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Case Report
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Incontinentia Pigmenti in a Male Infant: A Case Report

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ABSTRACT

Background: Incontinentia pigmenti (IP), also known as Bloch-Sulzberger syndrome, is a rare X-linked dominant genodermatosis with an estimated incidence of 0.7–1.2 per 100,000 live births. It is caused by mutations in the *IKBKG* gene. Affected women have a 50% chance of transmitting the defective gene, while male fetuses usually do not survive due to the lethal effect of the mutation. **Purpose**: This report aims to present a rare surviving male case of incontinentia pigmenti with early dermatological manifestations and to highlight the importance of clinical recognition and multidisciplinary follow-up. **Case**: A 4-day-old male newborn presented with blisters on the left leg since birth. Dermatological examination showed multiple papules and vesicles arranged along Blaschko's lines on erythematous macules without erosion. Based on clinical findings, the patient was diagnosed with stage 1 incontinentia pigmenti. Management included the use of moisturizers, topical antibiotics, and parental education regarding potential multi-organ involvement. Regular monitoring for neurological and ophthalmological manifestations was advised. **Discussion**: Incontinentia pigmenti is caused by an IKBKG gene mutation that disrupts NF-κB signaling, leading to increased apoptosis. It mainly affects ectodermal tissues such as the skin, hair, teeth, eyes, and CNS. The disease progresses through four skin stages: vesiculobullous, verrucous, hyperpigmented, and atrophic/alopecic. Diagnosis is mostly clinical, with histopathology or genetic testing used in atypical cases. Skin lesions usually resolve on their own, but preventing secondary infections is important. **Conclusion**: Incontinentia pigmenti in male infants is exceedingly rare. Early recognition, supportive care, and vigilant multidisciplinary monitoring are crucial to detect and manage possible systemic complications, improving survival and quality of life.

Keywords: Incontinentia pigmenti, Bloch-Sulzberger syndrome, Male newborn.

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BACKGROUND

Incontinentia pigmenti (IP), also known as Bloch-Sulzberger syndrome, is an uncommon X-linked dominant genodermatosis. Incontinentia pigmenti can impact all ectodermal-derived cells, including the skin, eyes, and teeth, and may be linked to neurological abnormalities.[1,2,3] The anticipated prevalence of incontinentia pigmenti is 0.7 to 1.2 cases per 100,000 live births.[3] Women with incontinentia pigmenti possess a 50% likelihood of transmitting the pathogenic variant of inhibitor of nuclear factor kappa B kinase regulatory subunit gamma (IKBKG) to their offspring, attributable to the X-linked inheritance pattern. Male infants with the defective gene generally result in miscarriage. The etiology of IP is the mutation of the IKBKG gene, which is associated with the NF-κB signaling pathway, formerly known as NEMO or nuclear factor kappa essential modulator. IKBKG is a gene located on Xp28 that suppresses the kappa light polypeptide gene enhancer in B-cells. Exons 4 to 10 of the NEMO gene are deleted in the most common mutation (80% of cases), which completely eliminates the function of nuclear factor B.[1,2,3,4]

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Individuals with IP may exhibit symptoms impacting multiple organs, including the integumentary system, ocular structures, central nervous system (CNS), and musculoskeletal tissue.[3] The clinical findings categorize cutaneous lesions of IP into four stages, although clinical variations often overlap and may complicate diagnosis. Stage I (vesiculobullous stage) typically appears within the first week of life as vesicular or bullous eruptions with erythema, distributed in a linear or whorled pattern on the trunk and extremities, usually sparing the face. Stage II (verrucous stage) follows, marked by keratotic eruptions resembling verrucous or lichenoid lesions, most prominent on the dorsal hands and feet. Stage III (hyperpigmentation stage) develops around 12–16 weeks of age, presenting as brown to gray-brown pigmentation along Blaschko's lines, which gradually fades by 4–5 years. Stage IV is characterized by residual changes such as alopecia, focal hypopigmentation, or atrophic scarring.[2,5,6]

CASE REPORT

A 4-day-old male neonate was referred to the dermatology department due to the primary concern of blisters on the left leg. The history revealed that the blisters had been present from the patient's birth. The assessment of any histories of pruritus was challenging. The patient's mother denied any history of the blisters, which were broad, increasing in number, and occurred in the eye and mouth. She also reported no prior use of topical treatments on the left leg area before the onset of the complaint. She also refuted any history of fever. All histories of food and medication allergies were refuted.

