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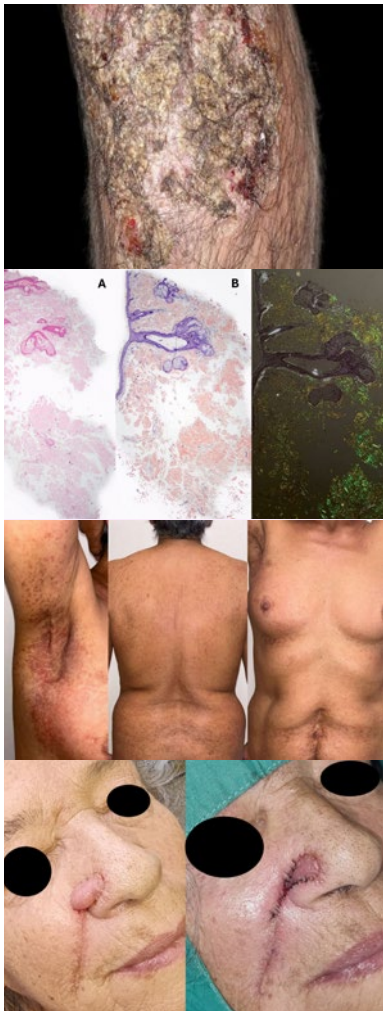

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CLINICAL CASE

Nasal mucosal melanoma: case report

Melanoma mucoso nasal: comunicación de un caso

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Abstract

Mucosal melanoma has an aggressive behavior and low survival.The diagnosis requires histopathological and immunohistochemical confirmation. Immunotherapy has a favorable impact on patient survival. We present the case of a 51-year-old man with nasal obstruction, rhinorrhea and epistaxis. An exophytic neoformation with an ulcerated surface with blood crusts is observed in the left nasal fossa.The histopathological study reports a malignant epithelial neoplasia and positive immunohistochemistry for S-100 and HBM-45 stains. He receives treatment with radiotherapy and immunotherapy. Mucosal melanoma has an unfavorable prognosis so early diagnosis is vital.

Keywords: *Melanoma. Amelanotic melanoma. Nasal mucosa.*

Resumen

El melanoma mucoso tiene un comportamiento agresivo y una baja supervivencia. El diagnóstico requiere confirmación histopatológica e inmunohistoquímica. La inmunoterapia tiene un impacto favorable en la supervivencia de los pacientes. Se presenta el caso de un varón de 51 años con obstrucción nasal, rinorrea y epistaxis. En la fosa nasal izquierda se observa una neoformación exofítica de superficie ulcerada con costra hemática. El estudio histopatológico describe una neoplasia epitelial maligna con inmunohistoquímica positiva para S-100 y HBM-45. Se indica tratamiento con radioterapia e inmunoterapia. El pronóstico del melanoma mucoso es desfavorable, por lo que el diagnóstico temprano es vital.

Palabras clave: *Melanoma. Melanoma amelánico. Mucosa nasal.*

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Introduction

Mucosal melanoma is a rare variety of melanoma that accounts for < 1-1.3% of all melanomas[1]. It has a low incidence rate, at 1.5 per million[2]. Unlike cutaneous melanoma, this type of neoplasm develops from melanocytes located in mucous membranes, so it differs in its biology, clinical presentation, and management. Mucosal melanoma mainly affects the head and neck (55%), followed by the anorectal region (24%), the vulva or vagina (18%), and the urinary tract (3%)[3]. The amelanotic presentation has been reported in 10-25% of cases, which confers a worse prognosis and a late diagnosis on most occasions[4]. The most appropriate treatment protocol for mucosal melanoma has not yet been well established, as it is a rare condition.

This is the case of a 51-year-old mannt diagnosed with amelanotic mucosal melanoma in the nasal cavity. Few cases of this variety of melanoma have been described, which highlights the importance of raising awareness about its clinical presentation, as well as timely diagnosis and treatment, since the overall survival is low.

Case report

A 51-year-old man, with no significant past medical history, began experiencing a sensation of nasal obstruction and increased volume in the left nasal cavity 1 year prior to his examination. This was accompanied by foul-smelling anterior rhinorrhea, occasional epistaxis, and a 10 kg weight loss in the previous 3 months. The examination revealed the presence of dermatosis located on the left nasal fossa mucosa, consisting of an exophytic neoformation with an erythematous, ulcerated surface covered by a bloody crust. In the oral cavity, an increase in volume was observed in the bony palate to the left of the midline, due to the protrusion of the tumor mass (Fig. 1).

During his examination, he progressed with proptosis of the right eye, diplopia, difficulty with visual fixation, and oppressive and intermittent frontal headache. The T1-weighted contrast-enhanced magnetic resonance imaging of the paranasal sinuses with gadolinium revealed the presence the tumor in the left nasal cavity, with avid enhancement with gadolinium, destruction of the nasal septum with extension to the ipsilateral orbit, erosion of the cribriform plate and the anterior wall of the sphenoid sinus, infiltration of the ethmoid air cells, and occupation of the left osteomeatal complex with extension to the maxillary sinus (Fig. 2).

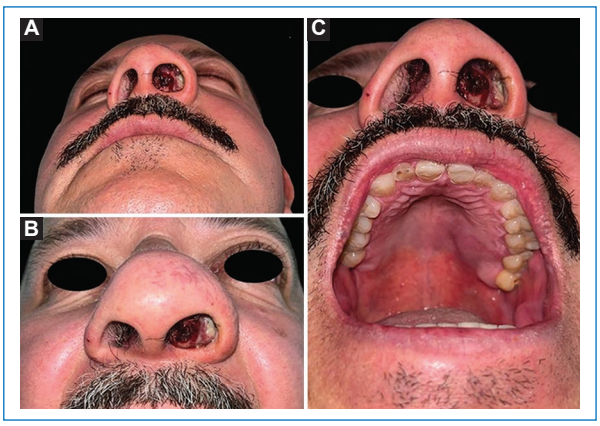

Figure 1. **A**: exophytic neoformation with an ulcerated surface covered by a bloody crust in the left nasal fossa. **B**: proptosis of the left eye. **C:** neoformation spread towards the left maxillary bone with protrusion through the bony palate.

The lesion was biopsized, and the histopathological study confirmed the presence of a malignant neoplasm consisting of small cells with scant cytoplasm, atypical nuclei with reinforcement of their membrane, prominent nucleoli, and numerous atypical mitoses, leading to a suspected non-Hodgkin lymphoma (Fig. 3).

The following immunohistochemical stains were performed: CD3, CD20, CD45, and CD138 all turned out negative; CD56 turned out cytoplasmically positive; CK AE1/AE3, chromogranin, and synaptophysin turned out negative; while vimentin turned out cytoplasmically positive. This ruled out the possibility of a B-cell and non-NK T-cell lymphoma, showing poorly defined immunoreactivity, and it was categorized as a poorly differentiated malignant neoplasm (Fig. 4). Due to suspected olfactory neuroblastoma or melanoma, S-100 protein and HMB-45 stains were requested and turned out positive (Fig. 5).

Based on the clinical presentation, the histopathological study, and the additional immunohistochemical stains, a diagnosis of amelanotic mucosal melanoma of the nasal cavity was established.

Surgical resection was technically impossible, and cytoreductive radiotherapy was decided. The patient received 30 sessions and a total dose of 60 Gy. He showed good tolerance to the initial treatment, with a decrease in diplopia and a slight reduction of the tumor mass within the first 8 weeks. Subsequently, metastases were evidenced in the lung, mediastinal and axillary lymph nodes, and multiple pancreatic nodules. We decided to start immunotherapy with nivolumab, an antibody against programmed cell death protein 1

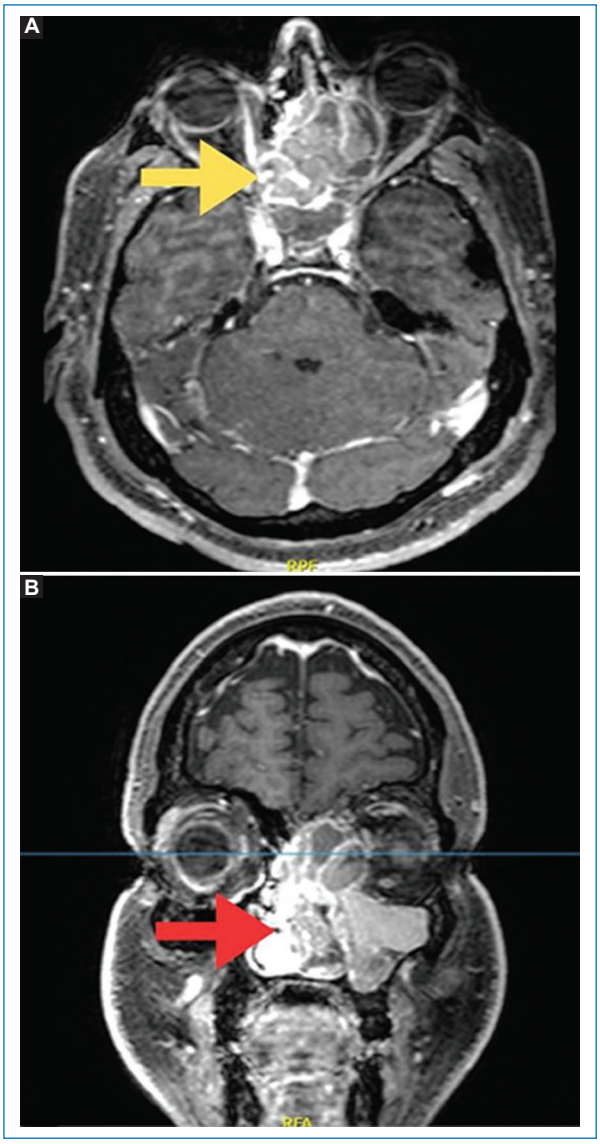

Figure 2. Magnetic resonance imaging of paranasal sinuses with gadolinium contrast, T1-weighted with fat suppression. **A**: heterogeneous enhancement of the tumor in the left nasal cavity, invasion of the orbit and displacement of the ipsilateral medial rectus muscle and optic nerve (arrow). **B**: extension to the left maxillary sinus (arrow).

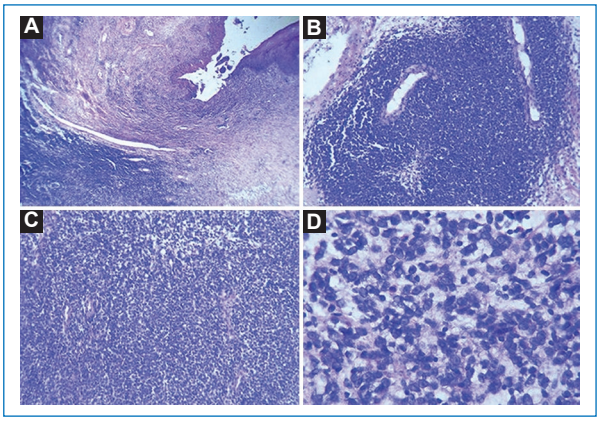

Figure 3. **A**: epithelium with focal ulceration. **B** and **C:** in the dermis, presence of an undifferentiated malignant neoplasm. **D**: small cells with scant cytoplasm, atypical nuclei, and numerous atypical mitoses.

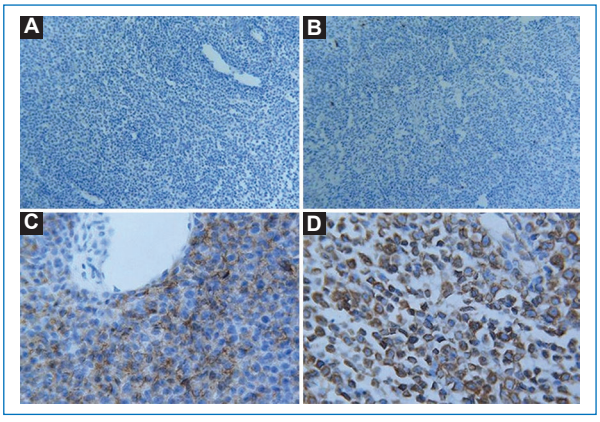

Figure 4. Immunohistochemical stains. **A**: CD3 negative. **B**: CD20 negative. **C**: CD56 positive. **D**: vimentin positive.

(anti-PD-1). However, the patient had progressive deterioration despite the targeted therapy and passed away 8 months after diagnosis.

Discussion

Mucosal melanoma is a rare neoplasm, originating from melanocytes or their precursors, characterized by its aggressive course. It has a prevalence of 1-1.3% of all melanomas. Its most common location is in the head and neck (55%), with involvement of the nasosinusal cavity, oral cavity, pharynx, larynx, and upper esophagus[1]. The incidence rate of mucosal melanoma of the nasal cavity is 0.03 per million. It occurs in older people, with a mean age of presentation of 64.3 years, with a predilection for the male sex (1:0.45)[4].

