an intertriginous rash caused by PLD in a 53-year-old woman with a history of clear cell ovarian cancer and histopathology findings that indicate epidermal dysmaturation. Only 3 similar cases including histopathological studies have been found in the dermatological literature.

The patient was a 53-year-old woman with a history including depression, fibrocystic breast disease, lumbar and sciatic pain from herniated discs L4-L5 and L5-S1, cholecystectomy, and appendectomy. She was admitted for left popliteal deep vein thrombosis. Abdominal-pelvic computed tomography (CT) revealed a lobulated mass was observed in the pelvis minor with cancer antigen (CA) 15.3 levels of 189.4 U/mL (normal values: 0.0-38.6 U/mL) and CA 125 levels of 23.5 U/mL (normal values: 0.0-30.0 U/mL). A total hysterectomy, double adnexitomy, and partial omentectomy were performed. A left adnexal tumor of 8 cm in diameter was found and histopathology showed a poorly differentiated clear cell carcinoma. The postsurgical thoracic abdominal and pelvic CT was normal, but CA 15.3 values of 54 U/mL were found. As this was a stage 1A cancer, adjuvant chemotherapy was initiated with 4 cycles of paclitaxel and carboplatin, but CA 15.3 levels rose to 72 U/mL. A further CT was normal, but the positron emission tomography showed an area of intense uptake suggestive of an adenopathic conglomerate in the paraaortic region. A new course of therapy was started with PLD 50 mg/m² every 4 weeks.

Three weeks after the second cycle of PLD the patient developed a pruriginous rash in the skin folds that was treated with 0.1% methylprednisolone aceponate emulsion for 10 days. The patient consulted at this point, presenting hyperpigmented plaques with scaly erythematous erosive and crusty areas on the axillas, groin, and waist (Figure 1).

A biopsy was taken from one of the lesions in the left axilla showing discrete hyperkeratosis and papillomatosis of the epidermis. There was a noticeable increase in size of the keratinocytes in the basal layer and middle layers, with enlarged atypical nuclei, occasional double nuclei, prominent nucleoli, and mitosis. Inflammatory infiltrate was present in a perivascular distribution in the middle papillary dermis. The infiltrate consisted of lymphocytes and scant neutrophils. This was in contact with the basal layer in some areas causing discrete disruptions and even penetrated into the epidermis in small groups (Figures 2 and 3).

A diagnosis was made of intertriginous rash with interphase dermatitis and epidermal dysmaturation caused by PLD, and treatment with the drug was continued at a reduced dosage of 40 mg/m². There was no recurrence of the complaint following the third infusion.

PLD frequently causes cutaneous toxicity. The most common reaction is palmoplantar erythrodysesthesia. This occurs in a third of all patients and consists of the development of erythematous lesions on the palms and plantar surfaces, accompanied by a sensation of dysesthesia. There can also be a recall reaction in areas were sunburn, radiotherapy, or extravasation of cytostatic agents has occurred previously. Other reported effects include...
Although there are many reported cases of PLD inducing a similar intertriginous rash,\textsuperscript{4,5} we have only found 3 articles describing the histopathological findings (Table).\textsuperscript{6-8} The condition is denoted “dermatitis or an intertrigo-like eruption” in order to distinguish it as an independent morphological entity, even though the pathogenic mechanism may be identical to that of “hand-foot syndrome.”\textsuperscript{5,8} Erythematous plaques appear several weeks after the last infusion in all cases of treatment with PLD, often producing bilateral erosive, pruriginous or painful areas on the axillas, groin, and areas of friction with clothing. Histopathological study shows an interphase reaction with epidermal dysmaturation (cytological atypia with apoptotic/dyskeratotic keratinocytes). Epidermal dysmaturation often presents during treatment with other chemotherapy agents like cyclophosphamide,\textsuperscript{10} and there have been many cases published recently of PLD-induced rashes with this histological pattern.\textsuperscript{7,11} As in our case, reducing the drug dosage resolved the skin lesions leaving some residual postinflammatory hyperpigmentation but no subsequent recurrence.\textsuperscript{6-8}

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Conflicts of Interest
The authors declare no conflicts of interest.

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<table>
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<th>Table. Patients With Intertriginous Rash Caused by PLD and Histopathological Study</th>
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<td>Skelton et al\textsuperscript{a}</td>
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<td>English III et al\textsuperscript{7}</td>
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<td>Korver et al\textsuperscript{b}</td>
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<td>Monteagudo et al (present case)</td>
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\textsuperscript{a} Interval between the last infusion of the drug and appearance of the rash.
W: woman.

