# Incontinetia Pigmenti in Males: Report of 2 Cases and Literature Review

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**Abstract:** Incontinentia Pigmenti (IP) is a rare X-linked genodermatosis.

Papules, vesicles and changes in pigmentation following the Blaschko lines during neonate period are distinctive with only few male cases reported in the literature. We report two cases of IP in males. One of the cases was associated with mild peripheral eosinophilia, which is characteristic. No extra-cutaneous manifestations were noted in neither of the cases. This report aims to be a reminder for clinicians to consider IP in newborns presenting with linear vesicles or papules, discuss the differential diagnosis and a brief review of the literature.

**Keywords:** Incontinentia pigmenti, male, newborn, NEMO.

## INTRODUCTION

Incontinentia pigmenti (IP) or Bloch-Sulzberger Syndrome is a rare X-linked dominant disease [1, 2]. Patients affected are more frequently female, since male individuals will more likely die in uterus when this defect is present [1].

Physiologically the pigment melanin is usually seen in the melanocytes of the basal epidermal layer, but in IP melanin is seen in the superficial layer of the dermis, giving its name to the condition.

IP is a genodermatosis in which the skin involvement occurs in all patients [1, 3], demonstrating papules, vesicles and changes in pigmentation following the Blaschko lines during neonate period. Additionally; other ectodermal and mesodermal tissues may also be affected such as the central nervous system, eyes, hair, nails and teeth [1, 4, 5].

IP originates in a single gene mutation, that has been mapped to Xq28, which encodes nuclear factor B essential modulator (NEMO) [1]. This gen codifies for the activator complex of the nuclear factor KB, which protects the cell against apoptosis, controlling gene transcription related to immune system, skin and skeletal morphogenesis [2].

It presents mainly in women, with a 40:1 predominance, and there are only a very few cases reported in men (sixty cases until 2007) [6], since men have only one X chromosome leading to death in utero most of the times, so their surveillance is proposed to be committed to three mechanisms: presence of an extra X chromosome (47XXY karyotype or Klinefelter Syndrome), the presence of somatic mosaicism for the NEMO gene mutation un just one chromatid (less severe mutation), or by the presence of hypo-morphic alleles with less deleterious mutations [3, 7]. Its incidence is about 1 in 50.000 alive new born [8].

There is no definitive treatment for IP and support therapy is mainly prescribed. The advance in molecular biology has contributed to the understanding of the disease and offers the possibility in the near future for new therapies development [7].

## CASE REPORT

### Case 1

40 weeks-old male newborn presented since birth with linear skin-colored papulo-vesicles on his right lower leg, which extended to the trunk. Initially herpes simplex virus (HSV) versus bullous impetigo was suspected, so treatment with Acyclovir and Cloxacillin was initiated, without any response. The patient was afebrile and blood cell count was performed showing 10% of eosinophils without leukocytosis. His mother had no history of HSV and no oral or genital lesions at delivery time. There was no history of preceding trauma, and he had unremarkable past medical family histories.

Physical examination revealed 1 to 2 mm skin colored papules with superficial vesicles, on the medial

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aspect of his right lower leg, on a linear band like distribution (Figure **1**). There was no tenderness to palpation. There was no palpable popliteal or inguinal lymphadenopathy, and had no eye or neurologic involvement.

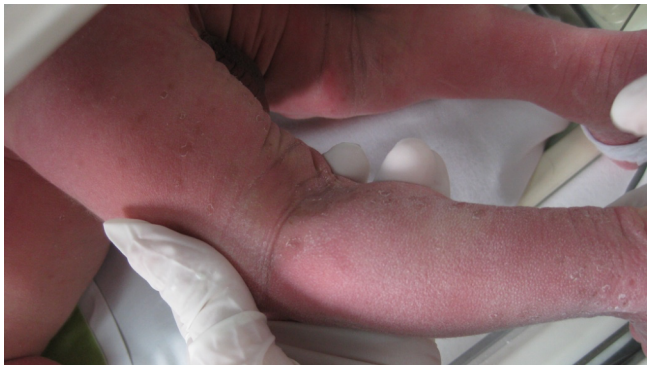

**Figure 1:**

An excisional biopsy was performed and the histopathology features are illustrated in Figures **2-3**, showing melanin incontinence and eosinophil-rich superficial epidermal layer.