Clinically, mucosal melanoma is characterized by neoformations with a polypoid appearance, with a color ranging from brown to black, and has an insidious and rapid onset[5,6]. In 10-25% of these tumors, there is a lack of pigment, a condition known as amelanotic, which confers a worse prognosis[4]. The most widely described symptoms are epistaxis or persistent rhinorrhea, nasal obstruction, and facial pain. In advanced cases, diplopia, proptosis, or neurological symptoms

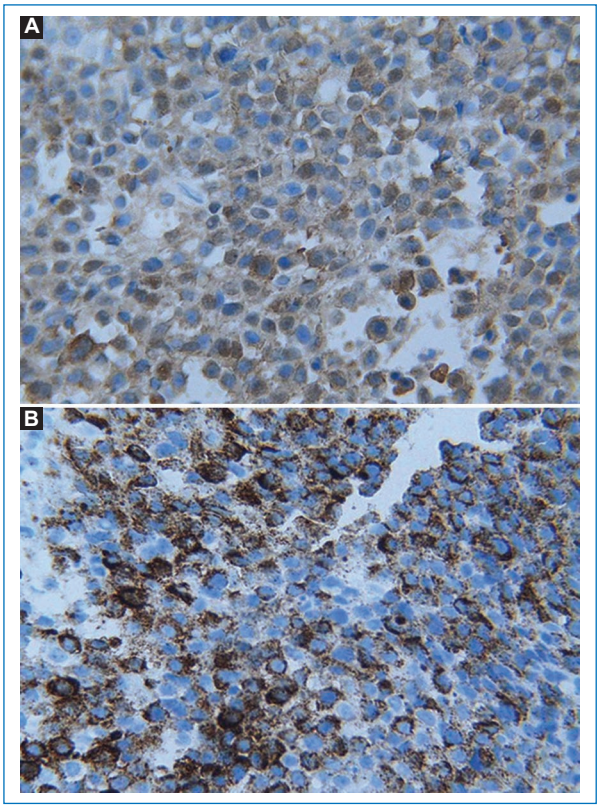

Figure 5. Immunohistochemical stains. **A**: S-100 protein positive. **B:** HMB-45 positive.

usually occur[2]. Diagnosis is established through clinical evaluation, imaging modalities, and histological confirmation. High-resolution magnetic resonance imaging is recommended, which is usually more accurate than tomography to determine the extent of the tumor and establish the staging. As it is an aggressive tumor, erosion of bone structures and invasion of adjacent soft tissues are a common finding[2].

Histopathology is characterized by a proliferation of neoplastic melanocytes with different phenotypes such as large epithelioid, spindle, or plasmacytoid cells[6]. The most widely used immunohistochemical stains are S100, HMB-45, NKI/C3, and MART-1/Melan-A[7]. The S-100 protein is known as the most sensitive melanocyte marker (sensitivity of 97-100% and specificity of 75-87%), while HBM-45 (sensitivity of 69-83% and specificity of 56-100%) and Mart-1/Melan-A (sensitivity of 75-92% and specificity of 95-100%) are more specific[8]. Although, clinically, they can be confused with nasal polyps[4], a differential histological diagnosis must be established with other tumors with undifferentiated cells, such as non-Hodgkin lymphoma, Ewing's sarcoma, and neuroendocrine tumors[1].

Dermoscopy faces limitations due to the relative difficulty of applying the lens in mucosal cavities and the lack of standardized diagnostic criteria. The most common dermoscopic findings in mucosal melanoma are a multicomponent pattern, asymmetric structures, polychromia, a whitish-blue veil, and polymorphic blood vessels[9].

The treatment of mucosal melanoma depends on its stage and location. Surgical resection is considered the first-line therapy whenever feasible[6]; however, it presents high rates of local (20%), regional (50%), and systemic (80%) recurrence[10]. For more advanced stages, adjuvant treatments such as chemotherapy, radiotherapy, and immunotherapy are chosen[6]. In patients with metastatic mucosal melanoma, immunotherapy with immune checkpoint inhibitors has been approved. Ipilimumab (anti-CTLA-4 monoclonal antibody) was the first agent that demonstrated improved survival in melanoma; nivolumab (anti-PD-1) has been shown to play a significant role on the survival of patients with advanced melanoma. The overall survival of mucosal melanoma with ipilimumab and nivolumab is 6.4 and 16.8 months, respectively[11].

The prognosis of patients with mucosal melanoma is poor because it has a tendency to recur and progress both regionally and distantly. The 3-year overall survival rate is 44%, and for head and neck mucosal melanoma, 39.6%, with a median survival of 26.4 months[12].

In the presented case, surgical resection was technically impossible, and second-line therapy with nivolumab was decided. Acceptable control of the disease was achieved, but at the follow-up, distant metastasis was evidenced and the patient finally passed away 8 months after diagnosis.

Conclusions

It is still not possible to define a therapeutic standard for mucosal melanoma due to its rarity. Surgery remains the first-line therapy when feasible. Currently, immunotherapy plays an important role with favorable survival results. The overall prognosis of the disease is poor, so a high index of suspicion is important for early diagnosis.

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The authors declared that this study was conducted with their own resources.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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CLINICAL CASE

Clinical, dermoscopy and ultrasonography findings in nail sarcoidosis: a case report

Hallazgos clínicos, dermatoscópicos y ultrasonográficos en sarcoidosis en las uñas: reporte de un caso

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Abstract

Although dermatological manifestations are frequent in sarcoidosis, nail involvement is rare and is related to chronic systemic disease. We present the case of a young female patient with significant nail involvement, highlighting the findings obtained by dermoscopy and high-resolution ultrasound. Cutaneous sarcoidosis is a granulomatous disorder with highly variable manifestations which poses a diagnostic challenge to all dermatologists. Diagnostic imaging, in particular ultrasound with color Doppler flow analysis, offers an inexpensive and widely accessible alternative to evaluate each component of the nail unit.

Keywords: *Sarcoidosis. Nail diseases. Dermoscopy. Ultrasonography. Doppler. Case report.*

Resumen

Aunque las manifestaciones dermatológicas son frecuentes en la sarcoidosis, la afectación ungueal es rara y se relaciona con enfermedad sistémica crónica. Presentamos el caso de una paciente joven con importante afectación ungueal, destacando los hallazgos obtenidos mediante dermatoscopia y ultrasonografía de alta resolución. La sarcoidosis cutánea es un trastorno granulomatoso con manifestaciones muy variadas que plantea un reto diagnóstico a todos los dermatólogos. El diagnóstico por imagen, en particular la ultrasonografía con análisis Doppler de flujo en color, ofrece una alternativa económica y ampliamente accesible para evaluar cada componente de la unidad ungueal.

Palabras clave: *Sarcoidosis. Enfermedades de la uña. Dermoscopia. Ultrasonografía Doppler. Reporte de caso.*

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Introduction

Nail involvement in sarcoidosis is uncommon but may indicate chronic systemic disease, with a reported prevalence ranging from 1 in 400 to 3 in 188 cases[1,2]. Nail alterations in sarcoidosis include hyperkeratosis, onycholysis, onychorrhexis, pitting, discoloration, fragility, pterygium, and dystrophy – the latter being the most frequently described (10.30% of cases)[3,4].

Assessment of nail changes in daily practice relies exclusively on clinical symptoms, which do not capture the entire disease process. Ultrasonography provides a widely accessible alternative to evaluate each component of the nail unit in real time. In addition, vascularity and blood flow can be assessed through color Doppler flow analysis[5].

We present the case of a patient with significant nail involvement, highlighting findings obtained through high-resolution ultrasonography and dermoscopy in the context of systemic sarcoidosis refractory to conventional therapy.

Case report

A 25-year-old Latin American woman worked as a typist at a call center (Fig. 1). In 2017, she presented with polyarthritis affecting the ankles and knees, as well as dactylitis in the third finger of the left hand. With negative autoantibody serology, rheumatoid arthritis vs psoriatic arthritis was suspected. Over a 3-year period, she was on several therapies, including anti-inflammatory analgesics, oral corticosteroids, methotrexate, and golimumab 50 mg/month for 6 months.

In 2021, she was hospitalized due to clinical relapse and GI intolerance apparently related to the immunomodulator. During this hospitalization she developed respiratory symptoms, raising suspicion of sarcoidosis, and a chest CT scan showed multiple apical mediastinal lymph node conglomerates. Lymph node biopsies revealed chronic non-necrotizing granulomatous inflammation, with negative staining for tuberculosis and fungi, suggestive of systemic sarcoidosis.

In 2022, she attended a dermatology outpatient clinic concerned about having “fungus on the nails.” Clinical evaluation revealed dactylitis and clubbing of the hands, and chromonychia with splinter hemorrhages in the nails (Fig. 2). Dermoscopy showed periungual erythema in the proximal nail fold, scaling on the nails of the right first finger and left second finger, and longitudinal ridging (Fig. 3). The fingertips showed hyperkeratosis and the Koebner phenomenon (a characteristic skin reaction in which lesions appear in areas previously exposed to trauma or irritation). A moderately infiltrated erythematous scaly plaque was also observed on the left nasal ala and dorsum. Histopathology of this lesion revealed non-necrotizing granulomas, confirming cutaneous sarcoidosis (Fig. 4).

High-resolution dermatologic ultrasonography was performed using an 18-MHz golf-club transducer on all nail units, with color Doppler flow analysis at baseline and at 3 months. The assessment was performed with the patient seated, hand supported, and fingers comfortably extended; the surface was dried and polish removed from unaffected units. Generous gel and high-resolution B-mode imaging – focused on superficial planes with moderate gain – were used to clearly visualize the nail plate, bed, matrix, and periungual folds. The protocol included longitudinal scans from the proximal fold to the distal edge (matrix, mid-third, and hyponychium) and transverse sections at the same levels. Evaluation of the extensor tendon insertion on the distal phalanx was also included. Doppler parameters were adjusted for low-flow detection, avoiding excessive transducer pressure and allowing seconds of stabilization prior to recording. Findings were compared with contralateral units when appropriate.

Ultrasonography revealed dystrophic changes in the nail plates with loss of normal trilaminar structure, thickening of the nail beds due to moderately hyperechoic nodules corresponding to sarcoid granulomas, and variable sclerotic changes in the distal phalanges. At baseline, both the matrix and bed showed significantly increased vascularity on Doppler examination, indicating an active phase of disease. Ultrasonography also included evaluation of all hand joints, allowing detection of synovitis defined according to the Outcome Measures in Rheumatology (OMERACT) criteria for musculoskeletal ultrasound: intra-articular echogenic material within synovial recesses, non-displaceable and non-compressible with transducer pressure, with or without Doppler signal, demonstrated in 2 perpendicular planes[6,7].

The patient was treated with 2 triamcinolone infiltrations (3 mg) at the periungual region, at the level of the eponychium. Lesions improved both clinically and ultrasonographically (Fig. 5). Due to refractory systemic involvement, she is on infliximab, with no further progression.

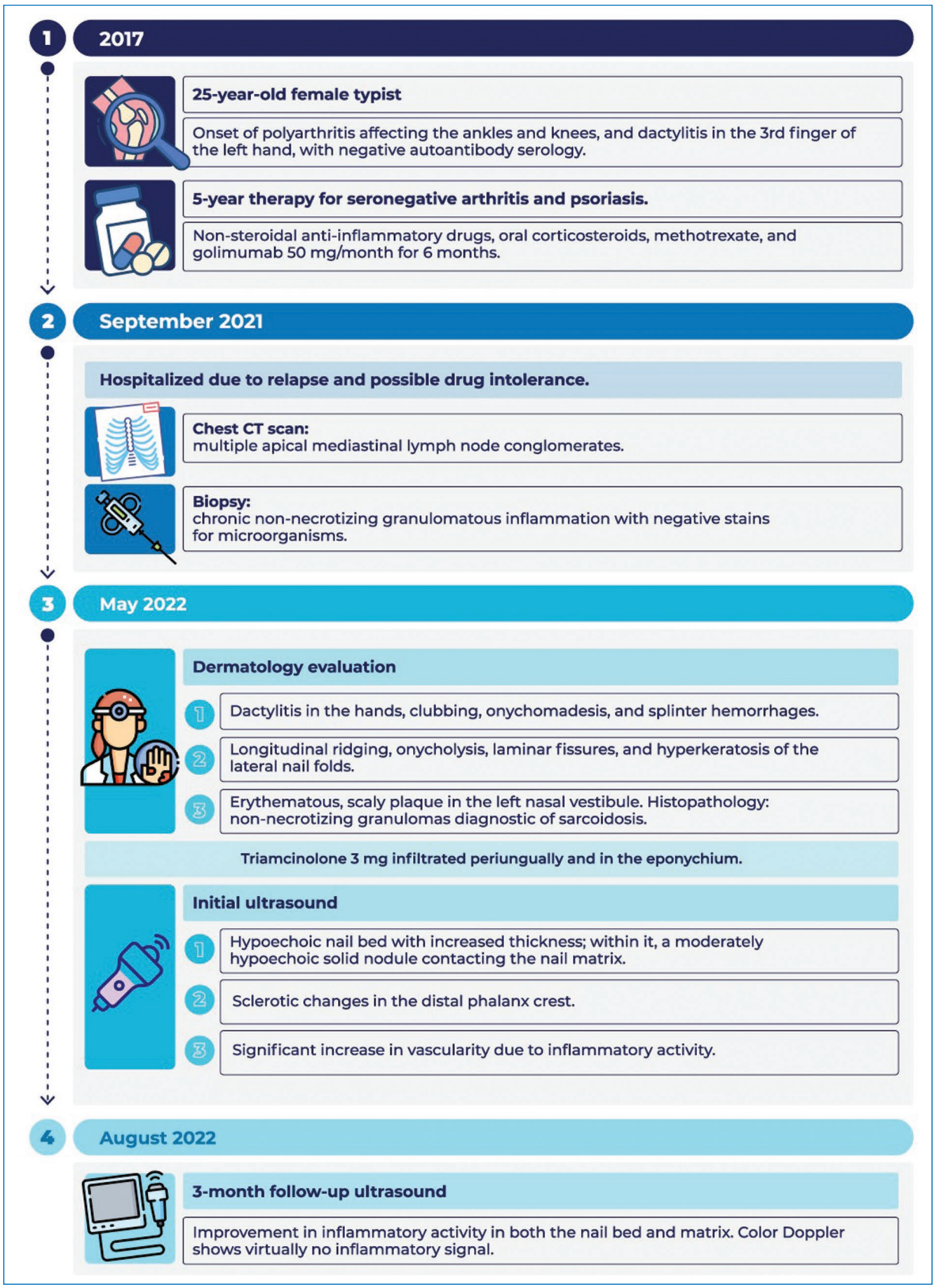

Figure 1. Timeline.

