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Authors

Xu, Michelle
Flamm, Alexandra
Shagalov, Devorah
et al.

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Case Report

Incontinentia Pigmenti presenting as a newborn eruption: two case presentations

Michelle Xu BA¹, Alexandra Flamm MD², Devorah Shagalov MD², Emily Hsu MD³, Sharon A. Glick MD FAAD FAAP²

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¹SUNY Downstate College of Medicine, Brooklyn, New York

²Department of Dermatology, SUNY Downstate College of Medicine, Brooklyn, New York

³Department of Pediatrics, Maimonides Medical Center, Brooklyn, New York (Hsu).

Correspondence:

Michelle Xu
SUNY Downstate College of Medicine
450 Clarkson Ave, Brooklyn, NY 11203
Email: michelle.xu@downstate.edu

Abstract

Linear vesicles or papules in a newborn can be a presenting sign of incontinentia pigmenti (IP). In this report, we present two cases of neonates with cutaneous manifestations of incontinentia pigmenti. In one case, mild peripheral eosinophilia was noted. No extra-cutaneous manifestations were noted otherwise in both cases after complete ophthalmological and neurological evaluations. These cases serve as a reminder for clinicians to consider IP in newborns presenting with linear vesicles or papules.

Case Synopsis



Figure 1. A 4-day-old baby girl presented with an expanding linear vesiculobullous eruption in a Blaschkoid distribution on the left anterior shin expanding to her left posterior thigh.

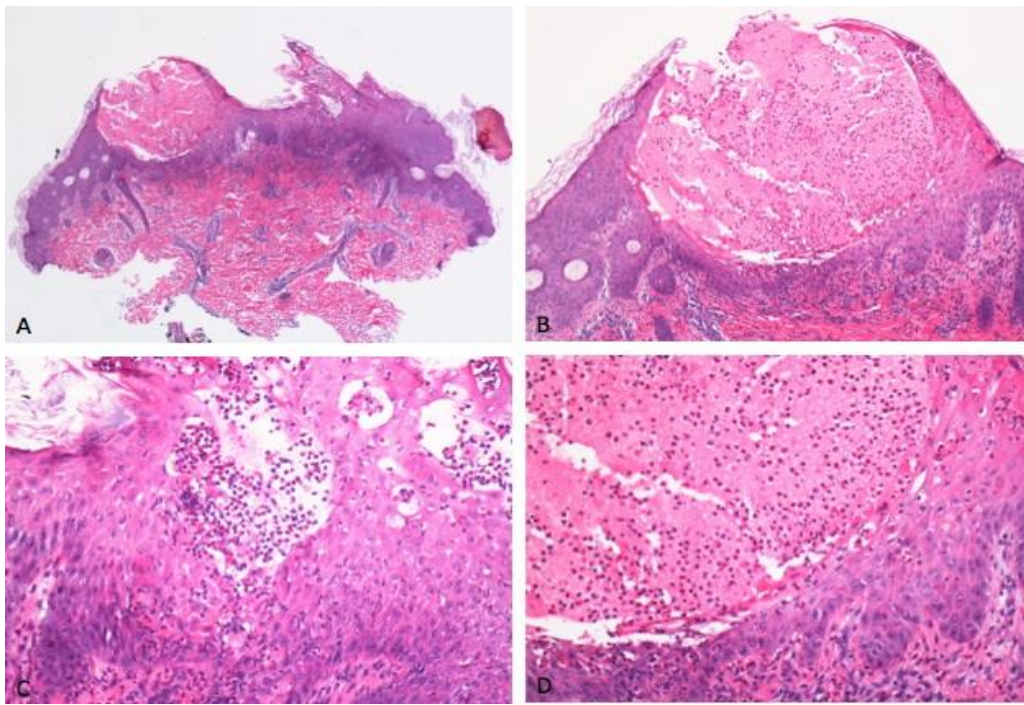


Figure 2. Punch biopsy of the linear vesiculobullous eruption, notable for epidermal spongiosis and intraepidermal vesiculation at 4x (A) and 10x (B). Numerous eosinophils are noted within the epidermis (C, 20x) and the blister cavity (D, 20x), consistent with a diagnosis of incontinentia pigmenti.

Case 1

A 4-day-old girl born prematurely at 34-weeks presented with linear vesicles, which started on the left anterior shin and expanded to involve the left posterior thigh and buttock over a span of 2-3 days (Figure 1). Maternal history was significant for multiple miscarriages; otherwise no other significant past medical history or maternal history was noted. Physical exam was notable for multiple vesicles arranged in a Blaschkoid distribution on the above locations. There were no associated fevers, vomiting, or diarrhea. Neurologic and ophthalmologic exams were unremarkable. Mild peripheral eosinophilia was noted at 6% with no other laboratory abnormalities. Skin biopsy was performed of the left anterior tibia, which demonstrated eosinophilic spongiosis (Figure 2), consistent with a diagnosis of incontinentia pigmenti. Viral and bacterial cultures were performed as well and were negative for organismal growth.



