SKIN

BRIEF ARTICLE

Incontinentia Pigmenti in a Female Infant: A Case Report

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ABSTRACT

Incontinentia pigmenti (IP) is an X-linked disorder characterized by a variety of findings that affect different systems, including cutaneous, ophthalmologic, neurologic, and dental. The cutaneous findings occur in 4 consecutive stages, generally referred to as vesicular, verrucous, hyperpigmented, and atrophic. The first stage is often observed in infancy, and this may be the first indication of IP in an infant. Early diagnosis is critical so that interventions can be implemented as soon as possible to monitor for complications and mitigate the effects of IP given the potential for multisystem involvement. Here, we describe a case of IP that was diagnosed in a female infant with no prior family history of IP. Prompt diagnosis and family counseling is critical, as early interventions can help optimize patients' quality of life and genetic testing may help families make informed future family planning decisions.

INTRODUCTION

Incontinentia pigmenti (IP), also known as Bloch-Sulzberger syndrome, is a rare condition characterized by a variety of findings including, cutaneous, ophthalmologic, neurologic, and dental manifestations.[1] IP is usually lethal in males in the prenatal periods. Thus, IP is typically seen clinically in females, and the first signs of this condition, usually cutaneous findings, may be observed at birth or in the first few days of life.

The cutaneous findings of IP classically appear in 4 consecutive stages: vesicular, verrucous, hyperpigmented, and atrophic. The skin lesions are typically distributed along the Lines of Blaschko,[1,2] which are lines on the surface of the skin that correspond to the developmental growth pattern that can be observed during epidermal cell migration.

Early diagnosis and treatment initiation is important for patients with IP, as this allows for prompt management of symptoms to prevent complications and minimize related cutaneous discomfort and prevention of secondary complications. Here, we describe the case of a female infant who presented for evaluation with typical cutaneous findings of IP, which was later confirmed with biopsy and genetic testing.

CASE REPORT

The patient is a 6-day old female who presented to the dermatology office with a chief complaint of a rash. At birth, her father

described the rash as pustules on the antecubital fossae. Two days after birth, the parents noticed the rash seemed to worsen and become widespread. The patient cried with dressing and undressing, but the parents were unsure if this was related to discomfort associated with the rash or typical newborn behavior. The patient was otherwise eating well, gaining weight appropriately, and making wet diapers. Review of systems was negative for fevers. There was no significant family history.

On physical exam, a vesicular rash was present on the arms in a Blaschko linear pattern with diffuse red patches on the scalp, trunk, and extremities, as shown in **Figures 1 and 2**.

Pathology of a punch biopsy demonstrated superficial perivascular dermatitis with eosinophilic spongiosis (**Figure 3**); histopathology results with the clinical correlation were consistent with IP. The parents were counseled on the features of this condition.

DISCUSSION

Incontinentia pigmenti (IP) is a rare, X-linked dominant, genetic disorder that primarily affects females and presents with a myriad of multisystemic manifestations. Cutaneous manifestations play a central role in the diagnosis of IP. The classic clinical course consists of four stages: vesicular, verrucous, hyperpigmented, and atrophic. Cutaneous findings are observable in 90% of patients by the age of 2 weeks. The vesicular phase typically occurs in infancy and is characterized by erythematous vesicles, which can evolve into pustules.[3] Stage 1 may last from several weeks to months. This stage can often appear similar to other blistering skin conditions so it is important to consider IP on the differential. In stage 2, plaques and warty papules overlying an erythematous base appear also along the lines of Blaschko. Stage 2 can overlap with stage 1, however, it may also occur slightly later, and last for a period of months. Stage 3 is characterized by the development of hyperpigmented, brown lesions that may appear where the lesions in stages 1 and 2 were. Stage 3 may appear between 6 and 12 months of age and can persist for several years, potentially into early adulthood. Stage 4 often appears during adolescence and is characterized by areas of atrophy and hypopigmentation, often on the lower extremities with absence of hair. These lesions develop the latest and may be permanent, following patients into adulthood, although some adults with IP may have no cutaneous manifestations of the condition.[1,3]

As the described patient was affected by the first stage of IP progression, eosinophilic and neutrophilic inflammatory infiltration with eosinophilic spongiosis was observed, which is consistent with histopathology of stage 1. Nail changes may also occur.[1]