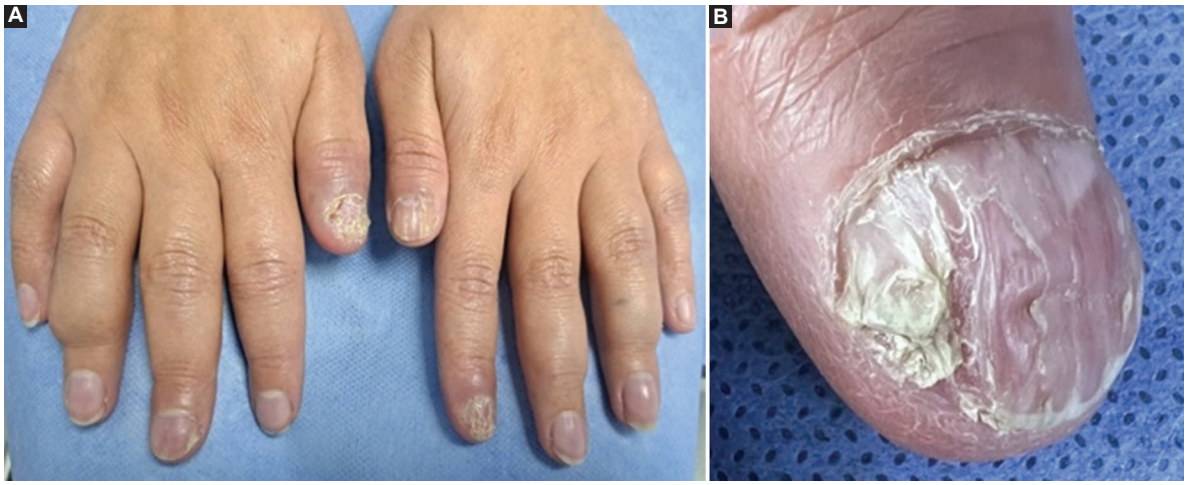

Figure 2. Clinical signs. **A:** dactylitis, clubbing, chromonychia, and onychodystrophy. **B:** hyperkeratosis, onycholysis, and splinter hemorrhages.

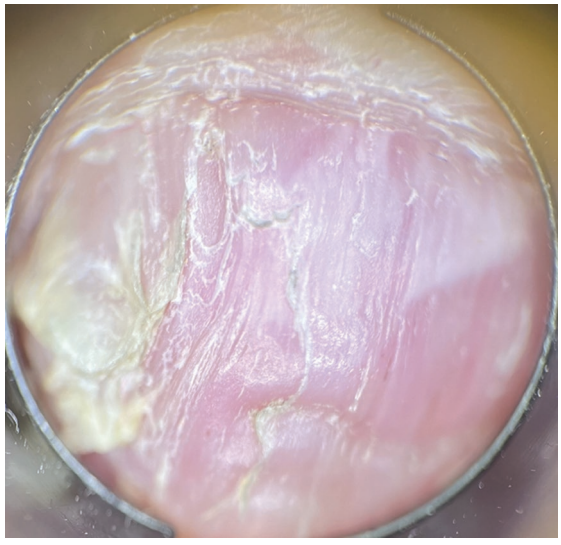

Figure 3. Dermoscopy of the right first fingernail. Longitudinal erythronychia, discontinuous longitudinal striations, lamellar fissures, and hyperkeratosis of the lateral edges are observed.

Discussion

Several presentations of sarcoidosis pose diagnostic challenges for involved medical teams, especially when signs are limited to a single organ system or are not immediately evident[8]. A common first step, once sarcoidosis is included in the differential diagnosis, is evaluation of the lungs and intrathoracic lymph nodes, the most frequently affected sites. However, involvement may be subclinical, and standard studies may be negative or inconclusive, requiring clinicians to search for signs in other systems. Among extrapulmonary manifestations, the skin is the second or third most widely affected organ, involved in up to one-third of patients. Cutaneous signs are highly variable and may represent the earliest signs of the disease[9,10].

Of note, macroscopic signs include sarcoid dactylitis, present in 0.2% of sarcoidosis cases, with swelling of the fingers and toes. It occurs more frequently in the middle than in the distal phalanges and is associated with poor prognosis, including increased risk of multisystem involvement and chronic progression with underlying bone involvement[11]. This was observed in our patient, who also had pulmonary disease. The Koebner phenomenon is also important in describing systemic sarcoidosis with bone and nail involvement[12]. Although the exact pathophysiology is unclear, it is hypothesized that T and B cells are recruited to sites of mechanical injury due to cytokine and autoantibody release. Given her occupation as a typist, repeated trauma may have significantly contributed to her clinical signs.

Some features of this case differ from those most frequently described in the literature. The 2nd and 3rd fingers are typically involved; therefore, the bilateral and predominant 1st-finger involvement seen in this patient is unusual. Longitudinal erythronychia is also uncommon, although a possible pathophysiologic mechanism has been proposed. It is suggested that these changes may result from sarcoid granulomas

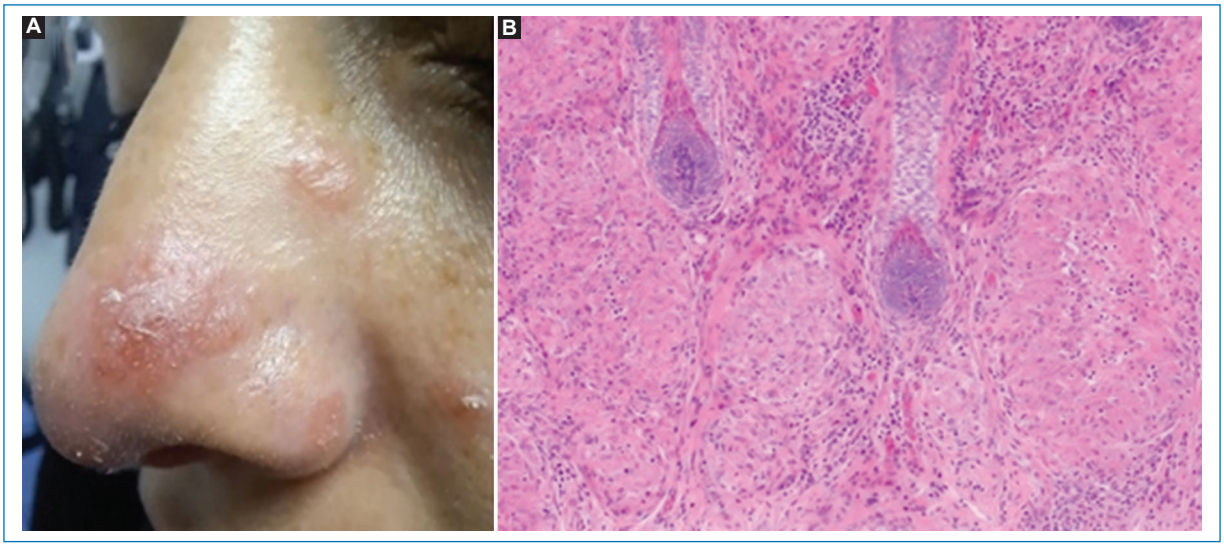

Figure 4. A: lesion on the nasal dorsum. **B:** histopathology reveals non-caseating granulomas, negative for microorganisms. Confirmed diagnosis of sarcoidosis.

within the nail bed, whose pressure on the dermis between the nail plate and distal phalanx generates the characteristic reddish linear change[3,4].

Dermoscopic findings are infrequently reported, and changes are more commonly located at the proximal nail fold. Typical findings include a pinkish background with linear vessels of varying calibers, hypopigmented whitish areas with scarring, white scales, and translucent orange globules. The nail plate shows subungual hyperkeratosis and splinter hemorrhages, while the nail edge shows only subungual hyperkeratosis[10]. Several of these nonspecific findings were present in our patient.

High-resolution ultrasonography of the nail unit has evolved into the imaging modality of choice for evaluating a wide range of conditions, including inflammatory and neoplastic diseases[5,13]. It is performed using a compact high-frequency linear transducer (≥ 15 MHz) and gel to prevent artifacts, avoiding pressure that may compress vessels[13]. Examination includes longitudinal and transverse planes, with 2D and Doppler imaging to assess vascularity. This non-invasive method is accurate and more accessible than MRI[5,14]. It also allows real-time evaluation of nail structure and vascularity, useful for diagnosing and monitoring conditions such as psoriasis, onychomycosis, subungual tumors, and nail lichen planus[15-18]. In psoriasis, it reveals thickening and vascular changes[18]; in onychomycosis, thickening and irregularity are observed[17]; and in subungual tumors, it shows their location and vascularization[16].

After her basic clinical evaluation and due to largely nonspecific findings, we performed ultrasonography. Examination of all nail units enabled a more comprehensive case description. This imaging technique demonstrated moderately hyperechoic solid nodules involving the matrix-bed junction. These nodules corresponded to sarcoid granulomas and represented the pathogenic process underlying the clinical findings. To our knowledge, this is the first ultrasonographic description of such findings in the literature. Previous reports have been limited to nonspecific cutaneous sarcoidosis. López-Llunell et al.[19] analyzed ultrasonographic patterns of cutaneous sarcoidosis and found the most frequent feature to be dermal and subcutaneous hypoechoic areas surrounded by hyperechoic subcutaneous tissue with hypervascularity. These patterns may be extrapolated to nail sarcoidosis, although in our case the nodules themselves were hyperechoic.

It is well established that inflammatory nail diseases, such as psoriasis, show ultrasonographic changes with Doppler flow analysis that help determine the degree of inflammatory activity and monitor therapeutic efficacy[18]. These dynamic changes were evident in our patient, and ultrasonographic evaluation of both the nail matrix and bed showed significant vascularity, suggesting an active disease phase. Follow-up Doppler examination after infiltration showed marked improvement with near-absence of Doppler signal, indicating that this non-invasive technique may play a role in monitoring sarcoidosis treatment response.

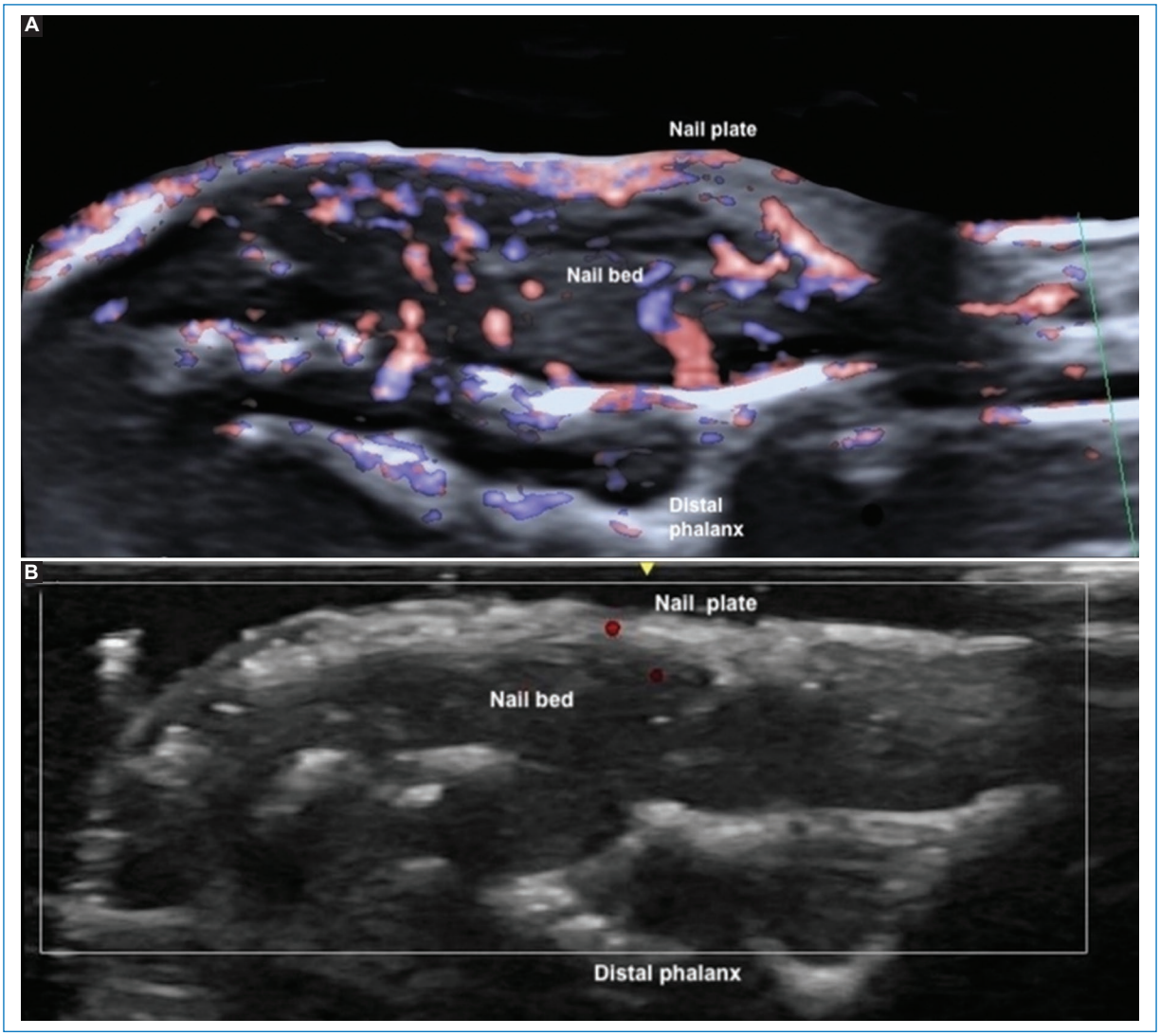

Figure 5. Initial ultrasonography and 3-month follow-up. **A:** hypoechoic nail bed with increased thickness, moderately hyperechoic solid nodule contacting the nail matrix, and increased vascularity due to inflammation. Sclerotic changes in the distal phalanx. **B:** improvement in inflammation of the nail bed and matrix after periungual and eponychial triamcinolone infiltration. Doppler shows almost no inflammatory signal.