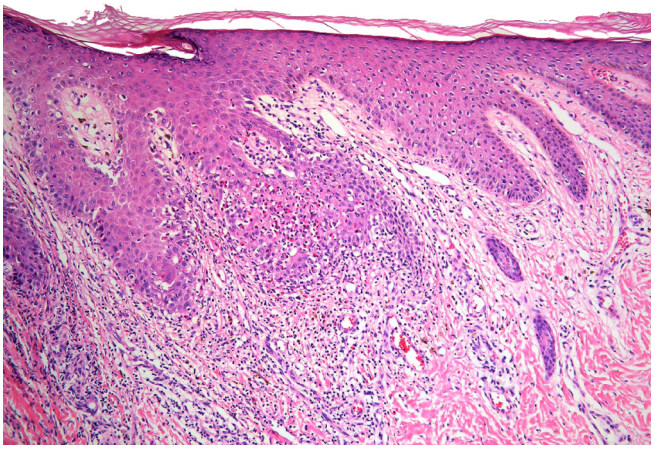

**Figure 2:**

## Case 2

38 weeks-old male newborn presented with papulo-vesicles on a linear distribution on his left lower leg since birth. He had no remarkable history, with healthy parents and good pregnancy history. Dermatology was consulted on his first day of life. Physical examination revealed an afebrile patient with a 2 to 3 mm pink papule with superficial vesicles without ulceration, on the medial aspect of the left lower leg (Figure **4**). There was no tenderness to palpation, and there was no palpable popliteal or inguinal lymphadenopathy, without any no eye or neurologic involvement.

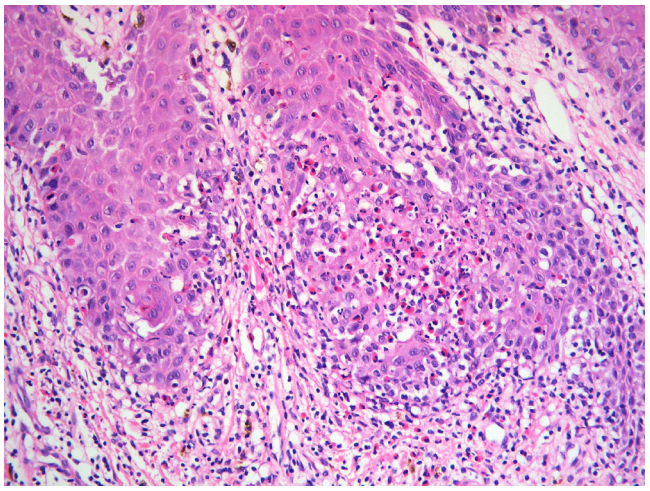

**Figure 3:**

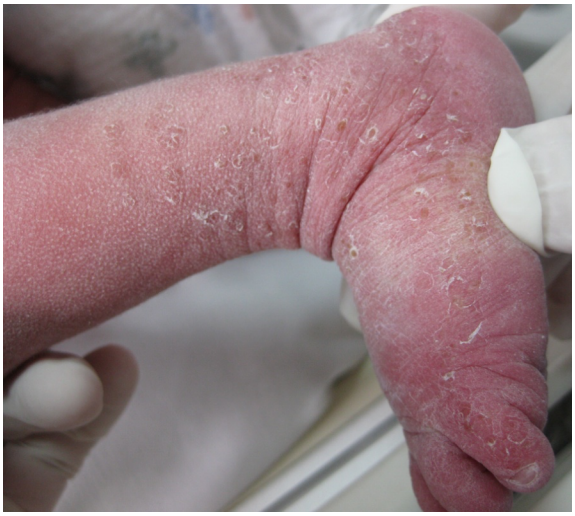

**Figure 4:**

An excisional biopsy was performed and the histopathology features are illustrated in Figures **5-6**, showing melanin incontinence and eosinophil-rich superficial epidermal layer.

