

Incontinentia Pigmenti: A Rare Genodermatosis in a Male Child

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ABSTRACT

Incontinentia pigmenti is rare X-linked dominant disorder. There is no consistent expression of Incontinentia pigmenti in female child, but in male child, they always lead to death in utero. Vesicular, verrucous, hyperpigmented, and atrophic stages are the four stages of Incontinentia Pigmenti and it is uncommon for all stages to be seen in a same case. It is a rare genodermatosis, with only very few cases of male child with Incontinentia pigmenti have been reported. Thus, we report this case due to its extreme rarity and the child showed all the first 3 stages on followup.

Keywords: Eosinophilia, Genes X-Linked, Melanins, Pigmentation

CASE REPORT

An 8-day-old neonate, second male child of nonconsanguineous parents, born out of an uneventful normal vaginal delivery, was brought with the complaints of erythematous papular skin lesions which was initially vesicular all over the body since birth. Mother had no history of miscarriage in the past and her 1st child was a 3-year-old healthy female. On examination, the child had papular lesion on an erythematous base that follows the Blaschko lines over the abdomen, face and trunk [Table/Fig-1] suggestive of Incontinentia pigmenti stage 1 (Vesicular stage). Hair and nails were normal. Systemic examination including that of eyes (Fundus), Central Nervous System, and skeletal system revealed no abnormalities. Complete blood count showed raised eosinophils on differential leukocyte count.

At 1 month follow up the child showed wide spread area of verrucous whorled papules on erythematous base with interspersed areas of

hypopigmentation in a blaschkoid distribution over the trunk and extremities [Table/Fig-2] suggestive of Incontinentia pigmenti Stage 2 (Verrucous stage). Dystrophic changes were found in the finger nails of the child [Table/Fig-3].

At 3rd month of life, the infant showed streaks and whorls of brown or slate-gray pigmentation along Blaschko lines [Table/Fig-4] suggestive of Incontinentia pigmenti stage 3 (hyperpigmentation stage). No seizures, no developmental delay and ophthalmic examination were normal. The parents were not willing for either CT brain or skin biopsy. Subsequently the infant was not brought for follow up.

DISCUSSION

The first probable case of Incontinentia pigmenti (IP) was reported by Garrod in 1906 as a peculiar pigmentation of the skin in an infant. Subsequently, Bloch and Sulzberger further defined the condition in 1926 and 1928, respectively [1,2].

Involvement of the tissues of ectoderm and mesoderm origin suggests that Incontinentia pigmenti is a systemic disease affecting the teeth, eye, central nervous system and cutaneous tissues [3].



[Table/Fig-1]: Papular lesion on an erythematous base that follows the Blaschko lines over the abdomen, face and trunk in a male child



[Table/Fig-2]: Wide spread area of verrucous whorled papules on erythematous base with interspersed areas of hypopigmentation in a blaschkoid distribution over the trunk



[Table/Fig-3]: Dystrophic finger nail



[Table/Fig-4]: Streaks and whorls of brown or slate-gray pigmentation along Blaschko lines

The pigment melanin is usually seen in the melanocytes of the basal epidermal layer, but in Incontinentia pigmenti 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 Incontinentia pigmenti [4].

The IP gene has been mapped to Xq28, which encodes nuclear factor B essential modulator (NEMO) [5]. IP is a single-gene disorder caused by mutations in the NEMO/IKK- γ gene. This gene encodes a protein that regulates the function of various chemokines, cytokines and adhesion molecules, and is essential for protection against tumour necrosis factor-induced apoptosis [6]. Criteria for making the diagnosis as follows,

Major Criteria

(1) typical neonatal vesicular rash with eosinophilia; (2) typical blaschkoid hyperpigmentation on the trunk, fading in adolescence; and (3) linear, atrophic hairless lesions.

Minor Criteria

(1) dental anomalies, (2) alopecia, (3) wooly hair, (4) abnormal nails, (5) ocular anomalies, (6) history of multiple miscarriages of male child, (7) typical features on cutaneous histology.

If NEMO mutation status is unknown, and Incontinentia pigmenti is not present in a first-degree female relative, at least 2 major criteria or 1 major and at least 1 minor criteria are required to make the diagnosis of sporadic IP.

If NEMO mutation status is unknown but Incontinentia pigmenti is present in a first-degree female relative, then any single major criteria or 2 minor criteria are required to make the diagnosis.

If NEMO mutation has been confirmed, the presence of any 1 major or minor criteria is required to make the diagnosis [7].

Since 2 major criteria were affirmative in our child, the diagnosis of Incontinentia pigmenti was confirmed.

Stages 1 (inflammatory or vesicular) and 3 (hyperpigmented) are more common than stages 2 (papular or verrucous) and 4 (hypopigmented or atrophic), all four stages are not always present in a same case. The child may develop lesions either immediately after birth or as late as the end of first week of life. Streaks and whorls of brown or slate-gray pigmentation along Blaschko lines is peculiar for Incontinentia Pigmenti and it may persist for many years. Dermatologic manifestations, being one of the most important aspects for the diagnosis of the syndrome, result in less damage to the patient.

Associated findings include developmental defects of eyes (cataract, uveitis, optic atrophy, strabismus, retrolental fibroplasia), teeth (delayed dentition, partial anodontia, cone- or peg-shaped teeth, or absence of teeth), skeletal system (skull and palatal defects), and central nervous system (epilepsy, microcephaly, mental retardation, and slow motor development) [8]. Generally the cutaneous lesions do not require treatment, although to hasten the resolution of lesions, topical tacrolimus and corticosteroids are used. Secondary bacterial infections of the vesicle in the inflammatory stage need emollients and topical antibiotics [9].

Oral hygiene and regular dental care is necessary, and dental restoration may be indicated. Seizures should be treated with anticonvulsants. Additionally, routine neurodevelopmental assessments should be made, with referral to occupational and physical therapists as warranted. Frequent ophthalmologic evaluations are indicated, especially during the first year of life, in order to diagnose and treat potential ophthalmologic complications.

The presence and severity of associated extracutaneous manifestations decide the prognosis. Morbidity and mortality primarily result from neurologic and ophthalmologic complications.

The inheritance of a mutant copy of this X-linked gene is generally lethal in males in-utero. Although there is case reports of men with IP submitted to mutation analysis, none of these patients has been shown to carry the common NEMO deletion. Several studies have demonstrated the presence of hypomorphic NEMO alleles, a finding suggesting that less severe NEMO mutations permit the survival of affected men [10]. There are also several reports of men with IP who present the 47, XXY karyotype (Klinefelter syndrome) [11].

CONCLUSION

This case is reported for its rarity in a male child and classical appearance of the stages of Incontinentia pigmenti on follow up. The aim is to increase awareness among paediatricians and dermatologists in making the diagnosis of Incontinentia pigmenti based on the aforesaid criteria.

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