A nail biopsy could not be obtained to provide definitive diagnosis. However, the combination of histopathological findings in the skin and hilar lymph nodes, dermoscopic and ultrasonographic results, and marked response to immunomodulatory therapy support sarcoidosis as the most likely diagnosis. Differential diagnoses include psoriasis, lichen planus, nail tumors, and onychomycosis, whose distinct features allow differentiation (Table 1)[20-25].

Treatment of cutaneous sarcoidosis has not been defined in depth. Currently, nail management is considered identical to cutaneous sarcoidosis in cases with mild or absent systemic signs[26]. Main therapeutic strategies include topical or oral corticosteroids or intralesional injections at the proximal nail fold; doxycycline, methotrexate, leflunomide, mycophenolate, and hydroxychloroquine. In cases with dactylitis or bone involvement, monoclonal antibodies targeting tumor necrosis factor – infliximab or adalimumab – are recommended[11]. They are likewise indicated in refractory sarcoidosis with unsatisfactory response to first- and second-line therapies[26]. Our patient is currently being treated with infliximab and intralesional injections and is seeking alternative employment. Meanwhile, Doppler ultrasonography has helped confirm a favorable therapeutic response.

Table 1. Differential diagnoses of nail sarcoidosis

Disease	Clinical and Dermoscopic Findings	Ultrasonography	Histology	Refs.
Nail sarcoidosis	Severe nail dystrophy, onycholysis, dorsal pterygium, nail plate thickening, subungual hyperkeratosis, yellow-brown discoloration, fragility, onychorrhexis, paronychia	Thickened nail plate, alternating hypo- and hyperechoic areas, increased Doppler vascularity, plate discontinuity	Non-caseating granulomas, lymphocytic infiltrates, fibrosis	10, 19, 20
Nail psoriasis	Pitting, oil spots, distal onycholysis, leukonychia, longitudinal ridging, subungual hyperkeratosis, yellow/brown discoloration	Nail plate thickening, loss of definition of the ventral plate, increased vascularity in the proximal region	Hyperkeratosis, Munro microabscesses, elongation of epidermal rete ridges	21, 22
Nail lichen planus	Onychorrhexis, longitudinal striation, loss of shine, nail plate thinning, extreme fragility, possible dorsal pterygium	Thinning of the nail plate, increased echogenicity of the nail bed, decreased Doppler vascularity	Vacuolar degeneration of the basal layer, band-like infiltrate, hypergranulosis	17, 23
Onychomycosis	Onycholysis, nail plate thickening, yellow or greenish discoloration, striae, subungual hyperkeratosis, fragility and crumbling	Diffuse plate thickening, subungual hypoechogenicity, irregular plate and posterior acoustic shadow	Fungal hyphae in keratin, hyperkeratosis, mild inflammation, neutrophilic microabscesses	5, 24
Nail-bed tumors	Nail deformity, palpable subungual masses, melanonychia, erythema, possible ulceration	Well-defined mass, increased vascularity in vascular tumors, possible distal phalanx erosion	Tumor cells with characteristic atypical proliferation in malignant lesions	16, 25

Conclusions

Ultrasonography with color Doppler flow analysis is a useful complementary tool for evaluating nail lesions associated with sarcoidosis, as it enables real-time characterization of structural and vascular alterations and may assist in diagnosing early disease. Furthermore, it may be highly valuable for monitoring therapeutic response. Nonetheless, histopathological examination remains the gold standard for definitive diagnosis. Further research is needed to explore the ultrasonographic signs of this rare condition.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. No experiments on humans or animals were performed for this research.

Confidentiality, informed consent, and ethics approval. The authors followed institutional confidentiality protocols, obtained informed consent from the patient, and received approval from the Ethics Committee. SAGER guideline recommendations were followed in accordance with the study design.

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CLINICAL CASE

Telangiectatic carcinoma as an unusual presentation of a cutaneous metastasis of adenocarcinoma of the colon

Carcinoma telangiectásico como presentación inusual de una metástasis cutánea de adenocarcinoma de colon

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Abstract

We present the case of a 52-year-old woman with a history of cervical cancer who underwent 26 radiotherapy sessions, with a 7-month history of evolution, characterized by lesions in the pelvis, abdomen and legs, associated with symptoms gastrointestinal. A biopsy was performed, which showed multiple atypical mitotic figures, in addition to permeation vascular and immunohistochemistry positive for CD20 and CDX2, confirming the diagnosis of telangiectatic carcinoma, with fatal outcome 2 months after diagnosis.

Keywords: *Skin metastasis. Colorectal cancer. Telangiectatic carcinoma. Tumor markers.*

Resumen

Presentamos el caso de una mujer de 52 años con antecedente de cáncer de cuello uterino, sometido a 26 sesiones de radioterapia y 2 de braquiterapia, con un cuadro de 7 meses de evolución, caracterizado por lesiones en la pelvis, el abdomen y las piernas, asociado a síntomas gastrointestinales. Se realizó biopsia, que evidenció múltiples figuras de mitosis atípica, además de permeación vascular e inmunohistoquímica positiva para CD20 y CDX2, confirmando el diagnostico de carcinoma telangiectásico, con desenlace fatal a los 2 meses del diagnóstico.

Palabras clave: *Metástasis cutánea. Cáncer colorrectal. Carcinoma telangiectásico. Marcadores tumorales.*

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Introduction

Telangiectatic carcinoma is a type of cutaneous metastasis almost exclusively associated with breast or lung cancer. It presents as prominent violaceous or purpuric nodules or papules, which may acquire a contusion-like, zosteriform, morphea-like, or armor-like appearance, among others. Diagnosis is challenging and requires an appropriate clinical examination accompanied by important tools such as dermoscopy, as well as extension studies that allow a final diagnosis, including biopsy and immunohistochemistry[1,2].

Case report

A 52-year-old woman from La Paz, Bolivia, with a history of stage III-B cervical cancer treated with 26 sessions of radiotherapy and 2 sessions of brachytherapy, presented to dermatology with a 7-month history of cutaneous induration affecting the abdominal, perineal, and bilateral thigh regions. Symptoms were accompanied by asthenia, a 5-kg weight loss over the past 3 months, abdominal pain, and difficulty ambulating. On physical examination, hot-to-touch neoformations were palpated, some coalescent, with papular morphology and bluish to black coloration, associated with local heat and pilosebaceous follicle atrophy (Fig. 1). Dermoscopy without polarized light of the abdominal region revealed asymmetric and heterogeneous pigmentation, with bluish and reddish areas, and absence of perifollicular openings (Fig. 2).

Given suspicion of a metastatic process, staging studies were requested. Abdominoperineal contrast-enhanced CT showed thickened colonic mucosa (18 mm). Because of the patient's poor general condition, gastrointestinal biopsy was not performed. Tumor markers revealed elevated CEA (681 U/mL) (Table 1). Biopsy of the cutaneous neoformations demonstrated stratified squamous epithelium with clusters of pleomorphic cells, multiple atypical mitotic figures, and vascular permeation (Figs. 3 and 4). Immunohistochemistry was positive for CK20 and CDX2 (markers of adenocarcinoma and colorectal carcinoma), confirming the diagnosis of telangiectatic carcinoma (cutaneous metastasis of colorectal adenocarcinoma) (Table 2 and Fig. 5).

The patient's course was unfavorable. She was evaluated by oncology, which recommended palliative care. She died 2 months after diagnosis.

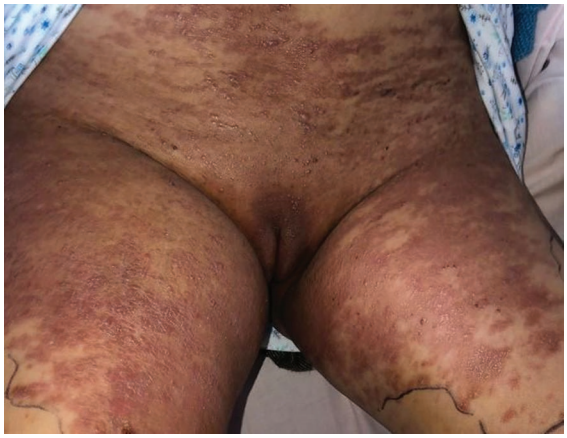

Figure 1. Disseminated dermatosis involving the abdomen, pelvis, and thighs, characterized by multiple erythematoviolaceous papular neoformations, confluent into an indurated, erythematous, warm plaque with cutaneous hardening, limiting abduction.

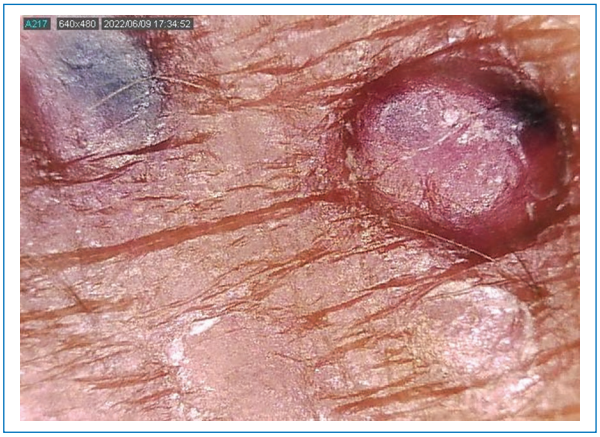

Figure 2. Papule with reddish, bluish, and blackish areas.

Discussion

Cutaneous metastases are rare in dermatology, with a prevalence of 0.6–0.9%. Dermatologists, however, may be the first to detect them. In men, the most frequent primary tumor is lung cancer, followed by colorectal cancer. In women, the most common primary tumor is breast cancer, followed also by colorectal cancer[3-6].

Colorectal cancer metastases have a prevalence of 0.7–5%, more frequent in women and in middle age. When they metastasize to the skin, they usually involve the abdominal and perineal regions[3-5].

Pathogenesis occurs when neoplastic cells detach from the primary tumor and disseminate to other sites, most widely through hematogenous and lymphatic routes[1,7]. Although treatment is individualized,

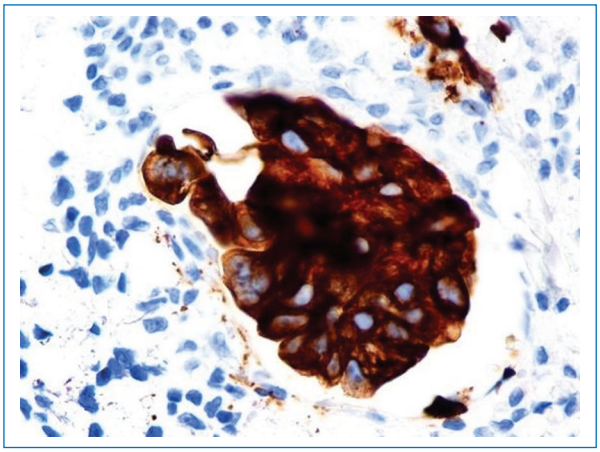

Figure 3. Hematoxylin-eosin, ×40: stratified squamous epithelium with clusters of pleomorphic cells.

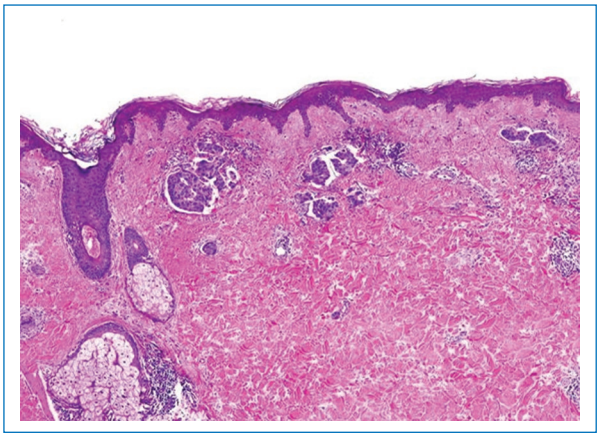

Figure 4. Hematoxylin-eosin, ×200: multiple atypical mitotic figures and vascular permeation.

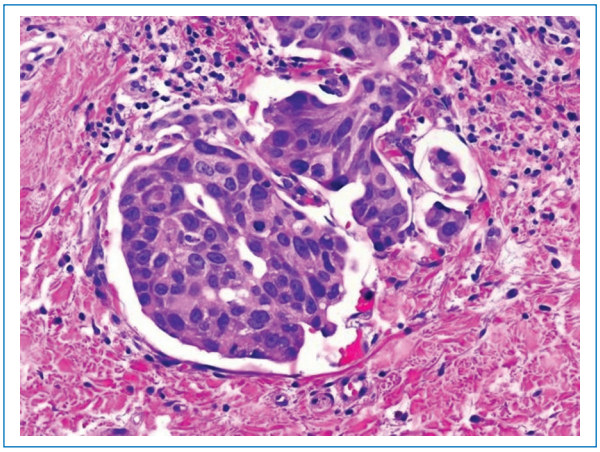

Figure 5. Immunohistochemistry: CK20 positive (GI marker).

Table 1. Tumor markers

Marker	Value
CEA	681.0 U/mL
AFP	4.4 U/mL
CA 125	90.4 U/mL
CA 19-9	26.3 U/mL
CA 15-3	16.9 U/mL

AFP: α-fetoprotein (normal); CA: cancer antigen (CA 125 elevated); CEA: carcinoembryonic antigen (elevated).

Table 2. Immunohistochemistry

Marker	Result
CK A1-A3	Positive
CK20	Positive
CDX2	Positive
Ki67	Positive

CDX2: intestinal cell marker; CK20: colorectal carcinoma marker; CK A1-A3: cytokeratins; Ki67: mitotic activity marker.

prognosis is poor, with survival ranging from 1-34 months[3]. Half of patients die within 6 months of diagnosis[4,8].

It is important to perform thorough screening and skin examinations in all patients with a history of neoplasia, in order to enable timely diagnosis, multidisciplinary management, and improved quality of life.

Conclusions

We contribute to the literature a new case of cutaneous metastasis whose diagnosis required detailed dermatologic examination. We highlight the importance of careful skin assessment in all oncology patients and the key role of dermatologists.

