

Onset of symptoms is minutes after exposure and is characterized by erythema, intense pruritus, and/or vesicular lesions on previous dermatitis lesions (i.e., on damaged skin, not healthy skin). PCD does not manifest as wheals, thus enabling it to be distinguished from chronic idiopathic urticaria.

The absence of symptoms after exposure in healthy skin can be explained by the fact that the allergens in PCD are high-molecular-weight proteins that do not come into contact with Langerhans cell receptors. In contrast, in ACD or chronic idiopathic urticaria, the allergens are low-molecular-weight haptens, which can cross the epidermal barrier easily.

Therefore, PCD leads to a positive result in the rub test on affected skin and a negative result on healthy skin, unlike ACD and chronic idiopathic urticaria, where the result is positive in both.

Patch tests are essential for distinguishing between these conditions and are negative in most cases of PCD. This makes it possible to establish a differential diagnosis with ACD. On the other hand, prick testing, which reproduces an IgE-mediated reaction, is positive in most cases of PCD and negative in ACD.

Treatment is based on 2 fundamental pillars: avoidance of the allergen involved in the reaction and treatment of the skin lesions, which depends on the degree of involvement and severity.

In the present case, the acute onset of symptoms, mainly pruritus after contact with shellfish, and the negative rub test result enabled us to reasonably rule out contact urticaria to shellfish.

This observation, together with the negative patch test results, made it possible to confirm the diagnosis of PCD to raw shellfish.<sup>2–4</sup>

The patient was recommended to avoid contact with shellfish and prescribed a topical corticosteroid. The lesions

resolved after a few months, and the patient has not experienced new flare-ups after 8 months of follow-up.

This condition should be suspected in patients with hand eczema who handle food. Since patch test results are mostly negative, it is necessary to perform immediate-type tests, with prick-by-prick being the most sensitive approach in these cases.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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## Dermoscopic Findings in Membranous Aplasia Cutis: Differential Diagnosis to Exclude Other Forms of Focal Alopecia in Infants<sup>☆</sup>



### Hallazgos dermatoscópicos en la aplasia cutis membranosa. Diagnóstico diferencial con otras formas de alopecia focal en lactantes

*To the Editor:*

Aplasia cutis congenita (ACC) is a rare congenital malformation. Membranous ACC is the most common of the 9 subtypes described. Its clinical presentation is highly variable, with

appearances ranging from eroded, ulcerated, or scar-like lesions to a glistening surface. The differential diagnosis is broad, and clinical diagnosis can be challenging. Dermoscopy may be a useful tool for the differential diagnosis, but few studies have analyzed its use in this setting.<sup>1,2</sup> We describe the dermoscopic findings of membranous ACC in an infant.

The infant was a 2-month-old boy with no remarkable personal or family history who was seen for a painful alopecic plaque on the vertex of his scalp. His parents reported that the plaque had appeared 3 weeks earlier following the use of a very rigid baby chair. They had applied disinfectants and healing creams, but there had been no clinical response. Physical examination showed a nonscaling erythematous alopecic plaque with a diameter of 8 mm that did not change on palpation (Fig. 1). Dermoscopy showed a shiny surface with thin telangiectatic vessels and bluish globules (Fig. 2). A diagnosis of membranous ACC was established. Transfontanellar ultrasound showed no underlying bone or brain defects. The parents were informed of the benign nature of the lesion. No specific treatment was prescribed.

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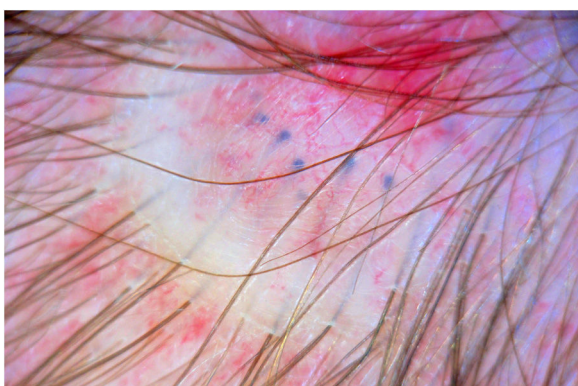
**Table 1** Dermoscopic Features of Diseases That Manifest With Alopecic Plaques in Neonates or Infants.

Aplasia cutis congenita	Translucency sign: shiny appearance, thin vessels, absence of follicular openings, visualization of hair bulbs (blue globules) Hair around the edge of the plaque (hair collar sign)
Sebaceous nevus	Yellow lobules or dots (not associated with hair follicles)
Tinea capitis	Comma, corkscrew, pigtail, zigzag, or Morse code–like hairs
Triangular alopecia	Regrowing hairs: short and upright, vellus, and pigtail hairs; terminal hairs at the edge of the lesion
Alopecia areata	Black dots, yellow dots, exclamation hairs, circular hairs
Impetigo	Scaling border, yellowish crusts, irregularly distributed dotted vessels

Source: Neri et al.<sup>2</sup> and Rakowska et al.<sup>4</sup>.



**Figure 1** Membranous aplasia cutis congenita. Erythematous alopecic plaque with a diameter of 8 mm on the vertex of the scalp.



**Figure 2** Dermoscopic features of membranous aplasia cutis congenita. Translucency sign: shiny surface, thin telangiectatic vessels, and blue globules corresponding to hair bulbs. Note also the absence of follicular openings.

