To the Editor:

Leprosy (Hansen disease) is a slowly progressive, infectious, chronic granulomatous disease caused by *Mycobacterium leprae*, it can be complicated by the appearance of lepra reactions.\(^1\) The skin and superficial peripheral nerves are most frequently affected.\(^1\)

Although its worldwide prevalence has fallen,\(^1\) leprosy continues to be a health problem due to its ability to cause permanent deformities. Bone disease is one of the principal prognostic factors\(^2\) and occurs in 15% to 29% of patients.\(^3\) Higher percentages (40%-95%) have been reported in the literature,\(^2,4\) in part because such data come from subjects in leper colonies and are therefore selected cases.\(^5\)

We present the case of a 34-year-old Nigerian man diagnosed with lepromatous leprosy (multibacillary) in August 2004 after clinical and histological study of multiple hypopigmented lesions on the trunk and limbs (Figure 1). The patient then did not return to the outpatient clinic until January 2006, when he was admitted for a type 2 lepra reaction, which resolved after treatment with oral corticosteroids. During the admission, a sensory-motor neuropathy of the cubital, median, and common peroneal nerves was detected, and areas of bone damage (acroosteolysis and bone cysts) in the distal phalanges of several fingers. Specific treatment was started with multidrug therapy for multibacillary leprosy (rifampicin, dapsone, clofazimine) and also with daily doses of vitamin D, oral calcium, and intramuscular calcitonin in order to halt the bone disease.

After discharge, the disease remained well controlled until June 2008, when he was seen in urgent outpatient consultation for a history of several days of swelling of right foot and fever up to 38°C. Physical examination revealed marked edema on the dorsum of the foot, with no crepitation on palpation. The peripheral pulses were present, but the third toe was a violaceous-black color and, on the sole, there was an ulcer with a dirty, exudative appearance under the head of the third metatarsal. An x-ray of the foot was requested, which showed signs of osteomyelitis and dislocation of the metatarsophalangeal joint of the third toe (Figure 2). In view of these findings, the orthopedic department considered it necessary to perform complete amputation of that toe (metatarsus and phalanges), together with systemic antibiotic treatment to be adjusted according to the results of the bone culture (positive for *Escherichia coli* and *Klebsiella* species).

Histological study of the surgical specimen showed signs of osteomyelitis, but without granulomas and with no *M. leprae* on Ziehl-Neelsen stain. The clinical course has been very satisfactory, and the use of a vacuum-assisted wound care system has achieved complete closure of the amputated region by second intention (Figure 3).

Leprous bone lesions mainly affect the hands and feet and, in more advanced cases, the bones of the cranium.
or axial skeleton. They may be divided into specific, nonspecific, and osteoporotic.

The specific changes are the direct result of bone invasion by *M. leprae*. They develop in bacteriologically positive patients and present mainly as geodes or bone cysts.

Nonspecific changes are much more common (approximately 2-fold) than specific changes. They are divided into 2 large groups that may overlap:

1. Neurotrophic lesions. This is the largest group of leprous bone lesions. The lesions are due to the characteristic neurological damage of the disease, leading to hypoesthesia-anesthesia, secondary metabolic alterations and disturbances of the autonomic nervous system, and deficient vascularization, favoring the appearance of trophic ulcers and recurrent trauma.

2. Lesions due to superinfection.

These usually present as acroosteolysis or bone reabsorption in the distal phalanges of the fingers and toes. Other possible clinical manifestations include acute and chronic osteomyelitis, dislocations, and spontaneous fractures.

Finally, osteoporosis is the second most common manifestation after the nonspecific changes. It can be caused by recurrent trauma or increased bone remodeling in the proximity of an active lesion. Hypogonadism and testicular atrophy due to infiltration by *M. leprae* may also be involved.

Leprous bone disease can progress even several years after having completed specific treatment for the disease, meaning that such treatment is necessary, but that it is not sufficient to cure the bone lesions. It is essential to achieve an early diagnosis and treatment of possible complications, and complete physical and radiologic examination must therefore be performed both at the time of diagnosis and at the periodic follow-ups. The reported benefit of the administration of calcium, vitamin D, and bisphosphonates is a matter of debate. In our case, due to the absence of other, well-founded therapeutic alternatives, we decided to use these treatments.

Patients should be instructed to examine their hands and feet periodically to search for any small wounds and to take adequate precautions both at home and at work. In our case, the episode coincided with the start of work in the building trade, which was probably the cause of recurrent trauma (favored by the sensory changes in the region), leading to the appearance of the plantar ulcer, which, in turn, was the trigger for the onset of cellulitis and osteomyelitis.

Correspondence:
Zuriñe Martínez de Lagrán  
Servicio de Dermatología, Hospital Santiago Apóstol  
Calle Olaguibel, 29, 01004 Vitoria, Spain  
Telephone: 945 00 77 45  
Fax: 945 00 79 01  
ZURINE.MARTINEZDELAGRANALVAREZDEARCAYA@osakidetza.net

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References
Collision Tumor Detected by Dermoscopy

I. Fernández-Canedo,* N. Blázquez,* M. de Troya,* and T. Pérez-Salguerob

*Servicio de Dermatología and *Servicio de Anatomía Patológica, Hospital Costa del Sol, Marbella, Málaga, Spain

To the Editor:

Collision tumors and combination tumors are terms used to refer to the association of various types of tumor in time and space. Although the majority are not of clinical importance, they can sometimes be significant, as they may combine a benign lesion with a malignant tumor. The clinical diagnosis in these cases is usually extremely difficult, particularly if one of the lesions is pigmented. Dermoscopy is a noninvasive diagnostic method that enables us to visualize morphologic structures not visible to the human eye, helping us to establish the diagnosis in this type of tumor.

We present the case of an 80-year-old man with a history of systemic hypertension; he reported occupational exposure to the sun and presented skin phototype III.