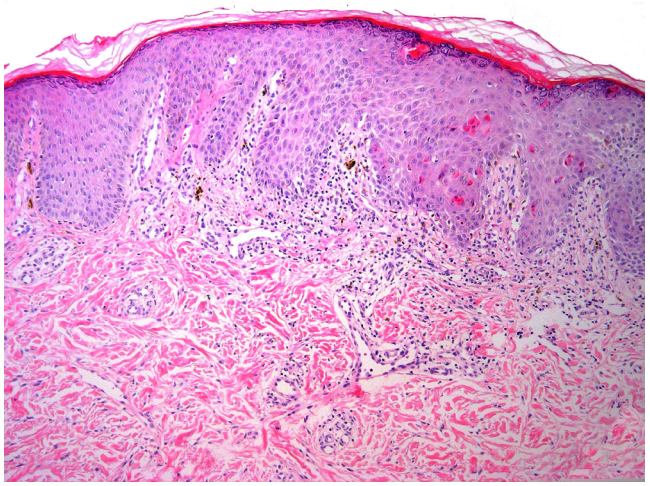

**Figure 5:**

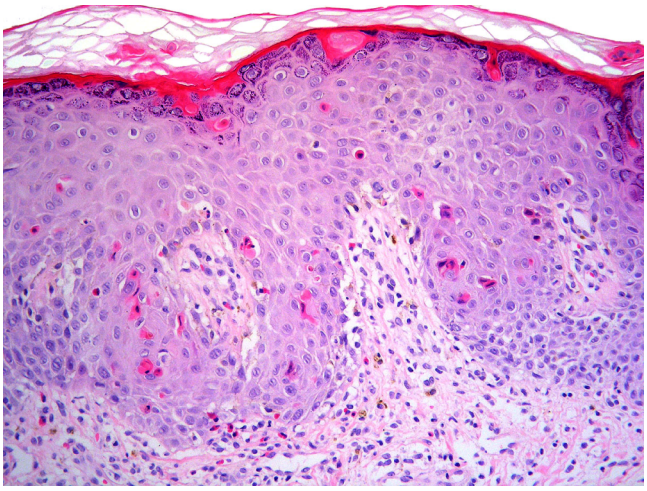

**Figure 6:**

## DISCUSSION

IP is an X-linked dominant syndrome associated with mutations in the IKBKG gene located at locus Xq28 and is typically seen in female patients, and only few cases have been reported in male patients due to its herency type and that they mostly die in uterus. Skin lesions are present at birth in approximately 50% of cases and in 90% of cases the skin lesions will appear in the first 2 weeks of life, eventually developing in all patients [9].

Dermatological findings in IP occur in four successive phases [10]. IP usually presents as an asymptomatic skin colored papule or vesicle, in a linear disposition following the Blaschko lines. The linear vesicles or papules in a newborn may be the presenting sign. There are four clinical stages in IP: Vesicular phase (stage1), verrucous phase (stage2), hyper-pigmented phase (stage3), and atrophic phase (stage4) [1, 10]. It is very uncommon for all stages to be seen in a same patient [1, 9].

The dermatological aspect is the most important for the diagnosis but there are other manifestations related to developmental alterations, such as eye defects (uveitis, cataracts, optic atrophy, strabismus, retrolental fibroplasia), teeth (delayed dentition, partial anodontia, cone or peg-shaped theeth, or even teeth absence), skeletal system (skull and palatal defects), and central nervous system (epilepsy, microcephaly, mental retardation, and slow motor development) [11].

In one of our cases, mild peripheral eosinophilia was noted, which is very characteristic. Histologically, IP is characterized by an incontinence of melanin. The pigment melanin is usually seen in the melanocytes of the basal epidermal layer, but in IP melanin is seen in the superficial layer of the dermis. Thus, this melanin incontinence by melanocytes is reflected in the name of the condition, as IP [12]. Histologic examination of our patients revealed eosinophil-rich epidermal spongiosis and interstitial dermatitis, associated to the melanin incontinence, which is consistent with IP.

Differential diagnoses are VHS infection (which should always be considered and ruled out), dermatitis herpetiformis, epidermolysis bullosa, dermatitis medicamentosa, acrodermatitis enteropathica and scalded skin syndrome [13].

As we commented above, the treatment suggested for IP is support and education of the parents. Generally skin lesions do not need specific treatment, but topical tacrolimus or topical corticosteroids could be used in order to accelerate their resolution. Secondary bacterial infections of the vesicle in the inflammatory phase could be treated with emollients and topical antibiotics [14]. Sometimes dental implantation is needed due to dental malformations. For seizures anticonvulsants may be indicated [1]. The prognosis is demarcated by the presence and the severity of the extra-cutaneous manifestations, mainly the neurologic symptoms.

## CONCLUSION

IP is an extremely rare genodermatosis, with distinctive **c**utaneous manifestations. We must be aware when we approach a neonate with vesicular lesions, and it should be considered as a differential diagnosis when we evaluate a newborn with characteristic skin findings, which may be the clue to diagnosis. After complete ophthalmological and neurological evaluations no extra-cutaneous manifestations were note in our cases, although the strict follow up is mandatory.

### Conflict of Interests

The authors report no conflicts of interest.

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