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The authors declare that this work was carried out with their own resources.

Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments were performed on humans or animals for this investigation.

Confidentiality, informed consent, and ethical approval. The study does not involve personal patient data and did not require ethics approval. The SAGER guidelines do not apply.

Declaration on the use of artificial intelligence. The authors declare that they did not use any type of generative artificial intelligence for the writing of this manuscript.

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CLINICAL CASE

Vegetative pyoderma gangrenosum: unusual presentation of a case

Pioderma gangrenoso vegetante: presentación inusual de un caso

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Abstract

Pyoderma gangrenosum is a neutrophilic, non-infectious, and progressive dermatosis. Superficial granulomatous or vegetative variety is advertised as the least typical. Diagnosis is difficult even for the dermatologist due to its large clinical spectrum. It has a lower association with systemic involvement and excellent response to topical corticosteroids or short oral courses of them. We present a 32-year-old male with no history of importance who presents two erythematous, warty and crusty plaques on the leg, asymptomatic, of two months of evolution; histopathology compatible with vegetative pyoderma gangrenosum. He had a good response to treatment with no recurrences 13 years after diagnosis.

Keywords: *Pyoderma gangrenosum. Vegetative variety. Corticosteroids.*

Resumen

El pioderma gangrenoso es una dermatosis neutrofílica, no infecciosa y progresiva. La variedad superficial granulomatosa o vegetante se anuncia como la menos típica. Su diagnóstico es difícil, incluso para el dermatólogo, por su gran espectro clínico. Tiene menor asociación con afección sistémica y excelente respuesta a los corticosteroides tópicos o en ciclos cortos orales. Presentamos el caso de un paciente de 32 años sin antecedentes de importancia que presenta en la pierna dos placas eritematosas, verrugosas y de aspecto costroso, asintomáticas, de 2 meses de evolución. La histopatología fue compatible con pioderma gangrenoso vegetante y tuvo buena respuesta al tratamiento, sin recidivas a 13 años del diagnóstico.

Palabras clave: *Pioderma gangrenoso. Variedad vegetante. Corticosteroides.*

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Introduction

Pyoderma gangrenosum is a rare inflammatory skin disease characterized by dermal neutrophilic infiltration[1,2]. According to reports, it predominantly affects women (up to 76% of cases), with an average age of onset of 59 years[3]. It commonly presents as a persistent, sterile, and deep ulceration affecting the lower limbs[4]. Approximately 50% of patients have an associated systemic disease, with the most frequent being inflammatory bowel disease and seronegative arthritis[5,6]. There are several subtypes, but the classical variant is the most common, accounting for about 85% of cases. The vegetative form is a superficial and uncommon variety of the disease, which generally is not associated with underlying systemic conditions[7]. It is often misdiagnosed as other pathological processes that produce vegetations and is therefore linked to delays in treatment[8].

Case report

A 32-year-old man with no history of chronic degenerative disease presented with a 2-month history of a rapidly progressing "dryness". On physical examination, a dermatosis was observed on the anterior-lateral aspect of the upper-middle third of the left leg, consisting of 2 erythematous-infiltrated verrucous plaques with well-demarcated borders. The larger lesion measured 23 cm × 12 cm × 1.0 cm and the smaller one 2.5 cm × 1.7 cm × 1.0 cm, both covered with meliceric and sanguinopurulent crusts (Fig. 1). Microbiological studies (including cultures on Sabouraud agar and stains such as Gram, Ziehl-Neelsen, and Grocott's methenamine silver) were negative. Histopathology showed epidermis with focal ulceration and fibrin deposits; in the superficial and mid dermis, there was an inflammatory infiltrate predominantly composed of neutrophils, as well as lymphocytes and histiocytes, and dilated blood vessels (Fig. 2). A diagnosis of vegetative pyoderma gangrenosum was established. An assessment to rule out associated diseases included complete blood count, blood chemistry, liver function tests, acute-phase reactants, antinuclear antibodies, fecal occult blood test, and rheumatoid factor – all of which were normal and negative. Due to the extent of the dermatosis, treatment was initiated with 60 mg of deflazacort, which was tapered weekly over a 2-month period until discontinued, leading to complete resolution with no recurrences 13 years after diagnosis.

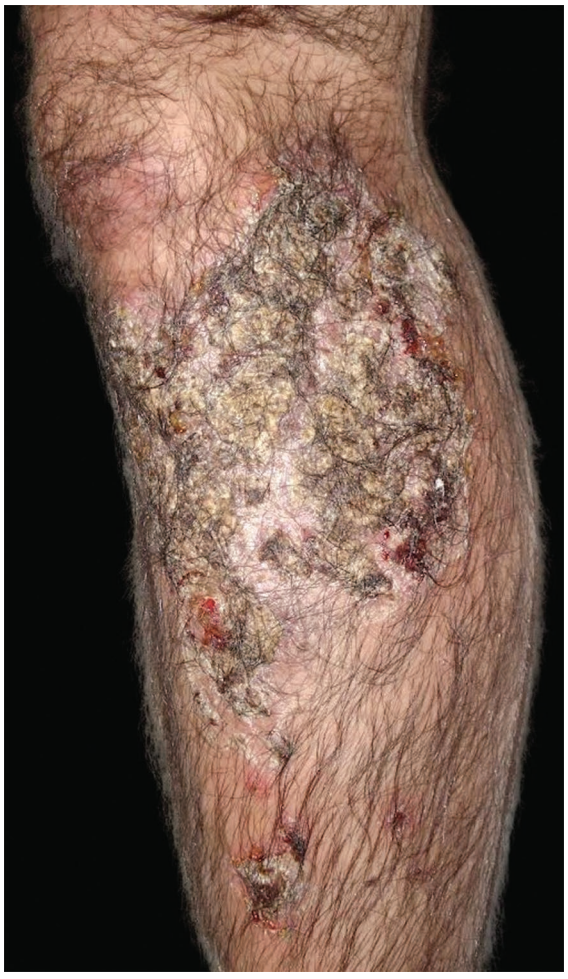

Figure 1. Verrucous-looking lesion on the left lower extremity.

Discussion

Pyoderma gangrenosum is a skin condition characterized by a painful erythematous lesion that rapidly progresses into a papule, blister, or pustule. Undermined ulcers with violaceous, irregular erythematous borders and necrotic areas are common and usually affect the lower limbs, although they can appear anywhere on the body[3,6,8]. Its etiology and pathogenesis have been extensively studied but remain diagnostically and therapeutically challenging[8], with some authors classifying it as idiopathic in 25-50% of cases[5,6,9]. It was initially described as a localized delayed hypersensitivity reaction to an unidentified endogenous or exogenous antigen, based on its response to immunosuppressants and association with pathergy[9,10]. Several studies suggest that the follicular unit may be an initial target of inflammatory cascades, leading to focal necrosis of

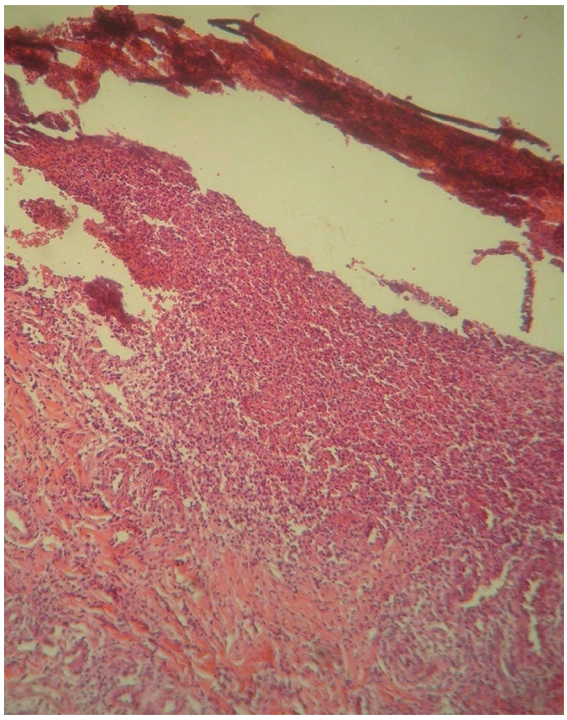

Figure 2. Histological section stained with hematoxylin and eosin (40 μm) showing an inflammatory infiltrate predominantly composed of neutrophils.

keratinocytes, followed by excessive stimulation of neutrophils and Th1 and Th17 lymphocytes. This in turn activates tumor necrosis factor-alpha (TNF-α), matrix metalloproteinases 2 and 9, vascular endothelial growth factor, and interleukins (IL) 1β, 8, and 17, inducing local infiltration and neutrophil activation that result in lesion formation[11]. A key feature of this inflammatory process is neutrophilic dysfunction, with abnormal trafficking and overexpression of IL-8 as a potent neutrophil chemoattractant. Neutrophil extracellular traps (NETs) have also been reported, apparently playing a significant role in pathogenesis. The location and depth of NETs seem to determine the various forms of pyoderma[11]. Currently, the initiating and perpetuating factors of these inflammatory processes remain unknown[11].

Five major clinical and histopathological variants are described: ulcerative, pustular, bullous, peristomal, and vegetative or superficial granulomatous[3,7]. Vegetative pyoderma gangrenosum is characterized by a benign course, favorable prognosis, and good response to conservative treatment[10]. First described in 1988 by Wilson-Jones and Winkelmann[9], it is the rarest form, accounting for < 2% of all cases[2]. Unlike other variants, vegetative PG can appear at younger ages, is not associated with systemic diseases, and evolves slowly and painlessly[7]. Morphologically, it presents as > 1 superficial ulcerated plaques, with non-purulent bases, no erythema, and exophytic or vegetative projections with well-defined, non-undermined borders[9]. It typically occurs on the trunk (52%), limbs (31%), face (9%), groin (5%), or scalp (2%)[2,7].

Diagnosis is achieved based on clinicopathologic correlation. Clinical and histological features help exclude conditions such as bacterial, mycobacterial, and fungal infections; autoinflammatory diseases; granulomatous diseases; or cutaneous neoplasms[7,9]. Due to its varied presentation, it is frequently confused with other disorders, requiring a broad differential diagnosis[1,2]. In vegetative PG, a diagnostic approach should consider the "verrucous syndrome" acronym *PLECT* (paracoccidioidomycosis, leishmaniasis, sporotrichosis, chromomycosis, cutaneous tuberculosis), as well as histoplasmosis and blastomycosis among infectious diseases[1,7]. Other differentials include vegetative pemphigus, granulomatous diseases, antiphospholipid syndrome, basal and squamous cell carcinoma, foreign body granuloma, vasculitis, syphilis, and drug eruptions, among others[3,9]. Additionally, histological findings depend on biopsy site and lesion evolution. They are nonspecific and mainly help to rule out other causes of ulceration. Ideally, biopsies should be taken from lesion borders, where the most useful findings are seen. A classic finding is the "3-layer granuloma," composed of a central area of neutrophils, an intermediate zone with histiocytes and giant cells, and an outer layer of plasma cells, eosinophils, and some dilated vessels, giving rise to a sinus tract appearance. Pseudoepitheliomatous hyperplasia may be observed in the dermis. Central biopsies may show vasculitis, which, if prominent, should suggest a primary vasculopathy[2,3,9,10].

As with any disease, a delayed or incorrect diagnosis can harm patient care, delay therapy, and worsen prognosis[6]. Recently, diagnostic criteria based on the Delphi method have been proposed, including one major criterion (compatible histopathological findings) and eight minor criteria (Table 1). Diagnosis requires the major criterion plus at least four minor ones[3,12,13], with 86% sensitivity and 90% specificity[13]. Our patient met the major criterion and four minor criteria: exclusion of infections, two ulcers on the anterior leg, ulcer size reduction after immunosuppressive therapy, and wrinkled-paper-like healing. We stress that not all proposed criteria apply to vegetative PG, such as a history of inflammatory bowel disease or peripheral erythema of the lesion.

Table 1. Criteria for the diagnosis of ulcerative pyoderma gangrenosum proposed using the Delphi methodology[13]

Major criterion	
Biopsy of the ulcer edge	Presence of neutrophilic infiltrate
Minor criteria	
Histology	Exclusion of infectious processes (including special stains and tissue cultures)
Medical History	Pathergy phenomenon (appearance of ulcers at sites of trauma)
	Personal history of inflammatory bowel disease or inflammatory arthritis
Physical examination (or photographic evidence)	Presence of papule, pustule, or vesicle that rapidly progresses to ulceration
	Peripheral erythema, undermined border, tenderness at the site of ulceration
	Multiple ulcers (at least one located on the anterior aspect of the leg)
	Cribriform or "crumpled paper" scarring after ulcer resolution
Treatment	Reduction in ulcer size after 1 month of immunosuppressive therapy

Treatment remains largely anecdotal, with no national or international guidelines. Management is based on underlying conditions, pattern, type, severity, and progression of the dermatosis[3,6]. Immunosuppressants are the mainstay of treatment, with systemic corticosteroids (prednisone 0.5-1 mg/kg/day) as first-line therapy. A hallmark of the vegetative form is its general response to topical therapy (creams, ointments, or intralesional drugs)[9,10,14]. However, this is not always feasible, especially in disseminated cases like ours, where non-systemic therapies were not a viable option. High-potency corticosteroids such as clobetasol 0.05% used as monotherapy show a 42.6% healing rate at 6 months, with relapses in 21.1% of cases. Topical calcineurin inhibitors (tacrolimus, pimecrolimus, cyclosporine) are applied twice daily for weeks until healing, then reduced to once daily for 2 months, and finally tapered to twice weekly for 6-12 months before discontinuation[15]. Lesion size at diagnosis is a significant predictor of healing time[15]. For disseminated superficial forms, systemic corticosteroid therapy in short pulses is recommended. Up to 39% of patients require more than one pulse of prednisone[1,2]. Although pathergy is seen in 20-30% of cases, the latest approach for refractory PG includes surgical management (gentle debridement of wound bed and borders, combined with autografts, xenografts, negative-pressure therapy, hyperbaric oxygen, flaps, or dermal substitutes), reported as successful in up to 86% of patients, always with adequate immunosuppression[16]. In our case, despite the lesion size, 2 months of systemic therapy were sufficient for complete resolution.