He was seen in our outpatient clinic for a long-standing pigmented lesion on the back; the lesion had changed color in the months prior to consultation. On examination, the patient presented an asymmetric, heterochromous pigmented lesion, slightly elevated on palpation, with a maximum diameter of approximately 1.5 cm. There were no other skin lesions and no palpable locoregional lymph nodes. Dermoscopic study revealed an asymmetric pigmented lesion with 4 different colors (light brown, dark brown, pink, and blue-gray). There were no criteria of a melanocytic lesion.1 A large part of the lesion was occupied by a blue-gray pigment stain, close to which there were large ovoid nests and maple-leaf structures, as well as a small area of ulceration and linear vessels (Figure 1). The rest of the lesion showed a homogeneous, brown pigment stain, in which keratin plugs and milia-like cysts could be seen. Interestingly, localized blue-gray spots could be seen around the borders of this homogeneous stain (Figure 2).

Histological study of the surgical specimen revealed 2 types of lesion in continuity. First there were nests of basaloid cells with peripheral palisading and, second, epidermal acanthosis with infundibular cysts. Beneath this epidermal acanthosis there was a band-like infiltrate of lymphocytes...
in the papillary dermis, with occasional melanophages (Figure 3). Based on these findings, a diagnosis of collision tumor (basal cell carcinoma and seborrheic keratosis with regressive changes) was established.

The pathogenesis of such collision tumors is unknown, although there are 2 hypotheses: the first suggests that different tumors can arise at the same site in an area of damaged skin, a process known as field cancerization; the second maintains that these collision tumors develop due to an interaction between the different parts of the tumor, in a way that one of the tumors stimulates the development of a second tumor through a paracrine effect. Clinical diagnosis is usually extremely difficult. The development of dermoscopy has helped to improve diagnostic accuracy, as it incorporates a series of distinctive dermoscopic features that, in the case of seborrheic keratosis, includes milia-like cysts, keratin plugs, fissures and crests, fingerprint-like structures, hairpin vessels, pigment network-like structures, and a sharp border. According to Menzies, the dermoscopic features of basal cell carcinoma are the absence of a pigmented network and the presence of at least one of the following: large blue-gray ovoid nests, multiple blue-gray globules, maple leaf-like areas, spoke-wheel areas, branching telangiectasias, and ulceration.

Our case presented large ovoid nests, maple leaf-like areas, ulceration, and telangiectasias specific to basal cell carcinoma, and also keratin plugs and milia-like cysts characteristic of seborrheic keratosis. In addition, at the border of the seborrheic keratosis, there was a coarsely granular blue-gray pattern characteristic of lichenoid keratosis. For some authors, lichenoid keratosis represents an immunological or regressive response of a pre-existing epidermal lesion, usually solar lentigo or, less commonly, seborrheic keratosis. Lichenoid keratosis also has certain dermoscopic features, such as localized or diffuse, coarse, bluish-gray granules without the features of a melanocytic lesion.

From a histological point of view, the large tumor masses of basal cell carcinoma correspond to the large, blue-gray, ovoid nests, the infundibular cysts to the keratin plugs of seborrheic keratosis, and the inflammatory infiltrate in the papillary dermis with melanophages to the coarse blue-gray granules of lichenoid keratosis.

There is no doubt that dermoscopy made it possible to reach the correct diagnosis in this case. In addition, it enabled us to alert the pathologists so that the histological sections of the excision biopsy could be orientated in such a way as to establish the most accurate diagnosis possible.

Correspondence:
Inés Fernández Canedo
Servicio de Dermatología y Anatomía Patológica
Hospital Costa del Sol
Carretera Nacional 340, Km 187
29600 Marbella, Málaga, Spain
inesbier@gmail.com

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The authors declare no conflicts of interest.

References
Eccrine Spiradenoma in a Zosteriform Distribution: Presentation of a Case

I. Alfonso-Trujillo, E. Arteaga-Hernández, and J.C. Pérez-Suárez
Hospital Clínico Quirúrgico Universitario Hermanos Ameijeiras, Ciudad de La Habana, Cuba

To the Editor:
Eccrine spiradenoma is a rare benign adnexal tumor of the eccrine sweat glands; very rarely it can undergo malignant change. It usually presents as a solitary nodule and, less commonly, as multiple lesions with a zosteriform distribution. The clinical diagnosis is often confused with neuromas, leiomyomas, neurilemmoma, neurofibroma, leiomyosarcoma, endometrioma, hidradenocarcinoma of the sweat glands, glomus tumors, lipoma, angiolipoma, dermatofibroma, hemangioma, angioleiomyoma, cavernous hemangioma, or lymphangioma.

There has been a significant increase in the number of cases reported in the literature in recent years, leading to the suggestion that this diagnosis is suspected more often; this will also lead to greater knowledge of its clinical features.

The patient was a 17-year-old woman with no past history of interest until 7 years earlier, when she started to develop tender, slightly bluish and mildly erythematous nodular lesions, that were round and had very clear margins. They were soft, with a smooth surface, and were about the size of a lentil (3-5 mm). The lesions were in a linear distribution that started in the left popliteal fossa and extended along the dorsal aspect of the thigh up to the inferior part of the ipsilateral gluteal region; 8 lesions were found on dermatologic examination (Figure 1). During the 7-year course of the disorder, the patient had been seen in various hospitals, though the diagnosis had not been reached. The patient therefore came to our hospital where, from a clinical point of view, we considered the following diagnoses: neuromas, neurilemmoma, and neurofibroma. Surgical excision of a nodule was performed for histological study. The histological diagnosis was benign eccrine spiradenoma (Figures 2 and 3); other disorders that could have caused clinical diagnostic confusion were excluded. All the lesions were removed surgically.
In 1896 Unna coined the term spiradenoma to describe a benign adenoma of the sweat gland arising from the secretory coil of the gland, in contrast to the syringoadenoma, which arises from the ducts.3-5 In 1956, Kersting and Helwig described this condition, referring to it as a rare benign tumor that develops from the secretory and ductal parts of the sweat gland.3-5

