

All That Is Vesicular Is Not Herpes: Incontinentia Pigmenti Masquerading as Herpes Simplex Virus in a Newborn

Morayo Faloyin*; Jacob Levitt, MD‡; Eric Bercowitz, MD‡; Daniel Carrasco, MD‡; and Jianyou Tan, MD§

ABSTRACT. Incontinentia pigmenti is a multisystem genodermatosis characterized by cutaneous, neurologic, ophthalmologic, and dental abnormalities. The skin lesions associated with the disease progress through 4 stages, the first being erythematous vesicles linearly distributed along the lines of Blaschko. We report a case of an infant who had incontinentia pigmenti and presented with 2 crops of vesicles and was initially thought to have herpes simplex virus. *Pediatrics* 2004;114:e270–e272. URL: <http://www.pediatrics.org/cgi/content/full/114/2/e270>; *incontinentia pigmenti, herpes simplex virus, Bloch-Sulzberger syndrome.*

ABBREVIATIONS. IP, incontinentia pigmenti; HSV, herpes simplex virus; CNS, central nervous system; WBCs, white blood cells.

First reported by Garrod in 1906,¹ the name incontinentia pigmenti (IP) is derived from the common histologic finding of incontinent melanin in the superficial dermis.^{1,2} The syndrome is not known to be more common to any racial group. As it is X-linked dominant, the vast majority of cases are seen in female individuals. The recently discovered genetic mutation in IP lies in the NEMO/IKK- γ gene that encodes a protein important in signaling pathways of apoptosis and inflammatory responses.³

CASE REPORT

A 3-day-old Chinese girl who was born by full-term normal spontaneous vaginal delivery, Apgar scores of 9 and 9, was noted to have 2 linear crops of erythematous vesicles on a red base on her right arm and leg (Fig 1). The infant was empirically started on intravenous acyclovir for suspected neonatal herpes simplex infection. The mother denied pre- or perinatal infection with herpes simplex virus (HSV) and was immune to varicella zoster virus. Of note, the mother had 2 miscarriages (genders unknown) and 1 healthy girl born full term.

Physical examination of the infant revealed a well-appearing, afebrile infant with the above-stated rash. Laboratory tests of the blister fluid were negative for HSV by direct fluorescent antibody. Cultures of stool, urine, and skin were negative for virus or bacteria. Cerebrospinal fluid analysis was normal, with negative reactive plasma reagent. Serum reactive plasma reagent was also negative. Complete blood count revealed normal eosinophil and basophil counts. Biopsy of a vesicle showed eosinophilic spongi-

osis with dyskeratotic epithelial cells, confirming the diagnosis of IP as shown in Fig 2. Acyclovir was discontinued.

DISCUSSION

IP, also known as Bloch-Sulzberger syndrome, is an X-linked dominant genetic disorder with prenatal lethality in boys. The disease, which has been found to be more prevalent among girls, is characterized by abnormalities of the tissues and organs embryologically derived from ectoderm and neuroectoderm.⁴

Diagnosis of the disease is aided by family history and history of miscarriages of male gender. Male patients with IP have rarely been reported, mostly in association with Klinefelter syndrome, in which the XXY genotype permits viability.⁵

IP is typically diagnosed by its cutaneous signs, which classically evolve through 4 stages. The vesicobullous first stage (stage 1) typically occurs from birth to the first 2 weeks of life and constitutes erythematous vesicles or bullae arranged linearly on the extremities, trunk, and scalp.⁴ The verrucous second stage (stage 2) manifests after several weeks of birth and could last for weeks. Stage 2 is characterized by the presence of hyperkeratotic, verrucous lesions on an erythematous base that usually affects the distal extremities.^{1,4,6} They may evolve from stage 1 or occur on previously uninvolved skin. The hyperpigmented stage 3 generally occurs between the ages of 3 and 6 months and could last from months to years.⁴ Features include asymmetrically distributed hyperpigmented streaks or whorls that occur along the lines of Blaschko, which refer to the common pattern of skin findings in specific skin disorders such as linear epidermal nevi, IP, hypomelanosis of Ito, and focal dermal hypoplasia.⁷ The hypopigmented stage 4 could become evident any time between the late infant and adolescent years and usually lasts a lifetime.⁴ Atrophic streaks or whorls of hypopigmentation, which are mostly apparent on the flexor surface of the lower extremities, are characteristic of this stage.⁴ Eccrine glands and hair follicles are not present in this stage, which can be subtle.¹ Careful examination of the mother for stage 4 lesions occasionally yields contributory diagnostic information.⁷ It is important to note that an infant can be born with any stage, in which case it is presumed that the previous stages occurred in utero.⁴