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CLINICAL CASE

Indolent systemic mastocytosis with response to phototherapy in a patient with other non-hematologic neoplasms: a therapeutic challenge

Mastocitosis sistémica indolente con respuesta a fototerapia en una paciente con otras neoplasias no hematológicas: un reto terapéutico

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Abstract

Mastocytosis is a rare clonal hematopoietic disorder characterized by the proliferation of neoplastic mast cells in the skin or other organs, including the bone marrow. It is classified into cutaneous, systemic, and mast cell sarcoma. Treatments focus on symptoms control or eliminating mast cells, with KIT inhibitors like midostaurin and avapritinib being effective therapies. Phototherapy has proven effective in symptomatic control in indolent systemic mastocytosis as in the presented case, improving quality of life.

Keywords: *Systemic mastocytosis. Indolent. Phototherapy. Quality of life. Multisystem involvement. Mast cells.*

Resumen

La mastocitosis es un trastorno hematopoyético clonal poco frecuente caracterizado por la proliferación de mastocitos neoplásicos en la piel u otros órganos, incluida la médula ósea. Se clasifica en cutánea, sistémica y el sarcoma de mastocitos. Los tratamientos se centran en el control de los síntomas o en la eliminación de los mastocitos, con inhibidores de KIT como la midostaurina y el avapritinib como terapias efectivas. La fototerapia ha demostrado su eficacia en el control sintomático en la mastocitosis sistémica indolente como en el caso presentado, mejorando la calidad de vida.

Palabras clave: *Mastocitosis sistémica. Indolente. Fototerapia. Calidad de vida. Afectación multisistémica. Mastocitos.*

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Introduction

Mastocytosis belongs to a group of hematopoietic stem cell proliferative disorders and is characterized by abnormal production and accumulation of mast cells in various tissues. It is a rare clonal hematopoietic disorder that manifests in the skin, bone marrow, and other organs.[1,2] Depending on the tissue affected and the mast cell burden, mastocytosis is classified into three main forms: cutaneous mastocytosis (CM)—the most frequent form in children, limited exclusively to the skin; systemic mastocytosis (SM); and mast cell sarcoma, an extremely rare, aggressive variant with poor prognosis that usually presents with extramedullary tumors[3] (Fig. 1).[4]

Indolent systemic mastocytosis (ISM) is the most common adult presentation of SM. It follows a benign, chronic course with mild multisystemic symptoms mainly related to mast cell mediator release. Life expectancy is similar to that of the general population.[5,6]

Another less common variant is systemic mastocytosis associated with neoplasms, which occurs with hematologic disorders such as chronic myeloid leukemia or myelofibrosis. Distinguishing this variant is crucial due to its prognostic impact.[5,6]

Mutations in the KIT proto-oncogene, particularly the D816V gain-of-function mutation, play a central role in disease pathogenesis. This mutation causes constitutive activation of tyrosine kinase, which stimulates uncontrolled mast cell proliferation. The discovery of these molecular alterations has been essential for the development of targeted therapies that not only focus on symptoms but also directly inhibit molecular pathways implicated in mastocytosis pathogenesis. Tyrosine kinase inhibitors (TKIs), such as imatinib and midostaurin, have shown efficacy in treating mastocytosis in patients with KIT D816V mutation. Midostaurin, in particular, has demonstrated effectiveness in controlling symptoms, reducing mast cell burden, and improving quality-of-life parameters in patients with advanced forms of the disease. The development of new inhibitors such as avapritinib and bezuclastinib offers an additional therapeutic strategy, especially in refractory cases or in those with a high mutational burden.[3]

Phototherapy, particularly narrowband ultraviolet B (NB-UVB), has become an effective therapeutic option for refractory cases of CM and ISM. This treatment helps improve symptoms such as pruritus and reduce lesion burden, including erythematous and hyperpigmented macules and papules.[5,7]

The objective of this manuscript is to highlight the efficacy of NB-UVB phototherapy as an effective strategy in the management of a patient with ISM, offering new perspectives to improve the quality of life of patients with this diagnosis.

Case report

A 57-year-old woman was referred in 2023 to the dermatology service of our hospital with a 16-year history of dermatosis, bilateral and symmetrical, involving the thorax, abdomen, and extremities. It was characterized by multiple hyperpigmented macules and papules, some erythematous, well defined, and intensely pruritic, with a positive Darier sign (Fig. 2).

Her past medical history included urticarial allergic reaction to nonsteroidal anti-inflammatory drugs, unilateral breast cancer in 2017 treated with breast-conserving surgery, radiotherapy, and adjuvant chemotherapy with anastrozole, as well as right-sided colon cancer in 2022 treated with surgical resection and oxaliplatin. At the time of presentation, she was undergoing treatment for diabetes, dyslipidemia, and chronic pain with gabapentin, venlafaxine, tramadol, metformin, and bezafibrate.

Histopathologic evaluation of a skin biopsy performed in 2017 reported superficial perivascular dermatitis with lymphocytes and CD117+ mast cells, consistent with cutaneous mastocytosis but not excluding systemic mastocytosis (Figs. 3 and 4). In a tertiary referral center, the diagnosis of systemic mastocytosis was confirmed. The patient met one major and two minor criteria for ISM: multifocal bone marrow infiltrates of CD117+ mast cells; expression of CD25 and CD30 by bone marrow and peripheral blood mast cells; and > 25% of mast cells in bone marrow biopsy displaying atypical immature morphology. Due to limited resources, serum tryptase levels were not assessed.

In 2017, treatment with midostaurin, prednisone, and loratadine was initiated, with minimal symptomatic improvement; however, there was no cutaneous response. Imatinib was added, also without therapeutic benefit.

In 2023, we initiated NB-UVB phototherapy with a Daavlin “Model 3 Series PC311-350 24/24” device, three sessions per week, starting at 150 mJ/cm² with increments of 100 mJ/cm² per session up to 1,500 mJ/cm², when therapeutic response was first observed. Loratadine 10 mg every 24 h was maintained.

The patient achieved approximately 80% cutaneous improvement, is currently asymptomatic, though still

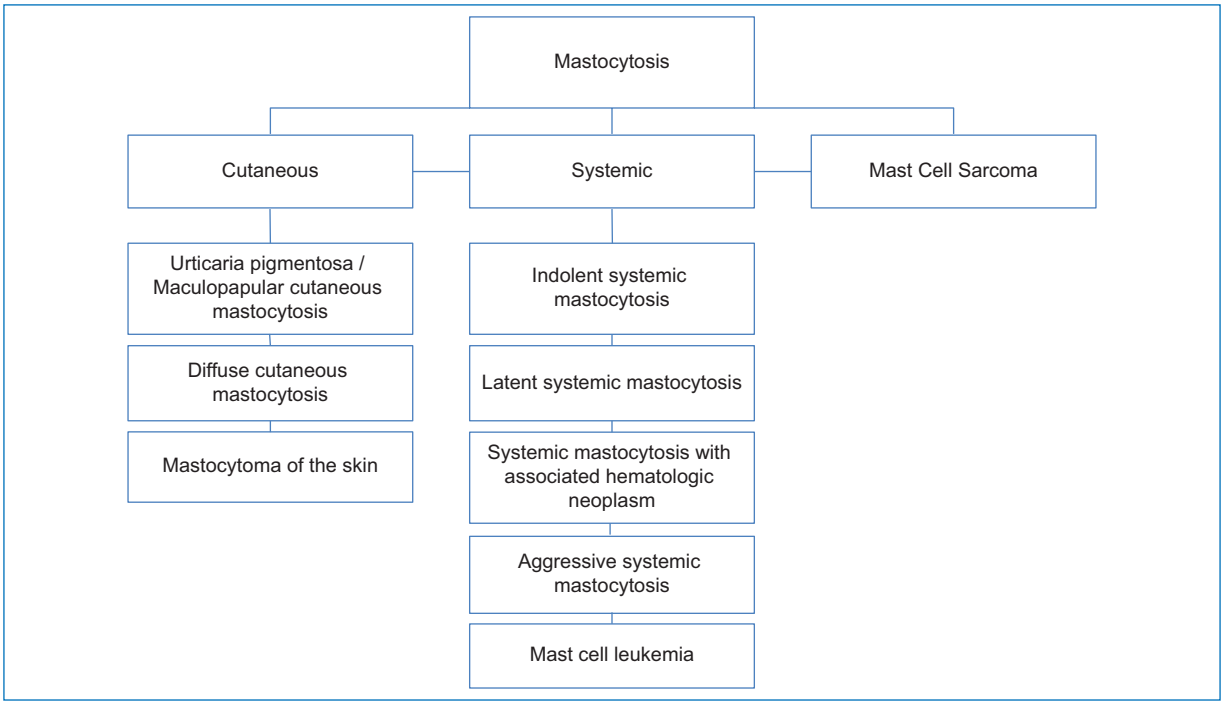

Figure 1. Classification of mastocytosis and its variants (*adapted from Horny et al., 2017*[4]).

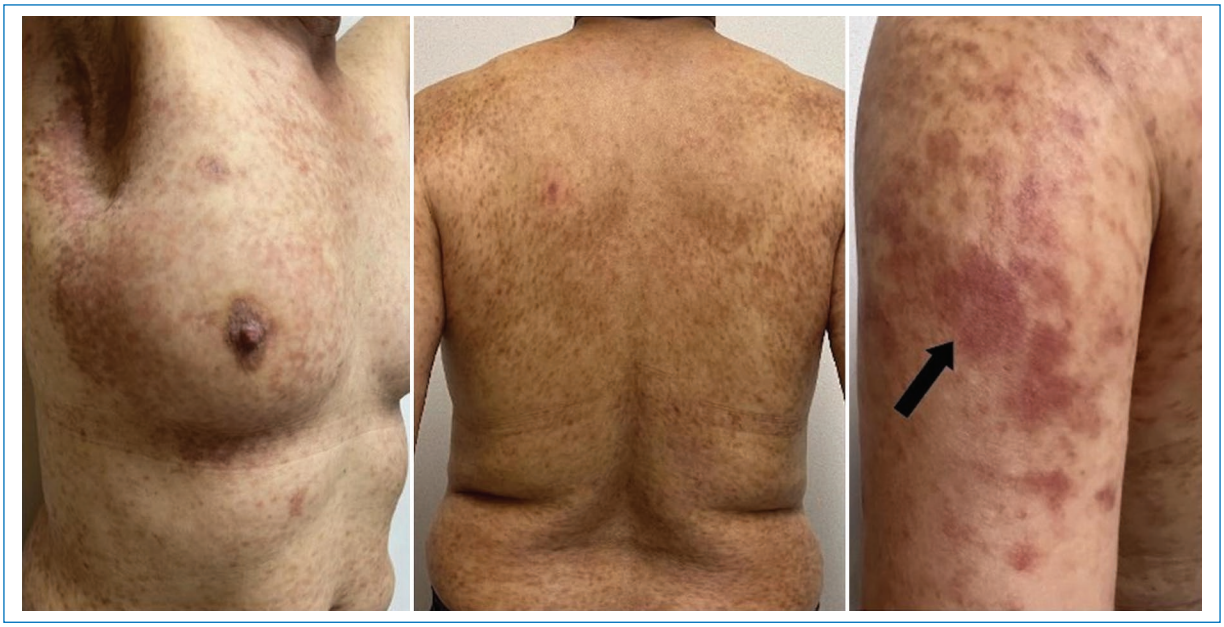

Figure 2. Multiple erythematous and pigmented macules and papules. Positive Darier sign (arrow). Before NB-UVB phototherapy.

presenting some hyperpigmented macules and a positive Darier sign. At the time of this report, she had received 207 sessions, with a cumulative dose of 292,532 mJ/cm² of NB-UVB (Figs. 5 and 6).

Discussion

Recent updates in the diagnostic criteria for SM have emphasized morphology and immunohistochemical

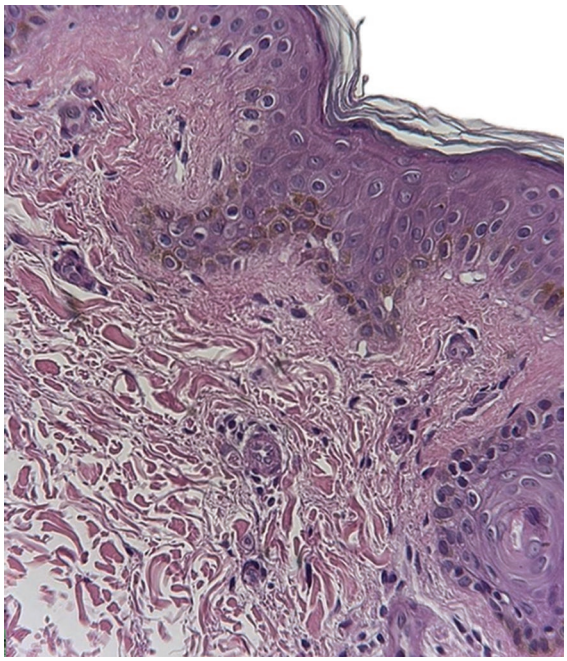

Figure 3. Hematoxylin-eosin stain showing perivascular infiltrate with predominance of lymphocytes and mast cells, some spindle-shaped (×60).