The cause of IP is a mutation in the *NEMO* (IKBKG) gene, which is located on the X chromosome. The *NEMO* gene results in the transcription of NF-κB, is essential for normal development and functioning of various tissues.[3] Random X-inactivation yields the wide range of phenotypic expressions. The mosaic pattern contributes to the characteristic skin findings, as well as the variability and complexity of clinical presentations.[4] Most cases are sporadic, and the phenotypically normal carrier females can pass this trait to their offspring unknowingly. While IP is usually lethal to males in utero, males with a condition called Klinefelter syndrome, characterized by an XXY chromosomal distribution, can be affected.[3] This may be an argument for males in families with females affected by IP to

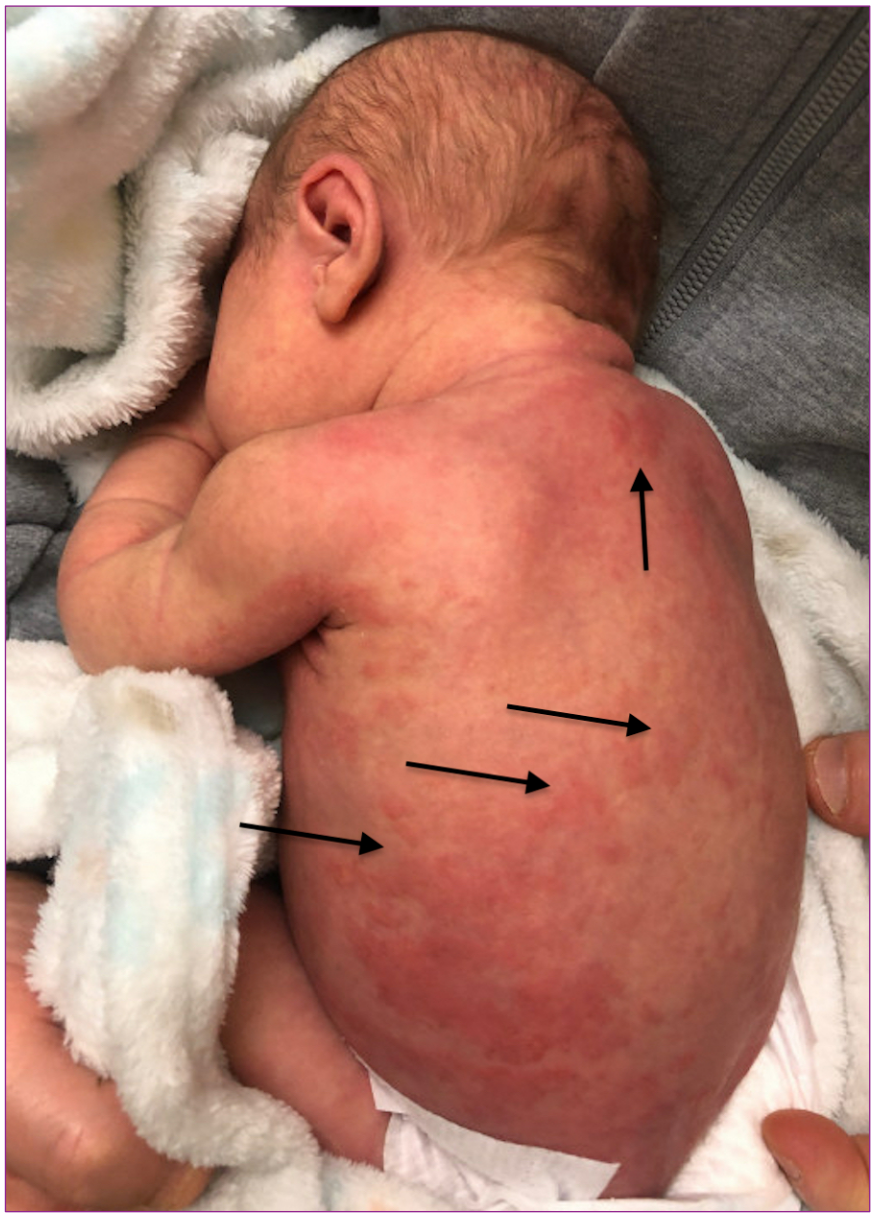

Figure 1. Vesicular rash in a Blaschko linear pattern with diffuse red patches on the back.