Merkel Cell Carcinoma at a Site of Vaccination

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To the Editor:

Adverse skin reactions from vaccination are very varied and can be local or generalized. Immediately after immunization, erythema, edema, pain, and induration may occur exclusively on the site of the injection, and these disappear spontaneously. Less frequently, papules or nodules appear that can persist for months or even years, consisting of nonspecific granulomatous or lymphoid reactions.1,2

Various tumors have also been described on the site of vaccine injections: basal cell carcinoma, squamous cell carcinoma, malignant melanoma, malignant fibrous histiocytoma, dermatofibrosarcoma protuberans (including the pigmented variant, Bednar tumor), dermatofibroma, and marginal zone B-cell lymphoma. The delay between vaccination and the appearance of the tumor varies widely, from days in the case of lymphomas, to more than 30 years in many patients with basal cell carcinoma.3-5

In this letter we report the case of an 84-year-old man who consulted with a tumor on the right arm that appeared a week after receiving an influenza vaccination in the same location. Histopathological and immunohistochemical studies provided the basis for a diagnosis of Merkel cell carcinoma (MCC).

The patient was an 84-year-old man with a history of Parkinson disease, referred to the Dermatology Department because of a fast-growing asymptomatic lesion in the right deltoid region present for 2 months. According to the patient and his family, the lesion first appeared on the site of the influenza vaccination received a week previously during the 2007 vaccination campaign (trivalent vaccine of inactive and fractionated viruses containing the following antigens: A/Solomon Islands/3/2006 [H1N1]-like strain, A/Wisconsin/67/2005 [H3N2]-like strain, and B/Malaysia/2506/2004-like strain). His physician initially diagnosed an abscess caused by administration of the vaccine, and prescribed oral antibiotics prior to draining.

Examination revealed a hard and poorly defined tumor, measuring 5 cm ×3 cm, located on the external surface of the right arm. The tumor surface showed many violaceous dome-shaped nodules (Figure).

A biopsy was taken to confirm a provisional diagnosis of pseudolymphoma or lymphoma caused by the vaccination and the ensuing histopathological study showed a tumoral infiltration of the dermis by rounded monomorphic cells of medium size with scant cytoplasm, round nuclei, and small nucleoli, forming solid masses or small trabecular structures. The mitotic index was high. Immunohistochemical study proved positive for cytokeratin 20, neuronal specific enolase, chromogranin A, and chromogranin B. There was no immunoreactivity to protein S–100, leukocyte common antigen, CD20, CD3, cytokeratin 7, or thyroid transcription factor 1. A diagnosis of MCC was made and the patient was referred to the Oncology Department.

MCC—first described by Toker in 1972—is a rare malignant cutaneous tumor of neuroendocrinal origin with poor prognosis and rapid progression. It tends to present as a fast-growing nodular erythematous lesion on the head, neck, or limbs in people aged over 65 years.6,7

The pathogenesis is unknown although various factors have been implicated: a) ultraviolet radiation—a greater
incidence in areas exposed to sunlight in patients with a history of basal or squamous cell carcinoma; b) other carcinogens—frequent occurrence in areas of irradiation, erythema ab igne, or following chronic exposure to arsenic; c) immunosuppression—from treatment in a liver or heart transplant setting or rheumatic diseases; and in patients with hematologic neoplasias or infection with the human immunodeficiency virus (HIV); d) cases described in patients with congenital ectodermal dysplasia or Cowden disease; and e) oncogenic viruses—although the role of Epstein-Barr virus has not been proven.8-10

In conclusion, we present a case of MCC located at a site of vaccination. As we have encountered no similar cases in the literature to date—even though the target population for anti-influenza vaccination overlaps extensively with those at greater risk of developing MCC (individuals aged 65 years or older and immunodepressed patients)—we believe this is a case of simple coincidence. However, the close temporal relationship could indicate that vaccination causes a local immune alteration through an unknown pathogenic mechanism that would facilitate the development of MCC patients with a predisposition to the disease.

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Conflicts of Interest
The authors declare no conflicts of interest.

References

Figure 1. Poorly defined tumor 5 cm × 3 cm in diameter, with multiple violaceous nodules on the surface, located on the outer surface of the right arm.

Eruptive Clear Cell Acanthoma
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To the Editor:
Clear cell acanthoma (CCA) was described by Degos et al1 in 1962. They suggested that this was a benign epithelial tumor of epidermal origin rather than a reactive hyperplasia of inflammatory origin, although they questioned this affirmation 8 years later. In recent years, several authors have vindicated the inflammatory nature of this lesion, and a number of writers view the condition as a localized form of psoriasis.2,3

Eruptive Clear Cell Acanthoma
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To the Editor:
Clear cell acanthoma (CCA) was described by Degos et al1 in 1962. They suggested that this was a benign epithelial tumor of epidermal origin rather than a reactive hyperplasia of inflammatory origin, although they questioned this affirmation 8 years later. In recent years, several authors have vindicated the inflammatory nature of this lesion, and a number of writers view the condition as a localized form of psoriasis.2,3
CCA is generally solitary and multiple forms are uncommon. However, there is one isolated description in the medical literature of an eruptive form of the disease with more than 400 lesions.