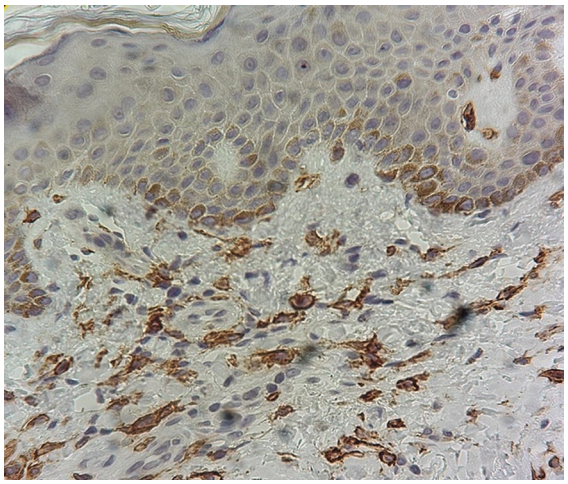

Figure 4. Immunohistochemistry: CD117 positive in numerous perivascular and interstitial mast cells (×60).

studies to identify mast cells positive for tryptase, CD117, CD25, CD30, and CD2. In addition, the detection of KIT activating mutations is now considered a minor diagnostic criterion.[2,6,7]

Treatment of ISM has been mainly symptomatic. In advanced systemic mastocytosis, therapeutic strategies have included cytoreductive therapy with interferon-α, which has shown variable results and has been replaced by TKIs such as imatinib, which is effective in SM without KIT D816V mutation.[3] We do not know if the patient carried this mutation, as testing for this genetic alteration was not performed; however, she did not experience clinical improvement with imatinib.

Midostaurin is very useful in aggressive SM, having produced significant responses with symptomatic improvement. Avapritinib, a multikinase inhibitor, has achieved high response rates in clinical trials and is considered first-line therapy for ISM. Bezuclastinib, selective for KIT D816V, has demonstrated early improvement in clinical signs and is now a promising therapy for refractory cases.[7,8] The patient described in this report had been treated with midostaurin, prednisone, and imatinib, without relief of pruritus and with persistence of cutaneous lesions.

Therapeutic combinations of TKIs with hypomethylating agents have also been studied to target diverse genetic clones, as well as allogeneic hematopoietic stem cell transplantation (allo-HSCT) as a potentially curative option.[3,6]

Phototherapy with NB-UVB or psoralen plus UVA (PUVA) is a therapeutic option for refractory cases, including patients with CM and ISM. The mechanism of action of phototherapy is based on suppression of mast cell activity, inhibiting the release of inflammatory mediators such as histamine and leukotrienes. It also helps reduce mast cell infiltration in the skin by modulating the expression of markers such as CD117. Furthermore, it has been shown to induce apoptosis in inflammatory cells and regulate the immune microenvironment, thereby reducing chronic inflammation. Recent studies also suggest that phototherapy can reduce serum tryptase levels, which correlates with symptom improvement.[9,10]

A study by Brazelli et al. compared these two modalities and demonstrated that both NB-UVB and PUVA are effective in the management of patients with CM and ISM. This work reported significant improvement in skin lesions, including reduction of pruritus and erythematous macules, after 20 sessions. Although both modalities showed benefit, PUVA was associated with better results in severe cases, but with higher risk of adverse effects.[5]

In our case, the patient presented generalized erythematous maculopapular lesions with significant pruritus. After antihistamine treatment, her symptoms persisted, justifying the initiation of NB-UVB phototherapy. Similar to the findings reported by Brazelli et al., our patient experienced a marked reduction of

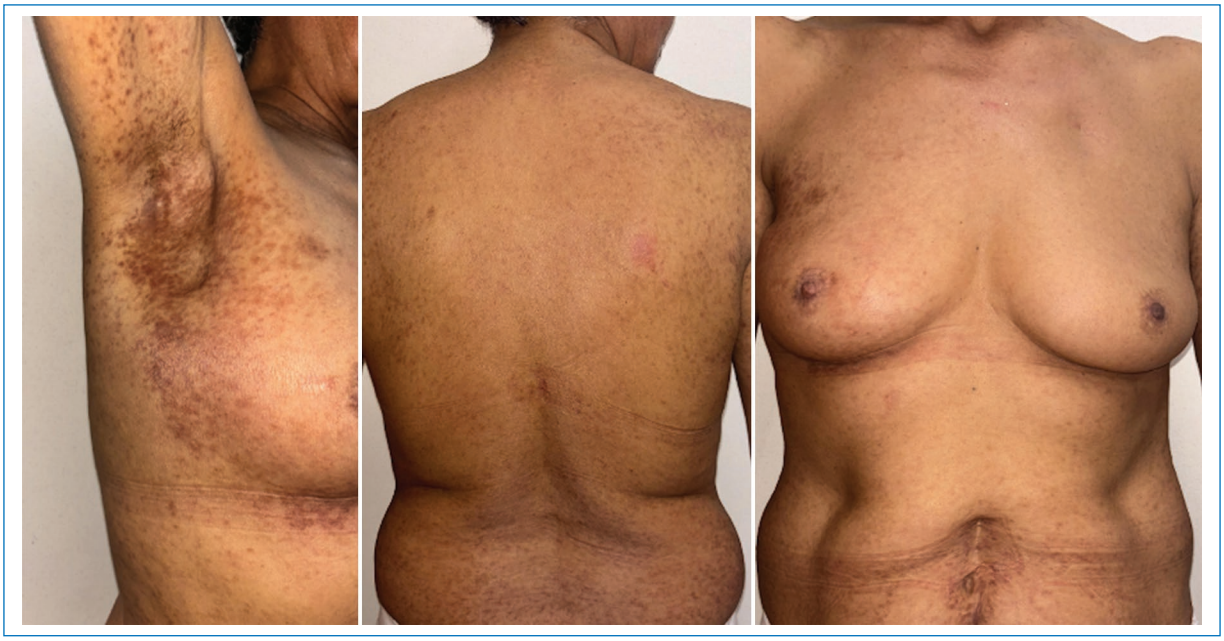

Figure 5. Residual hyperpigmented macules after 30 sessions of NB-UVB phototherapy.

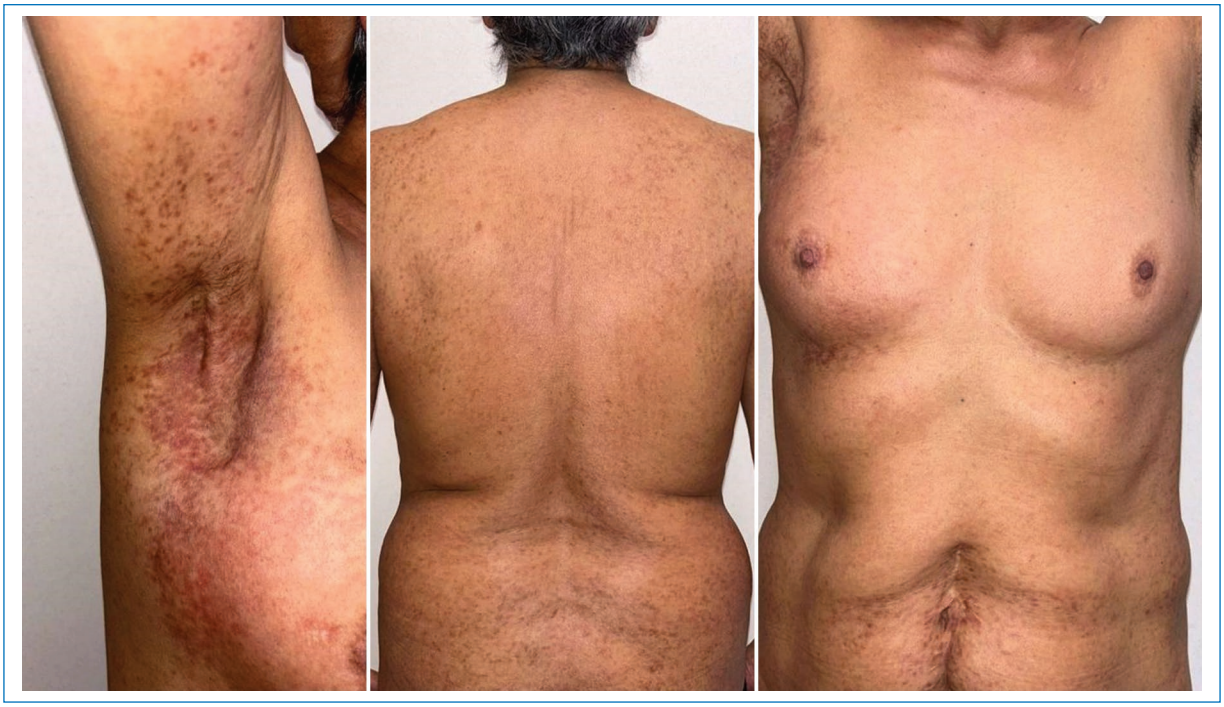

Figure 6. Follow-up after receiving narrowband ultraviolet B phototherapy (session 207).

pruritus, measured using the verbal numeric scale, and notable improvement in the appearance of cutaneous lesions, with only some residual hyperpigmented macules after 30 sessions.

On the other hand, the release of inflammatory mediators by mast cells may create a microenvironment that favors carcinogenesis. Meloti et al. found an increase in perivascular mast cells in rectal adenomas, possibly

representing an association in our patient with her history of colorectal carcinoma.[11] KIT gene mutations have also been found in other neoplasms, such as certain subtypes of breast and colon cancer, suggesting a possible shared genetic pathway.[12] Normal breast ductal epithelium is typically positive for this gene, but breast carcinomas rarely express it, indicating early KIT loss during tumor transformation.[13] Genetic testing was proposed for this patient—who had presented three different neoplasms—by the genetics service, but she declined, preventing determination of this potential association.

The use of new treatments and second- or third-line therapeutic combinations has produced complete responses and remissions, translating into improved quality of life and survival for patients.[7]

Conclusions

In ISM, therapeutic management focuses on symptom relief and prevention of anaphylactic episodes. Symptom burden can be significant, negatively impacting quality of life. Although phototherapy has proven effective for managing mastocytosis symptoms, it is essential to consider its potential association with increased skin cancer risk, particularly in patients with a history of neoplasm.

In this patient with ISM, NB-UVB phototherapy was effective in significantly reducing clinical symptoms and markedly improving quality of life. Although complete remission was not achieved, sustained improvement allowed for progressive reduction in treatment frequency to the minimum effective regimen, maintaining symptomatic control.

It has been demonstrated that in patients with mastocytosis associated with hematologic neoplasms, symptoms may worsen; in some cases, effective treatment of the neoplasm improves clinical manifestations. Although our case does not qualify as SM associated with neoplasia, continuous monitoring is necessary given the frequent relationship. The association between SM and nonhematologic cancers such as breast or colon requires further study, particularly in light of potential shared KIT mutations.

Advances in molecular identification and the development of targeted therapies have significantly improved the prognosis and treatment of systemic mastocytosis, although further studies are needed to optimize management strategies and define the role of allo-HSCT and phototherapy in its various modalities. A multidisciplinary approach involving dermatology and hemato-oncology is recommended for appropriate management and ongoing surveillance of these patients.

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Ethical considerations

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CLINICAL CASE

Waxy nodule on the nasal ala post-trauma: clinical presentation and surgical resolution

Nódulo ceroso en el ala nasal postraumático: presentación clínica y resolución quirúrgica

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Abstract

Primary cutaneous nodular amyloidosis is a rare type of amyloidosis where the deposition of amyloid is limited to the skin, and unlike macular or lichenoid amyloidosis, traumatic epidermal damage is not believed to play an etiopathogenic role. Must be studied and followed-up, because it is associated with Sjögren's syndrome and progression to systemic amyloidosis has been reported. Dermoscopy findings are yellow-orange background, bright white lines, and linear and serpiginous telangiectasias. The treatment is surgical excision, although various treatment options have been described. We report a unusual case of primary cutaneous nodular amyloidosis secondary to local trauma on the nose.

Keywords: *Amyloidosis. Localized cutaneous nodular amyloidosis. Local trauma. Dermoscopy. Yellow-orange background.*

Resumen

La amiloidosis nodular cutánea primaria es un tipo raro de amiloidosis en la que el depósito de amiloide se limita a la piel. A diferencia de la amiloidosis macular o liquenoide, se cree que el daño epidérmico traumático no desempeña un papel etiopatogénico. Debe ser estudiada y seguida, ya que se asocia con el síndrome de Sjögren y se ha reportado progresión a amiloidosis sistémica. Los hallazgos dermoscópicos incluyen un fondo anaranjado-amarillento, líneas blancas brillantes y telangiectasias lineales y serpiginosas. El tratamiento es la escisión quirúrgica, aunque se han descrito diversas opciones terapéuticas. Presentamos un caso inusual de amiloidosis nodular cutánea primaria secundaria a un trauma local.

Palabras clave: *Amiloidosis. Amiloidosis cutánea nodular localizada. Trauma local. Dermatoscopia. Fondo amarillo-naranja.*

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Introduction

Primary nodular cutaneous amyloidosis is a rare type of amyloidosis in which amyloid deposition is limited to the skin without involvement of other organs. Unlike macular or lichen amyloidosis, epidermal damage due to friction or scratching is not believed to play an etiopathogenic role. We report an unusual case of primary nodular cutaneous amyloidosis secondary to direct facial trauma.

Case report

An 84-year-old woman with a history of hypertension presented with a > 5-year history of a lesion on the nose that had progressively enlarged following a direct blow to the area during a fall. The lesion was neither painful nor pruritic but caused significant cosmetic concern.

On examination, a firm yellow-orange nodular lesion was observed on the right nasal ala (Fig. 1A). Dermoscopy revealed a homogeneous yellow-orange background with linear telangiectatic vessels and shiny white lines (Fig. 1B).

Histologic examination of a skin biopsy showed an extensive deposit of amorphous eosinophilic material in the dermis, with plasma cells (Fig. 2A). Congo red staining demonstrated apple-green birefringence under polarized light (Fig. 2B and C), confirming the diagnosis of nodular amyloidosis.

Additional work-up included complete blood count, metabolic panel, rheumatologic panel, serum and urine protein electrophoresis, chest X-ray, and electrocardiogram. All results were normal, ruling out systemic involvement.

