

A NEWBORN INFANT WITH VESICULOBULLOUS SKIN LESIONS

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ABSTRACT

Incontinentia Pigmenti Syndrome (IPS) is a rare hyperpigmentary disorder with an X-linked dominant inheritance. It is characterized by four phases, vesicular, verrucous, pigmentary, and hypopigmentary stages that often is associated with ocular, dental and central nervous system abnormalities. We describe an eleven days old girl with multiple erythematous vesiculobullous skin lesions were found at birth over distal part of her limbs and trunk. The family history for IPS was negative. The cause of incontinentia pigmenti has been traced to a defective gene on the X chromosome called NEMO, but genetic heterogeneity may exist. IPS may also arise as a spontaneous mutation.

KEY WORDS: Incontinentia pigmenti, X-linked dominant, newborn.

Pak J Med Sci April - June 2008 (Part-II) Vol. 24 No. 3 458-460

How to cite this article:

Sakha SH, Gharehbaghi MM. A newborn infant with vesiculobullous skin lesions. Pak J Med Sci 2008;24(3):458-60.

INTRODUCTION

Incontinentia Pigmenti Syndrome (IPS) also known as bloch-Sulzberger syndrome, is a rare X linked dominant inherited disorder that causes unusual blistering of the skin followed by increased pigmentation.^{1,2} Almost all cases are among females and the condition may be lethal in males.^{1,3} The initial skin lesions are usually present at birth and have four morphologic stages. Initially, there are inflammatory clear to yellow vesicles, which are arranged linearly and appear in crops during the first few weeks of life. The vesicular lesions occur on the

trunk and limbs and vary in density from few to many. Stage 2 is the verrucous stage, with linear or whorled warty, keratotic papules and plaques usually on the distal limbs. Stage 2 occurs between ages two and eight weeks. The third stage consists of patterned macular hyperpigmentation in streaks and whorls on the trunk and extremities. Occasionally, pigmentation accompanies some of the early lesions. Stage three occurs between ages 12 to 40 weeks. A fourth stage consisting of atrophic, hypopigmented streaks has been described in some patients.¹⁻⁴

Most patients with IPS have other problems. The central nervous system is involved in 10-40% of patients. The manifestations can include microcephaly, mental retardation, spasticity, seizures, ataxia, encephalopathy, hyperactivity and strokes.

The nails of the hands and feet may be involved in up to 40% of patients. About half of individuals with IPS have minor anomalies of their hair, usually a scarring alopecia on the crown of the head. Ocular changes are seen in

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* Received for Publication: December 10, 2007

* Revision Accepted: March 24, 2008

about one third of female patients and in two thirds of male patients in which it is lethal with incontinentia pigmenti. Skeletal and structural anomalies can occur in approximately 14% of patients but are associated with severe neurological deficits.²⁻⁴

Most cases of IPS are caused by a deletion in the NEMO gene. Approximately one half of all cases are spontaneous mutations. Most of the new mutations occur in the germline cells in the father's gonads.^{2,3,5} Usually, the diagnosis is made clinically on the basis of a history of sequential cutaneous lesions and associated features.^{1,2} There is often peripheral eosinophilia during vesicular phase of the disease. At least one major criteria is necessary for a diagnosis of sporadic incontinentia pigmenti, including the following:²

- * Typical neonatal vesicular rash
- * Typical blaschkoid hyperpigmentation
- * Linear, atrophic, hairless lesions.

Individuals with a history of first degree female relative who was previously diagnosed with IPS may also diagnosed with minor criteria which include the following:²

- * Dental involvement
- * Wooly hair, abnormal nails
- * Retinal diseases

Skin biopsy is used to confirm the diagnosis. The four cutaneous stages are associated with the following histologic findings.^{1,2}

Stage 1 has eosinophilic spongiosis that is characterized by spongiotic dermatitis with an eosinophilic inflammatory reaction, vacuolated basal cells and dyskeratotic cells. Stage 2 has papillated epidermal hyperplasia that is characterized by dyskeratotic cells in the dermis and epidermis, hyperkeratosis, acanthosis and vacuolated basal cells.

Stage three is the post inflammatory stage that is characterized by a thickened papillary dermis melanophages, deposits of melanin in the dermis and vacuolar alteration of epidermal layer.

Stage 4 is the atrophic hypopigmented stage that is characterized by decreased melanin in upper dermal layers, hyperkeratosis, atrophy, scarring and absence of appendages.

CASE REPORT

An eleven days old girl was brought to neonatal unit of Children's Hospital in Tabriz, Iran with multiple erythematous vesiculobullous skin lesions over distal part of limbs and trunk, since birth. The lesions were in the form of vesicles coalescing at places, arranged in linear configuration (Fig-1). These lesions gradually subsided leaving behind linear streaks of blackish hyperpigmentation. The infant had no involvement of central nervous system, ocular or skeletal system. The histologic examination of a small blister demonstrated a sub corneal vesicle filled with eosinophils. There was 18% eosinophilia in complete blood count.

She was born after a normal third pregnancy from a 33 year old mother. The family history was negative for similar skin lesions. In follow up visit at four months old, she had normal development with head circumference 41cm, and normal ophthalmologic, and neurologic examination. There was not hair and nail involvement.

DISCUSSION

Infants with IPS are born with blistering vesiculobullous lesions which appear as streaks. Most with IPS patients also have other problems including abnormal teeth, hair loss, and central nervous system abnormalities.¹⁻⁶ In the present case, the patient had skin lesions at her birth, which confirms that the disease can start in utero, as reported by other authors.² In follow-up study at 4 month old, the infant had normal growth and development, her head circumference, hair and nail were normal, and ophthalmologic examination was negative. The skin lesions were in hyperpigmentation stage with macular hyperpigmentation in a swirled pattern along the lines (Fig-2).

IPS is an X-linked dominant condition but genetic heterogeneity may exist, for this reason all the patients with it must have complete family physical studies.^{2,7} In our patient the examination of the other family members, did not show positive finding. We presume that this patient was a new mutation.



Figure 1 & 2: Vesiculobolous and pigmentary stages of incontinentia pigmenti in same patient.

No specific treatment is available for incontinentia pigmenti. The stage one lesions should be left intact and kept clean. Meticulous dental care is very important. Routine ophthalmologic follow-up is essential to prevent blindness as soon as possible after birth, and frequent examination during the first years of life. Neurological consultation is done only if neurologic abnormalities are present. Incontinentia pigmenti can also cause immunodeficiency in women and this may not manifest in the neonatal period.²

IPS is a genodermatosis and can be associated with malignancies (i.e, chromosomal

instability syndrome, such as acute myelogenous leukemia, Wilms' tumor, malignant rhabdoid tumors and retinoblastoma). Prognosis varies depending on the degree of central nervous system involvement and visual impairment.

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