Our patient was a 32-year-old woman with no relevant history, except for the presence of a crusty plaque on the occipital zone of the scalp during adolescence that disappeared spontaneously several years ago. The family history included a father and brother with psoriasis. The patient consulted for the progressive appearance of multiple erythematous papules on her legs and buttocks over the last 20 years (Figures 1 and 2). These were of an elastic consistency, with some slightly scaly lesions. The patient mentioned occasional bleeding when wearing tight trousers. She reported the appearance of similar papules on the trunk and arms over the course of the last year.

A diagnosis of lichen myxedematosus was proposed and biopsies taken of 3 papules, all with similar histopathological findings. Each biopsy revealed a psoriasiform hyperplasia with large cells and clear cytoplasm (Figure 3) that proved intensely periodic-acid-Schiff positive. The boundary with the adjacent healthy epidermis was very well defined in all 3 lesions.

CCA is generally solitary and is most often located on the legs, although the case described by Degos et al. was on the abdomen. The first case of multiple CCA was described in 1964 and some 30 articles have been published since then. Most of the cases described were CCA patients with between 2 and 20 lesions on the legs. The lesions sometimes appeared in association with ichthyosis, varicose veins, psoriasis, or xerotic skin, although whether this is coincidental has neither been confirmed or disproved. There is also one very interesting case of multiple CCA in a mother and her 2 children, but, as far as we are aware, this is the only familial example described.

These 30 cases include isolated incidences of patients with more than 100 lesions distributed across the trunk and limbs. However, we have only found one case similar to ours in the medical literature in which a woman had more than 400 lesions that appeared progressively.

The etiology of CCA is far from established, and even Degos recognized that the neoplastic nature of the lesions was still not fully confirmed 8 years after his initial description of the condition. Since then, many authors have suggested that CCA shows a psoriasiform reaction pattern, generally on the basis of the following 3 criteria:

1. Many of the CCA described are located within other inflammatory or reactive lesions, either stasis dermatitis, pilonidal cysts or psoriasis plaques.
2. CCA and psoriasis produce very similar histopathological findings and dermatoscopic patterns.
3. A recent study proved that the results of immunohistochemical analysis were similar to those for the normal epidermis and for psoriasis.
In view of the above it is possible to posit that our patient was simply experiencing an exceptional manifestation of familial psoriasis.

The patient reported that private phototherapy sessions several years ago had led to apparent improvements in the lesion, although they had later reappeared. We initially administered broad-band UVB phototherapy with no response. We then proposed PUVA treatment, but the patient has so far refused any further treatment.

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Conflicts of Interest
The authors declare no conflicts of interest.

References

Allergic Contact Dermatitis to Hydrocortisone as a Complication of Tattoo Care

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To the Editor:
Many complications have been described in the context of tattooing, including various types of infection, the appearance of tumors, granulomatous reactions, and contact allergy.1 Allergic contact dermatitis (ACD) has been described in these cases in relation to some of the pigments used, especially the red color. However, the person with the tattoo may also use many products to care for the tattoo—corticosteroids, antibiotics, healing or antiseptic ointments—that may provoke ACD. We describe 2 cases of ACD from hydrocortisone use in patients who applied an ointment containing hydrocortisone recommended by the tattooist for the localized care of their tattoos.

The first patient was a 21-year-old man who attended the emergency department with severe eczema on the left leg. The lesions were located around a permanent black tattoo created 10 days previously. The patient stated the tattoo was to be completed in 2 sessions and that the upper part was incomplete (Figure 1A). He applied Terra Cortril ointment (hydrocortisone and oxytetracycline in petroleum jelly as excipient; Farmasa Sierra Laboratorios) as recommended by the tattooist following the tattoo session, and the skin lesions appeared a week later. The emergency department prescribed Diprogenta cream (betamethasone and gentamicin; Shering Plough) and Dexa Tavegil (dexamethasone and clemastine; Novartis Consumer Health) and the lesions healed. Despite the recommendations, 2 months later the patient decided to complete the tattoo and apply Terra Cortril ointment, causing the skin lesions to return 2 days later (Figure 1B). Treatment with Diprogenta once more produced a good clinical response. Patch testing for contact dermatitis was performed with the Spanish Group for Research Into Dermatitis and Skin Allergies (GEIDAC) standard battery—showing a
positive reaction to tixocortol pivalate (+++D2, +++D4, +++D7); our series of corticosteroids (Table)—testing positive for 2.5 alcohol excipient (++D2, +++D4, +++D7) and hydrocortisone 17-butyrate (++D2, +++D4, +++D7) (Figure 1C); and a patch with 5% tetracycline in petroleum jelly—which showed no reaction.