ACC is a congenital condition characterized by absence of the epidermis, dermis, and, occasionally, bone or dura mater. It is mostly observed on the scalp, especially on the vertex or parietal scalp. The defects are usually small (typically 1–2 cm), although large lesions have been described. ACC has been linked to a number of causes, including

use of certain medications or drugs during pregnancy and embryologic malformations. The hair collar sign, a potential marker of neural tube defects, may be observed.<sup>3</sup> Transfontanelar ultrasound is recommended to rule out underlying bone or brain defects.

Because the lesions are so small, as occurred in our case, they can go unnoticed during the neonatal period, making clinical diagnosis even more challenging. Dermoscopy can be very useful for ruling out trauma or infectious (herpes virus, mycosis, impetigo), inflammatory (alopecia areata), or tumoral (sebaceous nevus) causes.<sup>4</sup> The translucency sign is a characteristic dermoscopic feature of membranous ACC. It consists of the presence of a shiny surface, thin arborizing vessels, and blue globules corresponding to hair bulbs.<sup>1,5,6</sup> Other possible features are an absence of follicular openings on the alopecic plaque and the hair collar sign (hair follicles distributed around the edge of the plaque). These features are quite specific to ACC and help establish a clinical diagnosis.<sup>1,2</sup> Findings for sebaceous nevi include yellow lobules or dots not related to hair follicles. In tinea capitis, findings include corkscrew hairs, comma hairs, zigzag hairs, pigtail hairs, and Morse code–like hairs. Features of alopecia areata, which is very uncommon in neonates and infants, are yellow and black dots, exclamation mark hairs, and vellus hair. Triangular alopecia, in turn, is characterized by short, upright regrowing hairs, vellus hairs, and pigtail hairs.<sup>4</sup> The dermoscopic features of diseases with focal alopecia in neonates and infants are summarized in **Table 1**.

High-frequency ultrasound can also be useful in membranous ACC, as it shows a thin or concave hyperechogenic line corresponding to the epidermis and absence of the dermis or subcutaneous tissue; it can also be used to assess bone status.<sup>7</sup>

Dermoscopy may be a useful diagnostic tool for membranous ACC as it helps rule out trauma, infections, inflammatory disorders, and tumors and may avoid the need for invasive diagnostic tests.

### Conflicts of interest

The authors declare that they have no conflicts of interest.

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## Scrotal Erythema: First Sign of a Cutaneous Drug Reaction to Pazopanib<sup>☆</sup>



### Eritema escrotal como manifestación inicial de toxicodermia por pazopanib

To the Editor:

Tyrosine kinase inhibitors (TKIs) are being increasingly used in oncology, replacing in many cases classic chemotherapy drugs. Reasons for their growing use include their superior efficacy and lower rates of adverse effects. Nonetheless, inhibition of molecular targets can result in previously undescribed adverse drug-specific reactions with an unknown etiology.<sup>1</sup> Pazopanib is a TKI indicated for the first-line treatment of advanced clear cell renal carcinoma (ccRCC) and advanced ccRCC refractory to cytokine therapy (interleukin-2 or interferon- $\alpha$ ). It is also indicated for adults with certain subtypes of metastatic soft-tissue sarcoma that are refractory to chemotherapy or that have progressed within 12 months of adjuvant or neoadjuvant chemotherapy.<sup>2</sup> The drug exerts a powerful inhibitory effect on vascular endothelial growth factor receptors (VEGFRs), platelet-derived growth factor receptors, and the stem cell factor receptor c-KIT.<sup>2</sup> A range of cutaneous adverse effects have been described for pazopanib, including hair depigmentation, alopecia, and nonspecific rashes.<sup>2,3</sup>

We report what is, to our knowledge, the first case of scrotal erythema associated with the use of pazopanib.

Case report. A 66-year-old man with a history of diabetes and metastatic ccRCC under treatment with pazopanib for

3 months presented with well-circumscribed erythematous, scaling plaques of 1 month's duration in the inguinal scrotal area (Fig. 1A, B). Bacterial and fungal cultures were negative. Histologic examination of a biopsy specimen showed psoriasiform dermatitis with exocytosis of neutrophils into the epidermis (Fig. 1C, D). Despite treatment with oral antihistamines and oral and topical corticosteroids, the lesions spread to the trunk and upper and lower extremities (Fig. 2A–C). Given the worsening of the lesions and their significant effect on the patient's quality of life and failure to respond to treatment, it was decided to interrupt treatment with pazopanib. This resulted in significant clinical improvement, with resolution of practically all the lesions (Fig. 2D, E). The scrotal lesions were the last to clear (Fig. 2F). Based on the clinical and histologic findings and the improvement observed following withdrawal of pazopanib, the diagnosis was TKI-induced toxic drug eruption.

Targeted therapy drugs can cause cutaneous adverse effects. The effects caused by TKIs are quite specific and are characterized by highly variable clinical manifestations and in most cases are dependent on dose and treatment duration.<sup>1</sup> Scrotal erythema is an uncommon cutaneous reaction consisting of well-circumscribed pruritic erythematous plaques, generally located in the scrotal area, although they can spread to the rest of the genital area, including the groin. Scrotal erythema has been described in patients treated with sorafenib, sunitinib, and cabozantinib,<sup>4,5</sup> but this is the first time it has been reported for pazopanib. The only specific changes reported by the few histopathologic studies that have investigated scrotal erythema are acanthosis and parakeratosis.<sup>6,7</sup> The pathogenic mechanisms are unknown, although it has been postulated that VEGF-induced neovascularization and increased vascular permeability and hypoxia-inducible factor 1 $\alpha$  may have an important role; nonetheless, as well known, the administration of VEGF inhibitors involves a feedback mechanism that results in increased plasma and tissue VEGF levels.<sup>6,7</sup>

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