In our patient, the condition started when she was 10 years old, some years earlier than those reported as most common in the literature reviewed.3,4 The literature suggests that this disorder usually presents in adolescents and young adults between 15 and 35 years of age, although congenital, familial, and multiple cases have been reported, and also cases related to other benign tumors of sweat glands with autosomal dominant transmission.3-5 This is a rare disease, and much more so in elderly patients. However, in 1998, Senol et al reported the case of a 60-year-old man with a superficial ulcer; the main symptom was spontaneous bleeding of the lesion rather than pain, and the diagnosis was confirmed by histological study.4,5

Although the disease affects both sexes, it is more common in women, with a ratio of 2 to 1.5

In the present case the nodules were situated on the posterior aspect of the left thigh. Other authors indicate that the lesions usually present on the anterior aspect of the trunk or upper limbs, but cases have been reported on the head (scalp, nasal cavity, and pinna of the ear); it is rare to find them on the palms of the hands, in the axillas, or on the areolae, perineum, or genitalia, as these are areas in which there is a predominance of apocrine glands.3 There are no reports of this tumor affecting a mucocutaneous junction or the nail bed.3-5

Our patient presented multiple, subcutaneous, nodular lesions that were very small (3-5 mm) and tender, and showed a linear (zosteriform) distribution. A similar condition to that of this patient has been reported as a rare form,1-4 though it was described at the same site (dorsal aspect of the thigh). These tumors may be associated with cylindromas and trichoepitheliomas. One case has been reported with multiple lesions with a linear, nevoid distribution affecting the right side of the body from the face to the pubis.1,3-5 The clinical course is chronic and, very rarely, malignant transformation can occur, with the possibility of developing metastases in regional lymph nodes, bone, lung, and brain, and it can be fatal.2,4 In the case presented here, there was no association with any other skin tumor nor was there malignant transformation of the lesions.

There has been a significant increase in the number of cases reported in the literature in recent years.1-3 We would therefore suggest that this diagnosis be kept more in mind. We consider it important to report the present case due to the low frequency of presentation of linear (zosteriform) eccrine spiradenoma and, in particular, because it has not been reported on the dorsal aspect of the thigh.

Correspondence:
Israel Alfonso-Trujillo
Calzada de Managua #1133 e/ Caimán y Quemados, Las Guásimas
Arroyo Naranjo
19320 Ciudad de La Habana, Cuba
israalfonso@infomed.sld.cu

Conflicts of Interest
The authors declare no conflicts of interest.

References
To the Editor:

Seborrheic keratosis is one of the most common benign epidermal tumors in dermatologic clinical practice. Although the association between seborrheic keratosis and other skin tumors was first reported in 1932, its malignant transformation is very rare, with less than 20 published cases. We present the case of a patient with seborrheic keratosis that underwent transformation into an invasive squamous cell carcinoma.

The patient was a 94-year-old woman who was seen in our outpatient clinic for a tumor on the abdomen that had been present for 30 years and that had increased in size over a period of months, causing pain and bleeding. On physical examination, a seborrheic keratosis with a maximum diameter of 12 cm was observed. On this lesion there were several hemorrhagic, lobulated tumors (Figure 1). Complete excision of the lesion was performed, with closure by tissue planes and primary suture under local anesthesia. Microscopic examination revealed different histological patterns within the same lesion (Figures 2 and 3), with images characteristic of ulcerated seborrheic keratosis, areas of transition between seborrheic keratosis and Bowen disease, and zones where Bowen disease infiltrated the dermis (invasive squamous cell carcinoma). The histological diagnosis was of invasive squamous cell carcinoma on seborrheic keratosis. Genotyping for human papillomavirus (HPV) was positive for type 59 in 1 of the 4 blocks sent. The patient remains disease-free after 1 year of follow-up in our clinic.

Seborrheic keratosis is rarely associated with other skin neoplasms such as basal cell or squamous cell carcinoma, Bowen disease, keratoacanthoma, or melanomas; in these cases it is most common to find that the lesion is adjacent to or contiguous with the other tumor.²,³ Malignant degeneration of seborrheic keratosis is very rare⁴ and, when this occurs, it usually develops as Bowen disease and

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**Figure 1.** Squamous cell carcinoma on seborrheic keratosis.

**Figure 2.** The right side of the image shows seborrheic keratosis with acanthosis, intraepidermal bridges, and the transition to Bowen disease, with keratinocyte disorganization and areas of dyskeratosis (hematoxylin-eosin, x10).

**Figure 3.** Infiltration of the dermis by squamous cell carcinoma with atypical, hyperchromatic epithelial cells with mitoses (hematoxylin-eosin, x20).
squamous cell carcinoma\textsuperscript{5,6}, the incidence is higher in men with long-standing lesions situated on the head, neck, or other areas exposed to sunlight.\textsuperscript{7}

The molecular mechanism of this transformation is not fully understood. A number of theories implicate the proteins involved in regulation of the cell cycle, alterations of which could lead to the appearance of other tumors. Carcinoembryonic antigen,\textsuperscript{8} growth hormone,\textsuperscript{9} and proteins p63, BCL2, and BCL6 have also been implicated in the pathogenesis of malignant change.\textsuperscript{10,11} In addition, the role of HPV in the appearance of squamous cell carcinoma is well known. In our case, HPV type 59 was detected in one of the blocks sent for study. This is a strain with a high oncogenic risk, although the viral load in the samples was very low.

In conclusion, rapid growth or transformation of seborrheic keratosis may be a sign of the appearance of a squamous cell carcinoma. In these cases, adequate and complete excision of the lesion is recommended.