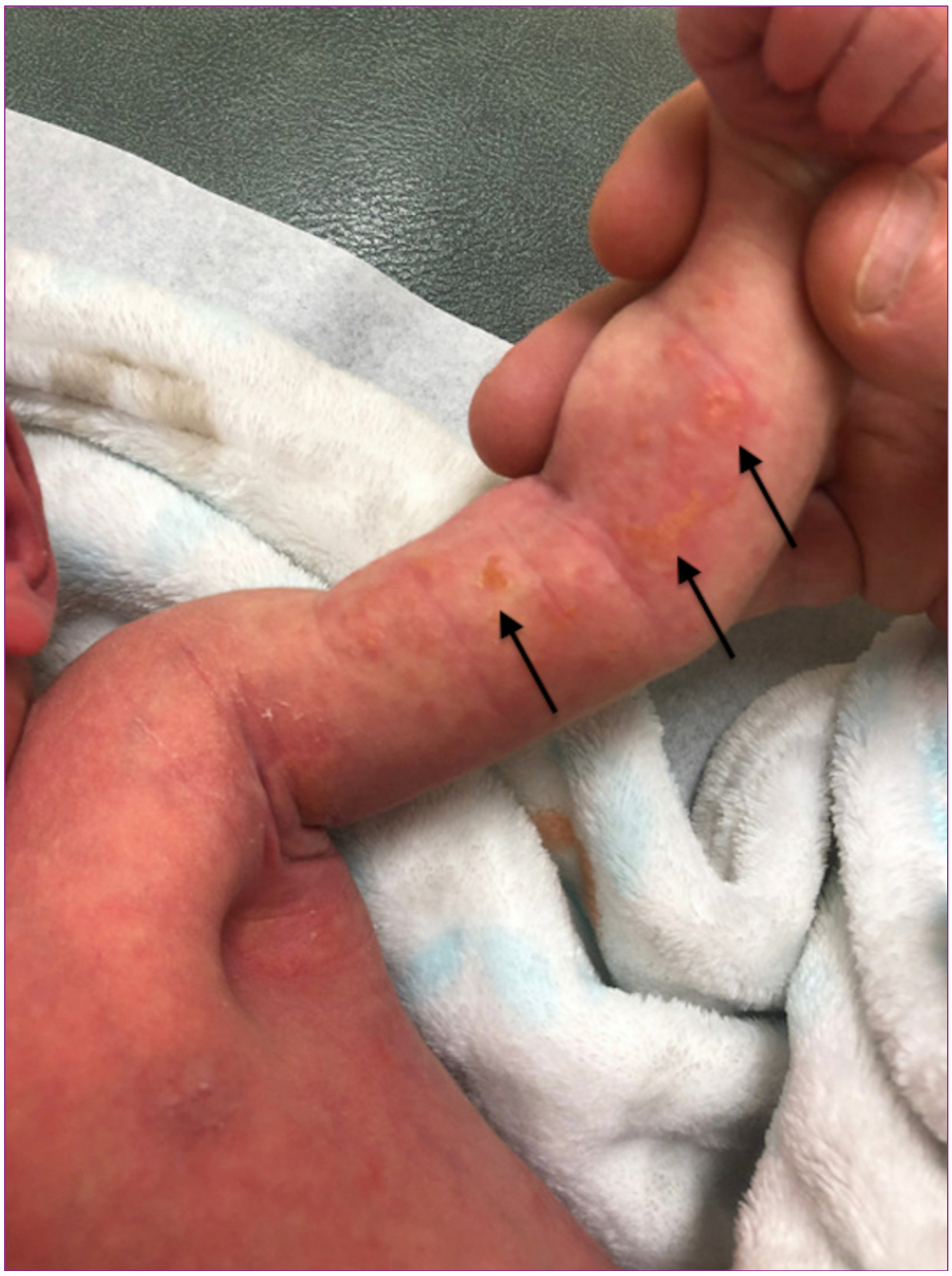

Figure 2. Vesicular rash in a Blaschko linear pattern with diffuse red patches on the left arm.