Figure 3. Incontinentia Pigmenti cutaneous stages in infant female (Case 2). **A)** Linear vesicular rash on right inguinal fold radiating down medial leg on day-of-life 6. **B)** Resolution of linear vesicles on day-of-life 8. **C)** Linear, warty plaques in same distribution as earlier vesicular rash on day-of-life 22.

Case 2

A 5-day-old girl born full term presented for linear vesiculopapules on the right inguinal fold radiating down the medial leg (Figure 3). Vesicles first appeared on the 2nd day of life, starting in the inguinal fold, progressing over the next several days to multiple vesicles in a linear distribution along the medial thigh and leg. Three similar lesions comprised of vesicles were noted on the right lateral leg. The patient's course was complicated by one episode of elevated temperature to 100.4F. Pregnancy was significant for recurrent maternal oral HSV. Mother denied history of miscarriages or stillbirth. A lumbar puncture and wound culture was performed and empiric treatment with acyclovir, vancomycin, and cefotaxime was administered. After one day of acyclovir, the vesicles and papules crusted over and appeared to be resolving. Labwork was negative for eosinophilia and all cultures were negative. On two week follow up, patient was noted to have developed linear, warty plaques in the same distribution as earlier vesicles, confirming the diagnosis of IP.

Discussion

IP is a rare genodermatosis with a prevalence of 2/1,000,000 [1]. It is a multi-system ectodermal disorder that exhibits cutaneous manifestations and can express anomalies in the eyes, central nervous system, hair, nails, teeth, and breasts [1]. This condition appears almost exclusively in females and is typically lethal in males given its X-linked dominant inheritance pattern. The disease is caused by a mutation in the NEMO gene, which codes for IKBKG, and alters NF- κ B's role in cell growth and apoptosis [2, 3]. The typical blaschkoid presentation is a factor of functional mosaicism and the nomenclature stems from the histological characterization of melanin incontinence from melanocytes in the epidermal basal layer into the superficial dermis [3]. These cases illustrate a common presentation of this rare condition.

The cutaneous changes of IP are described as occurring in four stages. The typical skin manifestations of each stage are distributed along Blaschko's lines, which represent a pattern of cutaneous mosaicism that appear in numerous skin disorders including IP [4]. The first stage is the vesiculobullous stage, which is seen in approximately 90% of patients. It presents at birth or appears within the first 2 weeks of life, as in the above cases [5]. This is followed by the verrucous stage, which is noted in about 70% of patients and consists of warty papules again in a linear distribution following Blaschko's lines. It appears between the 2nd-6th weeks of life. The third, hyperpigmented, stage occurs between the 12th-26th week of life with characteristic hyperpigmentation of brown/gray streaks and whorls. The fourth stage is the hypopigmented atrophic stage with histological absence of eccrine glands and hair follicles that may progress into adulthood. However, this stage is not present in all individuals [4].

Certain extra-cutaneous manifestations exist in those diagnosed with incontinentia pigmenti. Vision-threatening ophthalmological manifestations include retinal detachment, phthisis, and retinal ridges [5]. Neurological manifestations include seizures, infantile encephalopathy, or ischemic strokes [6]. Minic et al recently proposed an updated diagnostic criterion after different organ anomalies were analyzed in the context of applicability in the clinical realm (Table 1) [7].

Conclusion

These two cases illustrate the importance of doing a thorough physical exam and keeping a broad differential diagnosis to make the correct diagnosis of a common presentation of the uncommon condition of incontinentia pigmenti. The newborns had a characteristic linear vesiculobullous rash in a blaschkoid distribution that spread within several days. In addition, the maternal history of multiple miscarriages is supportive evidence of IP. Similarly, the presence of mildly elevated eosinophilia supports the diagnosis. In situations such as this, a dermatology consult is recommended to help diagnose IP because of the rarity of this condition.

A diagnosis of IP early on is crucial in allowing caretakers to begin proper follow-up with specialty consultations in the departments of ophthalmology, neurology, and genetics. No definitive treatment has been established but early intervention is of utmost importance to prevent irreversible neurologic and ocular sequela such as seizures or blindness.

Table 1. Minic et al's update to Landy and Donnai's IP criteria with conditions for establishing a diagnosis of IP [7].

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Major Criteria	Minor criteria	Conditions for establishing IP diagnosis
Typical IP skin stages distributed along Blaschko's lines: 1. Vesiculobullous	Dental anomalies Ocular anomalies (new) CNS anomalies ⁶ Alopecia Abnormal hair	No evidence of IP in a first-degree female relative: - If lacking genetic <i>IKBKG</i> mutation data, at least 2 or more major criteria

2. Verrucous	(sparse, wooly, eyebrow and eyelash anomalies)	or 1 major and 1 or more minor criteria are necessary to make a diagnosis of sporadic IP
3. Hyperpigmented	Abnormal nails Palate anomalies ⁷	- In the case of confirmed <i>IKBKG</i> mutation typical for IP any single major or minor criterion is satisfactory for IP diagnosis
4. Atrophic/hypopigmented	Nipple and breast anomalies ⁸ Multiple male miscarriages Typical skin pathohistological findings ⁸	- Evidence of IP in a 1 st -degree female relative: any single major or at least 2 minor criteria - In all cases eosinophilia and skewed X-chromosome inactivation supports diagnosis ⁹

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