Correspondence:
Lucía Carnero González
Servicio de Dermatología
Hospital Santiago Apóstol
C/ Olaguíbel, 29
01004 Vitoria, Álava, Spain
LUCIA.CARNERO@osakidetza.net

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The authors declare no conflicts of interest.

References

Facial Dystrophic Calcinosis Cutis Secondary to Acne

T. Saavedra, F. Mardones, I. Sazunic, and X. Wortsman
Departamento de Dermatología, Hospital Clínico, Universidad de Chile, Santiago, Chile

To the Editor:
Acne is a common condition in the general population, mainly affecting older children and adolescents. Physical sequela such as scarring and pigmentation disorders are often observed. However, other secondary lesions such as cutaneous calcification are occasionally reported in the literature.\textsuperscript{1} Calcinosis cutis occurs due to the deposition of calcium and phosphate salts in the skin and, in general, can develop around localized tissue damage or in association with systemic metabolic disorders. It is classified into 4 groups according to its etiology: dystrophic, metastatic, iatrogenic, and idiopathic; in some cases different mechanisms can coexist.\textsuperscript{2}

We present 2 cases of dystrophic calcinosis cutis of the face as a sequela of inflammatory acne.

The patients were women of 48 and 58 years of age, with no past history of note. Both patients reported that they had had severe inflammatory acne during adolescence, mainly affecting the face, making particular mention of the repetitive traumatic manipulation of the facial lesions. They attended our department for treatment of the residual scars on their faces.
The women presented numerous depressed pinpoint scars and multiple, hard, asymptomatic, skin-colored papules of 2 to 3 mm in diameter (Figures 1 and 2). There were no other significant clinical findings.

Ultrasound was performed of the soft tissues of the papules, showing, in both cases, numerous hyperechogenic foci of calcified appearance, located in the dermis.

Histopathological study of the lesions revealed the presence of calcified nodules in the dermis associated with signs of actinic damage (Figure 3).

Laboratory studies showed no abnormalities of the plasma levels of calcium, phosphate, parathyroid hormone, or the markers of renal function, and the study for connective tissue diseases (antinuclear antibodies, extractable nuclear antigen, scleroderma-70) was negative.

Finally, the diagnosis of facial dystrophic calcinosis cutis secondary to acne was made.

In view of the number, spread, and site of the lesions, it was decided to start medical treatment with diltiazem at a dose of 60 mg a day for a period of 2 months. At the end of this period there was no clinical improvement and, furthermore, the patients reported poor tolerance of the medication; the therapy was therefore withdrawn. In the end, abrasive treatment was prescribed to ameliorate the facial scars.

The deposits of amorphous and insoluble calcium salts in the skin are formed mainly of amorphous calcium hydroxyapatite or phosphate crystals. There appear to be multiple local and systemic mechanisms that lead to the onset of this condition.

In the absence of a tissue lesion, ectopic deposits of calcium salts develop when the calcium phosphate product in plasma exceeds 70 mg/dL. If tissue damage is present, it has been suggested that the following pathogenic phenomena may play a role: increased intracellular calcium concentration, denaturation of proteins that preferentially bind phosphate, genetic mutations of elastic fibers and collagen, and increased \( \gamma \)-carboxyglutamic acid.

The majority of cases of calcinosis cutis are associated with connective tissue diseases. Dystrophic calcinosis cutis is the most common form and develops around localized tissue damage, with no alterations of calcium or phosphate metabolism. In general the patients have a past history of an underlying disease, previous injury, or inflammatory dermatosis.

The majority of cases of calcinosis cutis have a gradual onset and are asymptomatic; however, the history and clinical course of the condition vary mainly according to
the etiology of the calcification. Clinical manifestations will also depend on the underlying disorder (if present), but usually there are multiple, hard, whitish papules, plaques, or nodules with a symmetrical distribution.

Morbidity depends on the extent and site of the cutaneous calcification; joints, muscles, and organs such as the lungs, kidneys, and intestine may also be affected. In addition, vascular deposits of calcium can give rise to distal ischemia and necrosis. Areas of ulceration or the transcutaneous elimination of a whitish-yellow, chalk-like material may be observed, and secondary infection can develop. The therapeutic measures used depend on the underlying disease; in general the outcomes are not very satisfactory and only the results of case reports are available.

Most medical treatments for calcinosis cutis have been described in patients with connective tissue diseases. They include warfarin, colchicine, probenecid, bisphosphonates, minocycline, and diltiazem.4-8 Success has also been reported with other treatment modalities, such as carbon dioxide laser and intralesional corticosteroid injection.9,10 Finally, surgery is a possible option to remove calcium deposits in necrotic or infected tissues.

In conclusion, calcinosis cutis is a rarely reported sequela of acne and represents a therapeutic challenge. Clinical suspicion and appropriate additional tests are required to reach the diagnosis.

Correspondence:
Felipe Mardones Valdivieso
Departamento de Dermatología
Hospital Clínico Universidad de Chile
Santos Dumont, 999 Santiago, Chile
fmardonesv@yahoo.com

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The authors declare no conflicts of interest.

References

Melanoma and Retinoblastoma*

S. Martínez-García, L. Martínez-Pilar, E. Gómez-Moyano, and V. Crespo
Servicio de Dermatología y Venereología, Complejo Hospitalario Universitario Carlos Haya, Málaga, Spain

To the Editor:
Retinoblastoma is an embryonal tumor derived from retina cells that affects 5 in every 100 000 newborns and accounts for 3% of cancers in those children aged less than 15 years. It is the most common type of malignant intraocular tumor in children and the second most common for all age groups after melanoma.1

Most cases are diagnosed in the first 4 years of life. Presentation is unilateral in 60% to 75% of cases, and 60% are classed as sporadic.2 The remaining cases are bilateral and mostly hereditary.