The lesion was surgically excised, and the defect was covered using a two-stage interpolated melolabial flap, with pedicle division at 3 weeks (Fig. 3A). The objective was complete resection while preserving the affected cosmetic unit. At 6-month follow-up, the patient showed an acceptable aesthetic outcome with no signs of local or systemic recurrence (Fig. 3B). She has been followed for 2 years after diagnosis with yearly basic laboratory testing, including rheumatologic panel and serum/urine electrophoresis, all without significant findings.

Discussion

Primary nodular cutaneous amyloidosis is an uncommon and distinct form of amyloidosis attributed to plasma cell proliferation and deposition of immunoglobulin light chains in the skin, without association with systemic amyloidosis or hematologic dyscrasias. The deposited amyloid is typically AL-type (immunoglobulin light chains, either kappa or lambda), resulting from a local proliferation of plasma cells[1,2]. Its exact cause remains unknown, and unlike macular or lichenoid amyloidosis, traumatic epidermal injury from scratching or friction is not believed to play an etiopathogenic role[1-3]. However, 1 reported case showed – through immunohistochemistry, chromatography, and tandem mass spectrometry – that the amyloid did not correspond to light or heavy chains but originated from keratinocytes, corresponding to AK-type amyloid[4]. Notably, there is only 1 documented case in the literature in which a nodular amyloidosis lesion developed after local trauma[4], similar to our patient. Both reports show a clear temporal relationship between traumatic injury and lesion development. Nevertheless, it remains unclear whether the amyloid derives from keratinocyte damage or plasma cells; further studies are required to clarify the causal relationship between trauma and nodular amyloidosis.

Clinically, it usually presents as a nodule, papule, or waxy pink-brown plaque, rarely multiple, and located mainly on acral areas, although cases on the face, scalp, and limbs have also been reported[1,2]. The,eam age at presentation is 55 years, with no sex predilection. It is generally asymptomatic[1], occasionally pruritic, and may cause cosmetic concern. Diagnosis is established by histopathology, showing deposits of amorphous eosinophilic material in the deep dermis and subcutaneous tissue, with apple-green birefringence on Congo red staining, usually accompanied by lymphoplasmacytic inflammatory infiltrate around vessels[2,3].

Dermoscopy has been proposed as a useful diagnostic tool in other forms of cutaneous amyloidosis, but information regarding dermoscopic findings in primary nodular cutaneous amyloidosis is limited[5]. Specific dermoscopic patterns include an orange-pink-yellow background, shiny white lines, and linear or serpiginous telangiectasias[5,6], likely correlating with deposits of amorphous material in the deep dermis and subcutis[5]. Our patient exhibited all 3 features.

Dermoscopic differential diagnoses include granulomatous conditions (such as sarcoidosis and necrobiosis lipoidica) and histiocytic disorders (such as Rosai – Dorfman disease and xanthogranuloma)[5].

Given the rarity of this dermatosis, several treatment options have been reported, including surgical excision, dermabrasion, laser therapy, electrodesiccation, curettage, intralesional corticosteroids, and cryosurgery, with variable effectiveness[2-4].

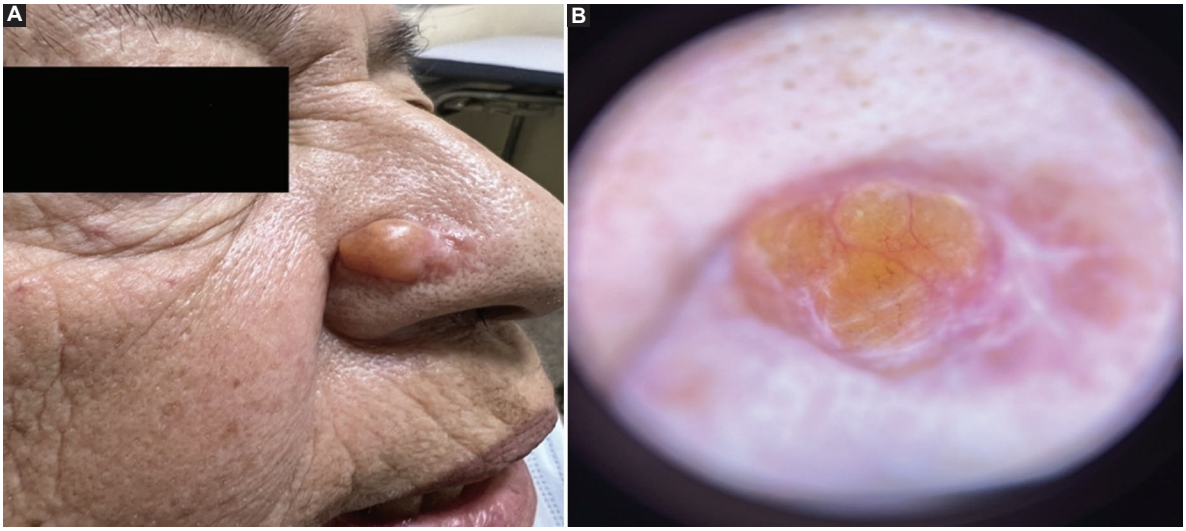

Figure 1. A: waxy-appearing, yellow-orange nodule, measuring 1 × 1.5 cm in diameter, well-defined, non-adherent, and firm on palpation. **B:** dermoscopy revealed a homogeneous yellow-orange background with linear telangiectatic vessels and shiny white lines.

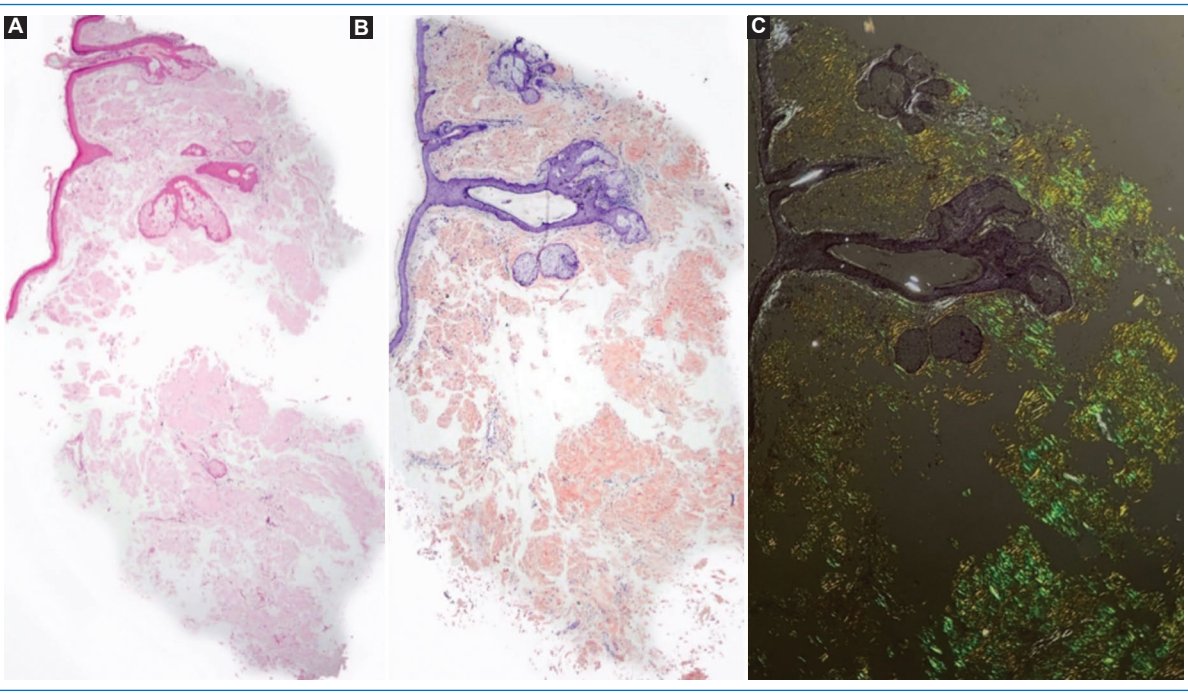

Figure 2. Histopathology (H&E ×100) showing infiltrate of acellular, amorphous, eosinophilic material extending into the dermis and subcutaneous tissue. **A:** sparse adnexal structures and mild lymphocytic infiltration. Congo red stain was positive **(B)**, with apple-green birefringence under polarized light **(C)**.

Regarding prognosis, it is not rare for patients with primary nodular cutaneous amyloidosis to also have other autoimmune connective-tissue diseases, with Sjögren syndrome showing the strongest association in up to 25% of cases[1]. The reported risk of progression to systemic amyloidosis is estimated at 1-7%[7], although paraproteinemia may be present in up to 40%[1,7]. At diagnosis, a complete physical examination and

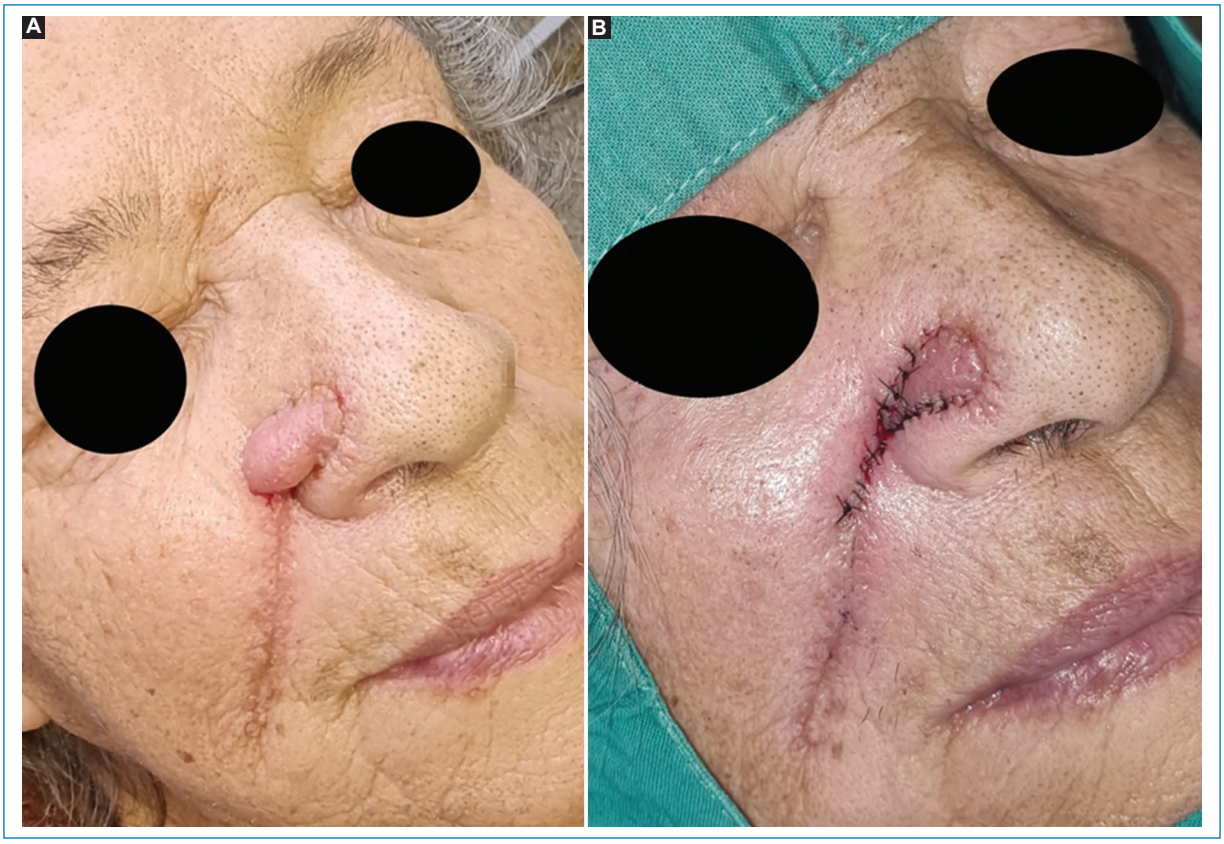

Figure 3. A: 2-stage interpolated melolabial flap with pedicle division at 3 weeks. **B:** acceptable cosmetic result at the 6-month follow-up.

laboratory evaluation – including CBC and metabolic panel – are recommended. The presence of monoclonal plasma cells outside cutaneous lesions is assessed by serum and urine electrophoresis and immunofixation. Depending on results, bone marrow examination may be considered to exclude monoclonal plasma cell populations. Some authors also suggest baseline imaging such as PET scan to assess possible systemic involvement, and an ECG to rule out cardiac disease[1].

It has been proposed that AK-type primary nodular cutaneous amyloidosis does not show these associations; therefore, extensive work-up may not be required if keratinocyte-derived amyloid is confirmed[4]. In our case, the amyloid subtype (AL vs AK) could not be determined, so clinical and laboratory follow-up was maintained for at least 2 years, with no relevant findings to date.

Given this, clinical suspicion of nodular amyloidosis is essential for timely diagnosis, evaluation of associated conditions, and appropriate follow-up[1-3].

Conclusions

Primary nodular cutaneous amyloidosis is an uncommon and distinct form of amyloidosis, generally due to plasma cell proliferation, often associated with systemic diseases – most commonly Sjögren syndrome. This case is reported because very few cases exist of primary nodular cutaneous amyloidosis developing after local trauma without systemic involvement. Additionally, dermoscopy and histopathologic findings contributed to diagnosis, and the patient achieved an excellent aesthetic result after surgical excision, which remains the treatment of choice when the lesion is resectable with minimal cosmetic impact.

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The authors declare that this work was conducted with their own resources.

Conflicts of interest

The authors declare no conflicts of interest whatsoever.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality, informed consent, and ethical approval. The authors followed their institution's confidentiality protocols, obtained informed consent from the patient, and received approval from the Ethics Committee. SAGER guideline recommendations were followed according to the nature of the study.

Statement on the use of artificial intelligence. The authors declare that no generative artificial intelligence tools were used in the writing of this manuscript.

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