No family member had the same major complaint as the patient, the third of three siblings. The patient's mother had a history of regular consultations with the obstetrician and denied any infections during the pregnant time. The patient's mother denied any history of miscarriage.

The patient was born at a gestational age of 37-38 weeks, weighing 3300 grams, and exhibited typical development. During the physical examination, we determined that the patient was compos mentis, showing no signs of anemia, cyanosis, respiratory distress, or lymphadenopathy. However, we observed minor icterus. Laboratory results indicated leukocytosis with a count of 14.420. A dermatological examination of the patient's left leg and thigh revealed several papules and vesicles, which ranged in size and followed the Blaschko lines, situated above an erythematous macule without any erosion. Regrettably, the patient's mother declined to consent to a histological examination.

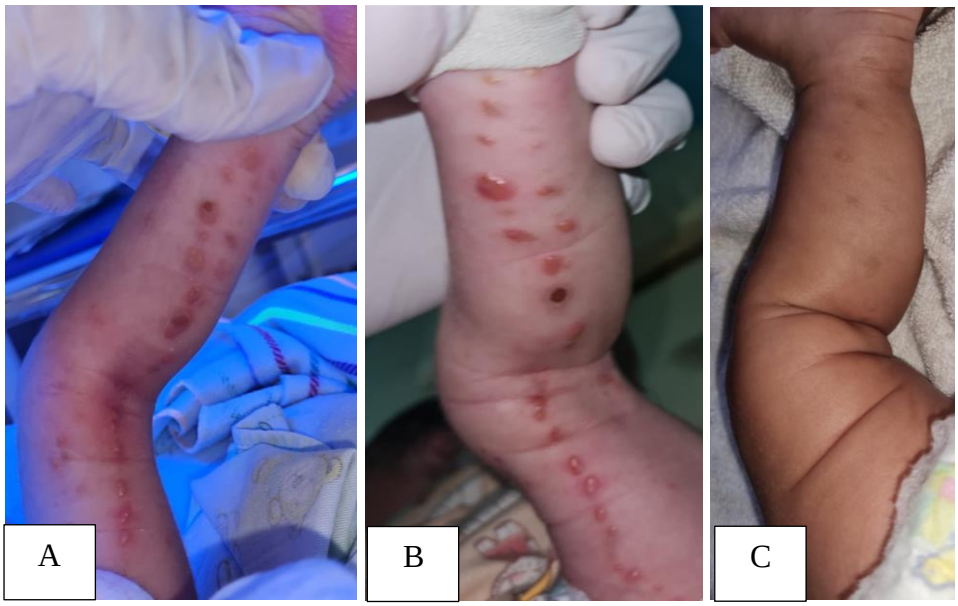

Figure 1A. Numerous papules and vesicles aligned along the Blaschko line above the erythematous macule, with no erosions observed during the initial examination. B. The lesion on the second visit on day seven. C. The lesion on day thirty.

The patient was diagnosed with stage I incontinentia pigmenti. A moisturizer was prescribed for bi-daily application, and a topical antibiotic was initiated to prevent secondary infection. The family was informed about the potential for a genetic condition that may involve multiple organs and was advised that regular monitoring for extracutaneous abnormalities, including those affecting the eyes, central nervous system, and teeth. Manipulation of the lesion was discouraged, and follow-up at the dermatology outpatient clinic was scheduled for subsequent evaluation.

DISCUSSION

Incontinentia pigmenti (IP) is a rare X-linked dominant genodermatosis caused by a mutation in the IKBKG gene on Xp28, which is typically deadly in male babies. Incontinentia pigmenti (IP) can damage the skin, eyes, central nervous system (CNS), and musculoskeletal tissue.[7,8] The clinical manifestation has four stages: vesiculobullous stage (stage 1), verrucous stage (stage 2), hyperpigmentation stage (stage 3), and may present as alopecia, focal hypopigmentation, or atrophic scars in stage 4. Molecular investigations can validate the clinical diagnosis of IP in neonates and babies.