Bilateral forms are caused by a double mutation in the Rb gene on the long arm of chromosome 13.3,4 The

*This case was presented as a poster in the XXXVI National Congress on Dermatology in Barcelona 2008 and was awarded a special mention within the Oncology section.
condition presents incomplete autosomal dominant inheritance with high penetrance.\(^5\)

Fifty-one percent of patients with bilateral retinoblastoma develop another cancer at some point in their life, the most frequent being osteosarcoma, followed by rhabdomyosarcoma, chondrosarcoma, neuroblastoma, glioma, leukemia, melanoma, and other neoplasms including ovarian, breast, lung, and bladder cancers.

We present the case of a 27-year-old man with a body weight of 155 kg, who underwent enucleation of the right eye for retinoblastoma at 16 months old. Later, at 9 years old, he was diagnosed with another retinoblastoma in the right eye that was treated by enucleation and complementary radiotherapy. His medical history includes poorly controlled psoriasis, as the patient did not apply treatment or attend follow-up sessions.

The family history includes a brother who died from bilateral retinoblastoma at 5 years old and a father diagnosed with unilateral retinoblastoma at 50 years old. There was no history of dysplastic nevi in the family.

In an examination during consultation for psoriasis, an abnormal pigmented lesion with a maximum diameter of 2 cm was noticed on the lower back (Figures 1 and 2). The lesion had been present for 8 months. The lesion was surgically removed and diagnosed as an invasive melanoma of Clark level III with a Breslow thickness of 1.3 mm, showing no ulceration or areas of regression. No lymph node involvement was palpated. No sentinel lymph node biopsy was carried out due to the anatomical limitations of the patient. The analysis of tumor spread (computerized tomography of the thorax, abdomen, and pelvis) produced no significant findings.

The link between retinoblastoma and melanoma has been described in the literature although the nature of the relationship between the 2 entities has not been identified.\(^6\)

Attempts have been made to establish a link between the predisposition of patients with retinoblastoma to other cancers and radiotherapy or cycles of cyclophosphamide treatment rather than with any genetic tendency to develop mutations.

There are few reported cases of links between melanoma and retinoblastoma. In 2002, Belt\(^6\) carried out a broad review of the literature and found 35 published cases, but some important contributions have come to light since.

Melanoma presents in between 3% and 25% of patients with hereditary retinoblastoma.\(^7,8\) Cases have been reported of bilateral retinoblastoma and melanoma in patients with no family history of retinoblastoma but with a history of melanoma.\(^9\) We have also found cases of bilateral retinoblastoma with melanoma where there is no family history.\(^1,8\) The risk of developing melanoma in families of patients with retinoblastoma is 10 times greater than among the general population.\(^10\)

The incidence of melanoma increases with age, especially after 20 years of age. Exceptional cases have been reported of melanoma during infancy in patients with retinoblastoma.

The role of radiation in the second carcinoma is not clear. It seems there is increased risk of osteosarcoma and
some forms of brain tumor; although such outcomes have not been demonstrated for melanoma.

The cells of retinoblastoma, melanoma and dysplastic nevus are derived from the neural crest. There are authors who postulate that patients with retinoblastoma and dysplastic nevus syndrome have increased genetic susceptibility to melanoma due to a primary anomaly in the neural crest.

The association between retinoblastoma and melanoma is a controversial issue potentially dependent upon genetic predisposition or the forms of treatment received. Patients with retinoblastoma have an almost 10-fold greater risk of suffering from melanoma than those with no history of retinoblastoma, especially in cases of bilateral or hereditary types. Consequently, close follow-up of these patients is vitally important, especially in patients with associated dysplastic nevus syndrome.

Correspondence:
Silvestre Martínez García,
Avda. Los Botijos, n.º 6 C1-1,
Benalmádena Pueblo, Malaga, Spain
silvestremg@eresmas.net

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The authors declare no conflicts of interest.

References

Parallel Ridge Pattern in Acral Melanoma: Biopsy Processing Technique Can Affect Histological Diagnosis

N. Blázquez, I. Fernández-Canedo, R. Fúnez, and M. de Troya
*Servicio de Dermatología, *Servicio de Anatomía Patológica, Hospital Costa del Sol, Marbella, Malaga, Spain

To the Editor:
The skin on the palms and soles presents anatomical and histological peculiarities suited to the particular pressures exerted upon it. Consequently, differential diagnosis of acral melanocytic lesions based exclusively on clinical and histological criteria can become a very complicated matter. Dermoscopy is a very helpful tool in difficult cases.

We present the case of a 45-year-old patient with no relevant history, of north African origin with phototype IV skin, who consulted for a slow-growing pigmented lesion on the sole of the right foot that had appeared 2 years previously. Examination revealed a well defined variegated macule on the heel, measuring 2 cm across. Dermoscopy revealed this to be a melanocytic lesion with a ridge pattern (Figure 1).
Two biopsies were taken from areas within the ridge pattern as clinical and dermoscopic examinations raised the possibility of melanoma. Both biopsies showed epidermal hyperplasia with isolated melanocytes at the dermal-epidermal junction—findings characteristic of an acrolentiginous nevus (Figure 2).

The possibility of melanoma led to the subsequent complete removal of the lesion. Sections of tissue were taken perpendicularly to the dermatoglyphs or skin markings for histological studies. Histology revealed a hyperplastic epidermis with atypical nests of melanocytes in the crista profunda intermedia, leading to a diagnosis of acrolentiginous melanoma (Figures 3 and 4).

The patient attended periodical follow-up appointments and remained free of the condition for 3 years.

Definitions of histological criteria for malignancy in other anatomical areas cannot be easily applied to the palms and soles. For instance, findings such as atypical junctional activity, reactive elongation of the interpapillary furrows, or the migration of melanocytes to the upper layers of the epidermis are all characteristic signs of nonacral dysplastic nevi that can also be seen in benign melanocytic lesions on volar skin. This overlap between the histological criteria for identifying malignant and benign tissue can complicate diagnosis immensely at times. Dermoscopy can increase diagnostic precision of melanoma by between 5% and 30% above visual inspection in such cases.