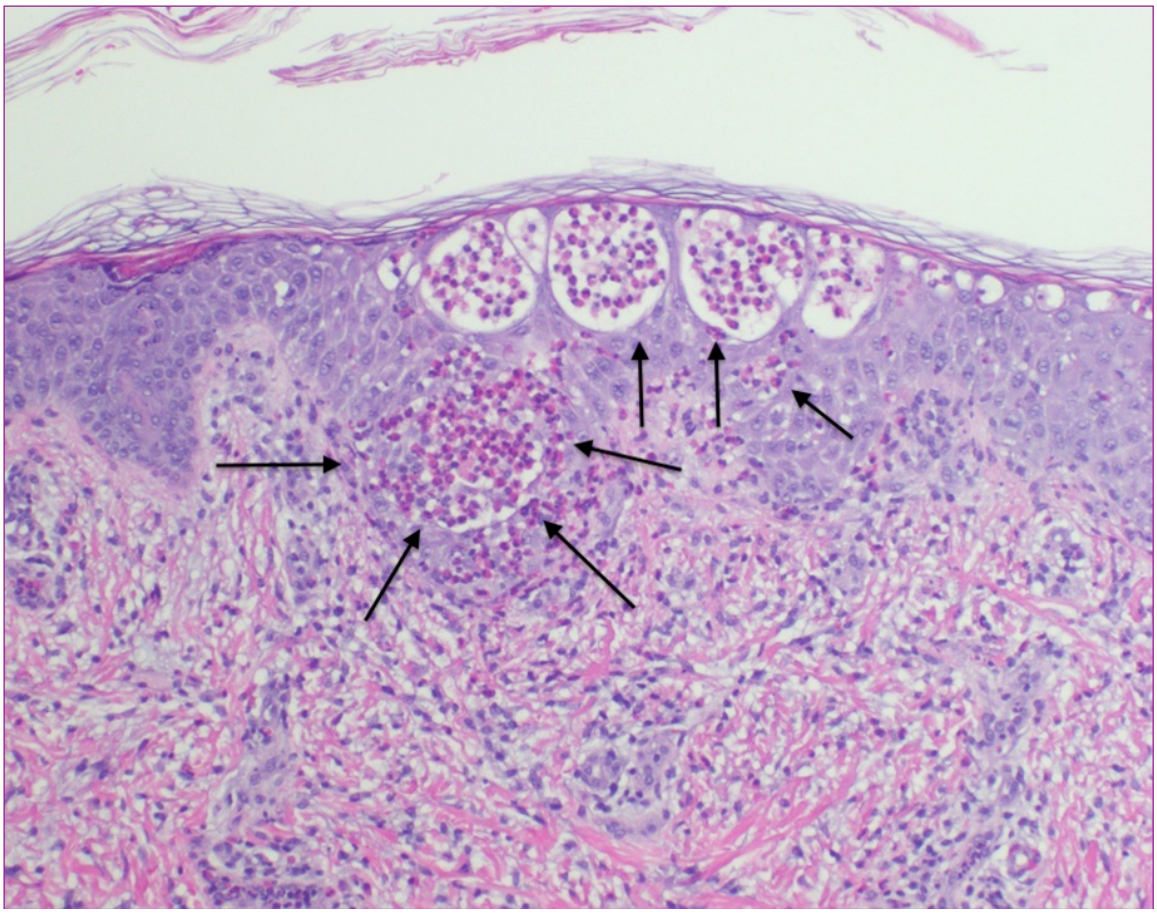

Figure 3. Superficial perivascular dermatitis with eosinophilic spongiosis (H&E, original magnification X20).

undergo genetic testing. Results of genetic testing of family members may also impact both medical management and reproductive decision making for patients and their families, which was the case in the described patient's family. Options for fetal testing are available for females with IP who desire pregnancy.[5]

The manifestations of IP are not strictly limited to the skin, as the eyes, teeth, hair, and central nervous system can also be affected. Thus, patients should be promptly referred to a multidisciplinary care team to assess specific cases, address these potential complications, and provide appropriate early interventions.

CONCLUSION

The described case highlights the importance of considering IP on the differential diagnosis when evaluating an infant with a vesicular rash. This is important not only so that prompt diagnoses can be made and treatment can be initiated for the patient, but also so that genetic counseling can be initiated for family members who may be affected or who may benefit from having this information for family planning purposes. Given that one of the first signs of IP can be the characteristic skin rash that the described patient presented with, it is important for the astute clinician, specifically pediatric providers, examining newborns to be able to recognize this rash and pursue the diagnosis efficiently. Further, it is important that patients promptly establish care with a team of specialists that can monitor patients regularly for complications, intervene when necessary, and provide the care that patients with IP need to achieve optimal outcomes.

Conflict of Interest Disclosures: None

Funding: None

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