Landy and Donnai (1993) proposed diagnostic criteria that remain a clinical cornerstone. Major criteria include typical cutaneous lesions following Blaschko's lines that evolve through four stages: vesiculobullous (stage I), verrucous (stage II), hyperpigmentation (stage III), and residual atrophic/alopecic/hypopigmented changes (stage IV). Minor criteria encompass dental anomalies, nail dystrophy, woolly hair or alopecia, and ocular or neurological involvement.[5,6]

Histopathology varies with the stage of presentation. Stage I typically shows intraepidermal spongiotic vesicles with prominent eosinophilic infiltration. Stage II demonstrates acanthosis, papillomatosis, and dyskeratotic keratinocytes. Stage III reveals pigment incontinence with dermal melanophages, while stage IV shows epidermal atrophy and adnexal loss.[7,8] Histopathology, although not mandatory when the clinical presentation is pathognomonic, can be useful in atypical cases or for ruling out differential diagnoses.[5,6]

This case illustrates the classical cutaneous presentation of IP in a male infant, a rare but documented occurrence. Male survival has been explained by mechanisms such as somatic mosaicism or Klinefelter syndrome, though these were not confirmed in our case. The absence of family history suggests a de novo mutation. Cutaneous lesions themselves are usually self-limited and rarely dictate prognosis. The major determinants of morbidity are ocular and neurological complications. Approximately 30% of patients develop CNS anomalies such as seizures, stroke-like episodes, or psychomotor delay, while ocular disease may result in retinal ischemia, neovascularization, and blindness if left untreated.[9-12] Recent studies have highlighted the role of microvascular ischemia in both CNS and retinal manifestations, underlining the importance of early multidisciplinary surveillance.[13,14]

This report describes a 4 day old male infant referred from the pediatrics department with blisters on the left leg that had been present since birth. The patient, the third of three siblings, had no family history of similar complaints, and the mother denied any infection during pregnancy. Dermatological examination revealed papules and vesicles arranged along Blaschko's lines on the left leg and thigh, located over erythematous macules without erosion. Histopathological examination was declined by the family. The patient was treated with a moisturizer and topical antibiotic, accompanied by education regarding the condition. At follow up, the lesions showed no new progression, and by one month, they had evolved into hyperpigmentation without active vesicles or papules.

The patient received a diagnosis of incontinentia pigmenti stage 1 following a comprehensive history and extensive physical examination. The diagnosis was established clinically based on the distinctive findings in the patient, specifically a typical skin rash along the Blaschko lines. Despite the lack of a histological examination, the lesion in the male neonate is indicative of IP. The cutaneous lesions may resolve spontaneously. However, topical antiseptics can be administered to prevent secondary infection. In neonates, vesiculobullous eruptions warrant careful evaluation. Differential diagnoses include neonatal herpes simplex infection, bullous impetigo, epidermolysis bullosa, and linear epidermal nevus. IP is distinguished by its distribution along Blaschko's lines and its characteristic evolution through cutaneous stages. Laboratory investigations such as Tzanck smear, bacterial culture, or biopsy may help exclude infectious and hereditary blistering disorders. Genetic testing of IKBKG mutations remains the definitive tool when clinical features are atypical.[2,9]

Male babies typically succumb in utero to incontinentia pigmenti, a condition that predominantly impacts female neonates.[7] Researchers have proposed several survival pathways for the unusual manifestation of incontinentia pigmenti in male patients, including the 47, XXY karyotype (Klinefelter syndrome), hypomorphic mutations, and somatic mosaicism. Furthermore, the absence of incontinentia pigmenti in the patient's family history suggests a de novo mutation.[8,9]

Skin lesions are not imposing the severity of IP; instead, ocular and neurological impairments, particularly blindness and psychomotor slowness, are the determining factors. Approximately 30% of individuals with incontinentia pigmenti are thought to have central nervous system impairments, including seizure disorders and spastic paralysis. Children with incontinentia pigmenti require prolonged and meticulous monitoring due to the severe manifestations of the condition.[5,7,10]

There is no specific curative therapy for IP. Cutaneous lesions typically resolve spontaneously, but supportive skin care, emollients, and topical antiseptics or antibiotics are recommended to prevent secondary infection. The long term management focuses on surveillance and early detection of complications. Dermatology follow up should be performed every trimester in the first year, then annually until at least age five, and as clinically required thereafter. Ophthalmology examinations should be conducted at 1, 2, 3, 6, 12, 18, and 24 months, followed by yearly visits if normal, given the high risk of retinal vascular disease in infancy. Neurological evaluation is essential during the first three years, and dental follow up is recommended throughout childhood and into adulthood.[5,11,15]

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