At present, 2 schemes are used for the classification of dermoscopy patterns in acral melanocytic lesions. An online consensus meeting on dermoscopy held in 2003 approved the classification provided by Saida et al due to its ease of use, and this is now the most widely used system. The basic classification cites 4 patterns associated with benign nevi: parallel furrow, lattice-like, fibrillar, and non-typical. Later additions to this list include patterns such as the homogeneous, globular and acral reticular, transition, and globulostreak-like.

On the other hand, the parallel ridge pattern (PRP) and irregular diffuse pigmentation are findings specific to melanoma. Although the diagnostic reliability of PRP is higher in the detection of acral melanoma in general and for in situ melanoma in particular, irregular diffuse pigmentation represents tumoral invasion, and so the sensitivity and positive predictive value increases in invasive melanoma.

Volar skin has characteristic parallel skin markings that are divided into ridges and furrows. In dermoscopic terms, PRP is characterized by the presence of pigmentation in parallel bands, along the ridges of the skin markings. This pigmentation can be due to iron deposits (in subcorneal hematomas) or melanin (in melanoma, macules with racial pigmentation, or Peutz-Jegher syndrome).

Histologically, the ridges of the skin markings overlie the crista profunda intermedia, whereas the furrows
between the ridges overlie the crista limitans that separates the interpapillary processes (Figure 5). Recent studies show the proliferation of atypical melanocytes around the acrosyringium (located in the crista profunda intermedia) is an incipient sign of the development of acral melanoma. PRP is a direct outcome of this proliferation of atypical melanocytes. It thus constitutes an early marker of acral melanoma, with high sensitivity (86.4%), specificity (99%), and diagnostic precision (81.7%) for melanoma.

However, the diagnostic yield of this dermoscopic indicator is frequently reduced in clinical practice when samples are selected and processed without due rigor. In 1999, Signoretti et al. showed that pathological findings of benignity in melanocytic acral nevi (symmetry, borders of the lesion or presence of columns of melanin) were detected more often if the tissue sections were cut perpendicularly to skin markings. Later, in an interesting study, Ishii et al. undertook a retrospective analysis of the dermoscopic-histological correlation of 22 acral melanocytic lesions with PRP where no clinical or histological diagnosis had been made. They observed that incipient pathological changes could be detected around the acrosyringia in 90.9% of these cases when the tissue section was cut perpendicularly to the skin markings, as this allowed for observation of the crista profunda intermedia. In our patient a diagnostic outcome was obtained only in a third biopsy, when the sample was cut according to the suggestions made by Ishii et al.

Another point worthy of consideration is that histological diagnosis of acral melanocytic lesions is based on the architecture of the lesion, information that can only be evaluated in tissue samples from complete surgical removal.

Unfortunately, despite all these considerations, histological diagnosis of some suspect pigmented lesions is rendered impossible by the low cellularity of the sample. In such cases, the use of molecular biology techniques would be advisable to detect chromosomal abnormalities associated with acrolentiginous melanoma (especially amplifications of the cyclin D1 gene).

In conclusion, while the ridge pattern cannot be considered an absolute marker of acral melanoma, it does constitute a highly specific parameter. In order to increase diagnostic yield, we therefore recommend excisional biopsy of all lesions presenting PRP on volar skin, with histological study of tissue sections cut perpendicularly to the skin markings.

Correspondence:
Nuria Blázquez Sánchez,
Servicio de Dermatología,
Hospital Costa del Sol,
Carretera Nacional 340, km 187,
29600 Marbella, Málaga, Spain

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References

Docetaxel-induced Psoriasis

I. Allende, R. González-Hermosa, M. Lázaro, and J.L. Díaz-Pérez
Servicio de Dermatología, Hospital de Cruces, Baracaldo, Vizcaya, Spain

To the Editor:

The taxanes are chemotherapy drugs that have been widely used since their introduction in the late 1980s.1,2 Various types of skin toxicity have been described due to their increased use and range of indications. We present a case of docetaxel-induced psoriasis that has not been previously reported.

The patient was a 65-year-old man with no known drug allergies, a history of silicosis and generalized arthrosis, and a brother with psoriasis. He was diagnosed with squamous cell carcinoma of the lung in 2007 and began treatment with docetaxel because of tumor progression in April 2008. Eight days after the first cycle of docetaxel, disperse psoriasis-like punctuate erythematousquamous lesions began to spread over his trunk and limbs (Figure 1). The nails, genitals, mucus membranes, and scalp were unaffected and the patient was in a generally good state with no systemic symptoms or arthritis. Tests confirmed only slight anemia, with a normal total and differential white blood count.

A biopsy was taken of a lesion to confirm the diagnosis made on the basis of symptoms and the family history of psoriasis. Pathologic study showed an epidermis with psoriasiform hyperplasia, acanthosis, parakeratosis, elongation of the interpapillary ridges, isolated lymphocytes, and a polynuclear infiltrate in the mid and upper layers of the epidermis forming spongiform pustules of Kogoj. The dermis showed a perivascular inflammatory infiltrate associated with dilated capillaries (Figure 2)—all compatible with psoriasis. Topical treatment with corticosteroids and calcipotriol was initiated and the patient responded well to treatment. The lesions returned in May 2008 with the
following cycle of Taxotere and resolved in a few days with the same treatment as before.