The second patient was a 19-year-old woman who attended the Emergency department with eczematous lesions in the lumbo-sacral region, at the site of a tattoo completed 3 days previously (Figure 2). The patient related the inflammation to the application of Terra Cortril ointment recommended by the tattooist. Dexa Tavegil and Diprogenta were prescribed with good clinical response, and patch tests were performed with the standard battery, corticosteroids and 5% tetracycline in petroleum jelly, with results identical to the first case: tixocortol pivalate (+ day 2 [D2], ++ day 4 [D4], +++ day 7 [D7]) hydrocortisone 2.5 alcohol excipient (+D2, ++D4, +++D7) and hydrocortisone 17-butyrate (+/−D2, +D4, +D7).

Table 1. Battery of Corticosteroids Used in the Skin Allergy Section of the Consorcio Hospital General Universitario de Valencia, Spain

<table>
<thead>
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<th>No.</th>
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<tr>
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<td>Betamethasone dipropionate 0.5% pj</td>
<td>pj</td>
</tr>
<tr>
<td>2</td>
<td>Clobetasol 17-propionate 1% pj</td>
<td>pj</td>
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<tr>
<td>3</td>
<td>Betamethasone 17-valerate 1% pj</td>
<td>pj</td>
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<td>4</td>
<td>Triamcinolone acetonide 1% pj</td>
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<td>5</td>
<td>Hydrocortisone 17-butyrate 1% alc</td>
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<td>6</td>
<td>Alclometasone 17:21-dipropionate 1% pj</td>
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<td>7</td>
<td>Dexamethasone 21-phosphate 1% pj</td>
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<tr>
<td>8</td>
<td>Prednicarbate 1% pj</td>
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<tr>
<td>9</td>
<td>Prednisolone 5% pj</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Dexamethasone 21-acetate 1% pj</td>
<td>pj</td>
</tr>
<tr>
<td>11</td>
<td>Fluocinolone 0.25% pj</td>
<td>pj</td>
</tr>
<tr>
<td>12</td>
<td>Betamethasone base 1% pj</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>Dexamethasone base 1% pj</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Hydrocortisone acetate 25% pj</td>
<td>pj</td>
</tr>
<tr>
<td>15</td>
<td>Hydrocortisone 2.5% alc</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Hydrocortisone base 25% pj</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>Triamcinolone acetonide 5% pj</td>
<td>pj</td>
</tr>
<tr>
<td>18</td>
<td>Betamethasone 17-valerate 5% pj</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: alc: alcohol; pj: petroleum jelly.
Although the use of topical corticosteroids is extremely common, it is rare to find positive patch tests for these. In Spain, incidence of sensitivity to corticosteroids is less than 1%.

Hydrocortisone belongs to group A of the Coopman classification. This system is based on different substitutions on the D ring or in the C20-C21 position of the lateral chain of the steroid molecule, and attempts to explain cross-reactions between corticosteroids. Three corticosteroids have been described as contact allergy markers: tixocortol pivalate—as a group A marker; budesonide—as a group B marker; and hydrocortisone 17-butyrate—as a group D marker. Allergic reactions to group C corticosteroids are extremely uncommon. Most cross-reactions occur between corticosteroids in the same group, and also between group A and D. In our cases cross-reaction was observed between hydrocortisone (group A) and hydrocortisone 17-butyrate (group D), however, betamethasone and dexamethasone—both from group C—were well tolerated by both patients.

When a corticosteroid responsible for a contact allergy is administered orally, dermatitis is reactivated in the affected locations. Immediate reactions such as urticaria and anaphylaxis have been described, but these are uncommon.

Contact allergy to corticosteroids must be suspected when there is no improvement in chronic dermatitis. The existence of ulcers on the legs, stasis dermatitis, chronic dermatitis, and multiple drug sensitivity are considered risk factors in developing a contact allergy to corticosteroids. In our experience many patients use creams containing corticosteroids in caring for damaged skin following the tattooing process. In conclusion, on the basis of our observations, we suggest tattoos be considered among the group of risk factors for developing contact sensitivity to corticosteroids, in this particular case, to hydrocortisone.

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Conflicts of Interest
The authors declare no conflicts of interest.

References