Additional cutaneous findings include abnormalities of hair (scarring alopecia, coarse hair, hypoplasia of eyebrows and eyelashes), nails (dystrophy resembling onychomycosis, subungual fibromas associated with bony deformities of the underlying pha-

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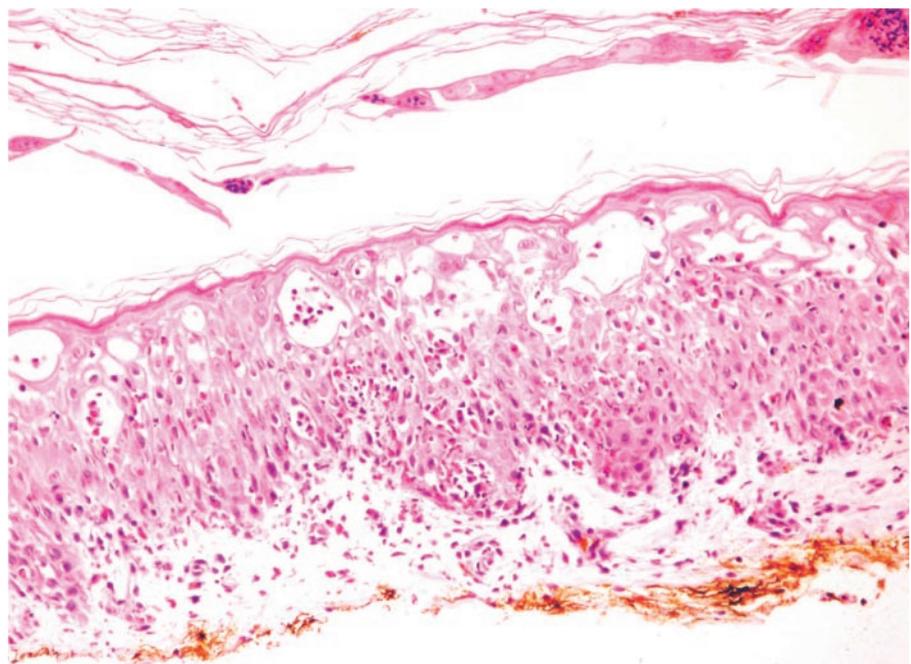
Fig 1. Crops of vesicles in linear distribution on lower extremity.



langes), and teeth (delay or malformation of teeth, eg, pegged teeth).^{4,6} Although the cutaneous findings are benign, they must prompt investigation for more serious central nervous system (CNS) and ophthalmologic involvement. Specifically, patients with IP have been found to have seizures, mental retardation, spasticity, and ataxia in 30% of cases.⁶ A myriad of ophthalmologic findings can include retinal detachment, proliferative retinopathy, and cataracts in 30% of patients.^{4,6,7} The presence of CNS involvement, such as seizures, in the neonatal period is a poor prognostic sign.^{1,4,8} If ocular and CNS abnormalities do not appear by the age of 1 year, then prognosis for normal vision and normal neurologic development is good.^{9,10}

The differential diagnosis of the vesiculobullous first stage of IP includes neonatal HSV, herpes zoster, congenital candidiasis, congenital syphilis, bullous impetigo, epidermolysis bullosa simplex (Dowling-Meara type), transient neonatal pustular melanosis, congenital self-healing reticulohistiocytosis, Letterer-Siwe disease, blistering drug eruption, epidermolytic hyperkeratosis (also known as bullous congenital ichthyosiform erythroderma), allergic contact dermatitis, and neonatal dermatitis herpetiformis.^{1,4,6,9,11} The histologic differential diagnosis of eosinophilic spongiotic dermatitis includes IP, allergic contact dermatitis, arthropod assault, drug eruption, nummular dermatitis, and, occasionally, bacterial or fungal infection.¹²

Fig 2. Skin biopsy showing eosinophilic spongiosis.



In this case, HSV infection was the initial leading diagnosis on the basis of clinical morphology and the leukocytosis. The linear distribution of the vesicles and maternal history of spontaneous abortions swayed our thinking toward IP, and the characteristic cutaneous histopathology confirmed it. Of note, leukocytosis is known to accompany the first stage of IP.³ This case highlights the importance of skin biopsies in atypical vesicular lesions that do not perfectly fit the criteria for herpes simplex infection. Nevertheless, given the serious sequelae of neonatal HSV infection, we wish to emphasize the importance of early initiation of acyclovir in neonatal vesicular eruptions until a more thorough physical and laboratory evaluation can be conducted.

For additional information and patient support, please contact Incontinentia Pigmenti International Foundation, 30 East 72nd St, #16, New York, NY 10021; Phone: 212-452-1231; Fax: 212-452-1406; E-mail: ipif@ipif.org; web site: imgen.bcm.bmc.edu/IPIF.

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