The taxanes—paclitaxel (Taxol) and docetaxel (Taxotere)—are cytotoxic chemotherapy drugs used in the treatment of various malignant diseases.1,2

Taxotere is a concentrate of a solution for infusion that contains docetaxel in trihydrate form. Docetaxel is a semisynthetic taxane obtained from the leaves of the European yew tree Taxus baccata. It is an antineoplastic agent that acts on the microtubules detaining the cell cycle and stopping cell proliferation. It also induces cell apoptosis and inhibits angiogenesis. The drug is administered intravenously and has a half-life of 12 hours.1

Docetaxel is indicated in both monotherapy and in combination with other antineoplastic drugs for the treatment of solid malignant tumors such as breast, prostate, or stomach cancer, and non-small cell lung cancer. It is generally administered as an infusion for 1 hour every 3 weeks.1,3

The most common adverse drug reactions include myelosuppression and consequent neutropenia (reversible and nonaccumulative). Others include neuropathy, hypersensitivity, anemia, nausea, vomiting, stomatitis, diarrhea, myalgia, fluid retention, and asthenia.1

Dermatological adverse reactions include toxic skin reactions in 50% to 70% of patients5—one of the most common nonhematological adverse events.

Acute reversible skin reactions have been observed following intravenous administration of the drug, although these are generally of a weak to moderate intensity. Lesions vary from a single erythematous and edematous plaque close to the site of infusion (fixed erythrodysesthesia) to maculopapular drug eruption lesions, diffuse or predominantly acral erythema, urticariiform lesions, to maculopapular drug eruption lesions, diffuse or close to the site of infusion (fixed erythrodysesthesia) vary from a single erythematous and edematous plaque these are generally of a weak to moderate intensity. Lesions following intravenous administration of the drug, although common nonhematological adverse events.

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Reversible alopecia (anagen and telogen effluvium) is a common adverse effect in these patients—an adverse effect also common to other chemotherapy drugs.

Nail abnormalities due to docetaxel present in 35% to 58% of patients.2,4,5 Nail symptoms include: onycholysis, onicomedesia, subungual suppuration, acute paronychia, subungual abscesses, nail pigmentation, subungual hemorrhage/hematoma, Beau lines or transverse leukonychia, nail bed hyperemia, nail bed dyschromia, subungual hyperkeratosis, and periungual erythema.2,4,6

Another adverse cutaneous reaction is erythrodysesthesia of the palms and soles,5,7,8 which occurs in 5% of cases7 and manifests as confluent erythema that resolves in a matter of weeks following scaling.7 There have also been cases reported of stomatitis, mucositis, radiation recall reaction, squamous eccrine syringometaplasia, generalized pustular reaction, inflammation of preexisting actinic keratoses, and fixed drug eruptions.9

Flagellate erythema,10 subacute cutaneous lupus erythematosus and sclerodermiform changes7 have also been reported following the administration of docetaxel.

We consider this case worthy of publication as there have been no previous reports of a dermatological complication in the form of generalized psoriasis following treatment with docetaxel—a widely used chemotherapy drug with an ever broader range of indications.

Correspondence:
Irati Allende Markixana,
Servicio de Dermatología,
Hospital de Cruces,
Plaza de Cruces s/n,
48903 Baracaldo, Vizcaya, Spain
iratialiende@telefonica.net

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References
To the Editor:

Lichen striatus is a self-limiting inflammatory dermatosis that is characteristically distributed along the Blaschko lines. It is usually seen in children although cases, with different histopathological features, have been reported in adults. In view of the characteristic clinical features of the disease in adults—with its papulovesicular aspect—it is known as blashkitis. Subsequently, different attempts have been made to define these conditions.

A 70-year-old man with a family and personal history of atopy attended the clinic for a pruriginous multilinear papulovesicular eruption on the trunk and right leg that had appeared 6 months earlier. Treatment over the preceding month with methylprednisolone aceponate applied as a 0.1% cream had led to no improvement. The multilinear eruption took the form of a papulovesicular eruption that followed the Blaschko lines on one side of the body; it was more intense on the leg (Figures 1A, C, and E).

Histopathological study showed a lichenoid inflammatory infiltrate that extended to the mid-dermis (Figure 2A). The composition of this infiltrate was polymorphous, with the presence of lymphocytes, plasma cells, histiocytes, and a notable presence of eosinophils. The epidermis showed irregular epidermal hyperplasia, with compact hypergranulosis and hyperkeratosis but no parakeratosis. Limited spongiosis was present. No transepidermal migration of inflammatory cells was observed. In addition, clefts were observed between the dermis and epidermis, along with basal apoptotic keratinocytes and pigmentary incontinence (Figure 2B). Perieccrine thickening of the deep dermis was observed.

Once lichen striatus had been diagnosed, the patient was instructed to apply an ointment containing 0.1% tacrolimus twice a day for the first month to the lesions on the trunk, which disappeared, and to the legs in the second month, with the same results (Figures 1B, D, and F). After 6 months of follow-up, no recurrences had been reported.

Lichen striatus is an uncommon, self-limiting, linear dermatosis, which usually affects children and is rare in adults. It is distributed unilaterally, although some cases of bilateral distribution have been reported. At present, given its distribution pattern, it is considered a somatic mosaicism. The cause is unknown, although an immune mechanism has been proposed whereby killer T cells eliminate keratinocytes with a postzygotic mutation.

Lichen striatus is often associated with atopic dermatitis, and it has also been suggested that the altered immune status of these patients might act as a predisposing factor to trigger the process. Tacrolimus, an inhibitor of inflammatory cytokine production by T cells, has been shown to be useful in the treatment of isolated cases of lichen striatus. In our case, as the patient was treated in 2 different areas at 2 different times and a rapid response was obtained, the resolution of clinical symptoms can probably be attributed to topical tacrolimus and not the natural course of the disease.
There is no clear consensus about whether to consider lichen striatus and adult blaschkitis as the same entity. The term was initially coined by Senear and Caro in 1941; “adult blaschkitis” was first used in 1990 by Grosshans and Marot for a case in an adult with a multilinear, papulovesicular, and pruriginous eruption, with histologic features of spongiotic dermatitis. In view of the appearance of similar cases and in an attempt to differentiate the entity from lichen striatus, other terms such as acquired relapsing self-healing Blaschko dermatitis or acquired Blaschko dermatitis have been used. Thus, blaschkitis is considered more common in adults, presents as a multilinear and bilateral papulovesicular eruption, usually on the trunk, and heals quickly though relapses are common. Histopathology is the same as that of spongiotic dermatitis. In contrast, lichen striatus is more common in children, appears more frequently on the limbs, is distributed along a single line or a few lines at most, and is usually papular without the formation of vesicles. Resolution is slower—leaving transient hypopigmentation—and recurrence is rare. Histopathological study reveals features of both lichenoid and spongiotic dermatitis. However, certain overlap of these features is common, giving rise to terms that try and encompass both aspects such as “Blaschko linear acquired inflammatory skin eruption”.

