

A full-term female newborn, with no history of consanguinity in the parents, presented at birth with generalized vesicles, pustules and blisters, appearing in crops, with preferential distribution on the limbs. She was otherwise well and was afebrile. A herpetic infection was considered, so after taking swabs, she was started on intravenous acyclovir. After an initial good response, the dermatosis worsened, assuming a roughly linear pattern [Figure 1] and manifested with an impressive blood eosinophilia. The infectious cause was excluded (Tzanck test showed no giant cells, and there was a negative PCR for HSV, VZV and bacteriologic examination), and a skin biopsy was performed, which revealed spongiotic intraepidermal vesicles with a rich eosinophil infiltrate [Figure 2]. Her mother recalled a history of a similar rash in her infancy, and displayed faint linear hypopigmented streaks on her calves, which were better observed with the Wood's lamp [Figure 3], conical incisor teeth and vertex alopecia.



Figure 1: Generalized vesicobullous rash. Note the linear configuration best seen on upper limbs

WHAT IS YOUR DIAGNOSIS?

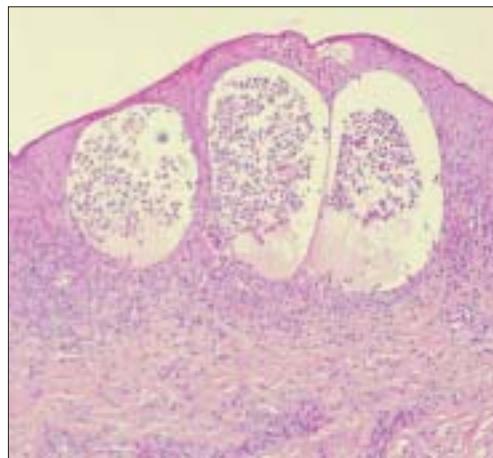


Figure 2: Skin biopsy showing spongiotic epidermal vesicles with an abundant eosinophilic infiltrate (H & E, $\times 100$)



Figure 3: Linear hypopigmented streaks on the calves of the mother, observed with the Wood's light

Diagnosis: Incontinentia pigmenti

DISCUSSION

Incontinentia pigmenti (IP) is an uncommon X-linked dominant genodermatosis characterized by peculiar cutaneous findings and alterations in teeth, nails, hair, along with variable ophthalmologic and nervous system manifestations. This disease has an incidence of 1:50, 000 births and is typically lethal in males *utero*.^[1] It is caused by inactivation mutations on nuclear factor k-B essential modulator (NEMO) gene, mapping in X chromosome (q28). A familial history is found in about 50% of the cases.^[2]

The cutaneous presentation of IP, although impressive, subsides spontaneously and is best regarded as a marker for multisystemic disease. Characteristically, evolves through 4 stages, which may overlap or skip. The first stage occurs in 90% of the patients and presents perinatally to the fourth month with erythema, vesicles and pustules, accompanied with blood eosinophilia. Verrucous lesions appear later, usually resolve by the sixth month and are followed by hyperpigmented streaks or whorls. The pigmentation fades during infancy, leaving hypopigmented hairless patches on the skin, which persist through adulthood.^[2] The lesions distribute along the lines of Blaschko, reflecting the functional mosaicism due to X chromosome inactivation. This phenomenon also explains the wide variability in phenotypes in the same family. The evolution of the disease is caused by the selective elimination of the cells carrying the mutant X chromosome and their gradual replacement by normal cells.^[3]

Extracutaneous manifestations include dental anomalies in 80% of the cases; nail alterations emerge in 40%. Ocular manifestations occur in 25% to 77% of the patients. Neurologic alterations arise in 30% of the cases. There are some reports of immunodeficiency, cardiovascular abnormalities and musculoskeletal manifestations.^[1]

This case represents, according to the diagnostic criteria,^[2] a typical case of IP. Nevertheless, an infection should always be ruled out, particularly herpes, as the clinical presentation is initially indistinguishable, and there are some reports of concurrent herpetic infection.^[4] Other diagnoses to eliminate in the vesicular stage include erythema toxicum neonatorum, Langerhans

cells histiocytosis, epidermolysis bullosa and bullous mastocytosis. Immune-mediated bullous diseases, such as dermatitis herpetiformis, epidermolysis bullosa acquisita, bullous systemic lupus erythematosus, linear IgA bullous dermatosis, bullous pemphigoid and neonatal pemphigus vulgaris should also be considered, but feature distinctive in histological and direct immunofluorescence findings. Rarely, IP has been confused with child abuse.^[1,2]

At the time of the diagnosis, complete neurological and ophthalmologic evaluations are mandatory, with regular follow-ups. In this case, these assessments were normal, highlighting the lack of correlation between blood eosinophilia and internal organ involvement. Indeed, extracutaneous abnormalities have not been found after one year of follow-up, heralding a good prognosis.

The investigation of the whole family and genetic counselling are invaluable. The genetic study result of both mother and daughter was positive with regard to the deletion of exons 4 to 10 of the NEMO gene in heterozygosity.

After investigating three generations, we concluded that the mother was the first affected member (probably by a germline paternal mutation),^[1] and transmitted the disease to her second female child. The genetic mutation detected is associated with 80% of the cases of the disease.^[5]

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REFERENCES

- Ehrenreich M, Tarlow MM, Godlwska-Janusz E, Schwartz RA. Incontinentia pigmenti (Bloch Sulzberger Syndrome): A systemic disorder. Cutis 2007;79:355-62.
- Berlin AL, Paller AS, Chan LW. Incontinentia pigmenti: A review and update on the molecular basis of pathophysiology. J Am Acad Dermatol 2002;47:169-87.
- Nelson DL. NEMO, NFκB signaling and incontinentia pigmenti. Cur Op Gen Develop 2006;16:282-8.
- Stitt W, Scott G, Caserta M, Goldsmith L. Coexistence of

- incontinentia pigmenti and neonatal herpes simplex infection.
Pediatr Dermatol 1998;15:112-5.
5. Aradhya S, Woffendin H, Jakins T, Bardaro T, Esposito T, Smahi

A, *et al.* A recurrent deletion in the ubiquitously expressed NEMO (IKK- γ) gene accounts for the vast majority of incontinentia pigmenti mutations. Hum Mol Genet 2001;10:2171-9.