In our opinion cases such as ours, in which there is overlap of the features that define adult blaschkitis—such as multilinear papulovesicular lesions located on the trunk—with lichenoid histopathology with involvement of skin adnexa and features of spongiotic dermatitis, suggest that lichen striatus and blaschkitis are different expressions of the same process. Therefore, in our case, and given the lack of other information to allow differentiation between lichen striatus and blaschkitis, we consider these terms to be synonymous.

Correspondence:
Antonio Tejera-Vaquerizo
"Departamento de Dermatología
Hospital Infanta Margarita
Avda. Góngora s/n
14940 Cabra, Córdoba, Spain
antoniotejera@aedv.es

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References
Pigmented Cyst of the Median Raphe of the Scrotum in a Boy

I. Colmenero, N. Sastre, I. de Prada, and A. Hernández-Martín

Servicio de Anatomía Patológica and Servicio de Dermatología, Hospital Infantil Universitario Niño Jesús, Madrid, Spain

To the Editor:

Cysts of the median raphe (CMR) are uncommon lesions that result from abnormal embryologic development. In most cases, a urothelial-type or squamous epithelial lining is present, but other rarer histologic variants have been described. One of these, reported infrequently in the literature, is characterized by the presence of melanocytes and melanic pigment in the epithelial lining.

A 3-year-old boy was referred to our hospital for surgical removal of a cystic tumor that had been present in the median raphe of the scrotum for 2 years. The lesion was initially a single cyst, but further cysts subsequently appeared along the median raphe of the scrotum. These grew and became progressively pigmented. All cysts were less than 1.5 cm in diameter, soft, painless, and with no signs of inflammation. The lesion was completely excised. On sectioning the surgical specimen, there was a longitudinal canal measuring 0.2 cm in diameter, running the full length of the tissue sample, with several cystic dilatations along its path, the biggest measuring 1.5 cm. The canal and the cysts were filled with a yellow pasty material. Histologically, both the canal and the cystic dilatations showed an epithelial lining in which areas of pseudostratified cylindrical epithelium (Figure 1) alternated with keratinized stratified squamous epithelium (Figure 2). Many areas containing intracytoplasmic melanin were observed in the epithelium, both at the basal level and in upper strata (Figure 3). In addition, some vacuolated melanocytes could be observed in...
the basal layer. In some areas, the presence of isolated subepithelial melanophages was detected along with a moderately-intense mixed inflammatory infiltrate. No decapitation secretion, mucosal secretion, or ciliated cells were observed and there were no myoepithelial cells in the cyst wall. Likewise, no atypia or mitosis was observed. The histopathological diagnosis was a pigmented variant of mixed-type CMR.

CMR is a rare lesion that may develop at any site between the anus and the urinary meatus. The region of highest incidence is the ventral aspect of the penis, often near to the glans. CRM is generally diagnosed in patients under 30 years of age. Three clinical forms have been described. The most common is a solitary cyst, but multiple cysts or a canal along the median raphe have also been reported. Our case has the particular characteristic that the canal had multiple cystic dilatations along its path.

Three theories have been put forward to explain the pathogenesis of CRM. The first proposes that they occur during embryonic development, after primary closure of the urethral and genital folds, as a result of evagination of the urethral epithelium followed by subsequent growth; the second postulates that the lesion arises from epithelial debris originating from incomplete closure of the urethral folds; and the third considers that these lesions could be due to the presence of dilated ectopic periurethral (Littre) glands. We agree with Nagore et al. in that these 3 mechanisms may be complementary and are not necessarily exclusive.

Histologically, 3 patterns can be described:

1. Urethral type, lined by a pseudostratified columnar epithelium (70%)
2. Epidermoid type, with a stratified squamous epithelium (10%)
3. Mixed type (4.6%), as is the case in our patient, in which both types of epithelium are present.

In addition to the above, some uncommon histological variants of CRM have been reported. The pigmented variant, as in the case we present here, is one of these, and to our knowledge, only 3 other cases have been published previously. Histologically, it shows a pseudostratified columnar, squamous, or mixed lining, with melanin granules in the cytoplasm of the basal cells and occasionally in the upper layers. Dendritic melanocytes are also observed interspersed among the epithelial cells, and subepithelial melanophages.

Although it was believed for a long time that, in superior warm-blooded vertebrates, melanocytes migrating from the neural crest were limited to the epidermis and specialized organs, such as the eye or the pia mater, they have been shown to be present in other sites such as the esophagus, larynx, prostate, vagina, uterine cervix, and urothelial epithelium. The migration of undifferentiated melanoblasts from the neural crest to the urothelium explains the etiology of this variant of CRM.

The treatment for CRM recommended by most authors is simple excision followed by primary closure in order to prevent infections or symptoms associated with the site. In our patient, this procedure proved successful. Until present, no cases of malignant transformation of CRM have been reported.

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Correspondence:
Isabel Colmenero
Servicio de Anatomía Patológica
Hospital Infantil Universitario Niño Jesús
Avda. Menéndez Pelayo, 65
28009 Madrid, Spain
isabelcolmenero@gmail.com

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The authors declare no conflicts of interest.

References