

Case Report

INCONTINENTIA PIGMENTI

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ABSTRACT

Incontinentia pigmenti (IP) is an uncommon X-linked dominant genodermatosis characterized by four cutaneous stages and frequent association with dental (90%), central nervous system (33%) and ocular (35%) anomalies. The exact pathogenesis of this disorder remains unknown.

Herein, we report a newborn girl with inflammatory vesiculobullous and warty skin lesions and a positive family history of IP, with blood leucocytosis (eosinophilia and also lymphocytosis), but no other extracutaneous findings.

Iran J Med Sci 2001; 26(3&4):178-181

Key Words • Incontinentia pigmenti • leucocytosis • inflammation

Introduction

Incontinentia pigmenti is a rare X-linked dominant disease which affects the ectodermal tissues, and is usually lethal in males. Most patients have cutaneous manifestations within the first week of life. Cutaneous features include vesicles, papules, verrucous plaques and splash-like hyperpigmentation, although in some cases hypopigmented atrophic streaks or scarring alopecia may be seen.¹

Case report

A 7-week old female infant with bullous and warty cutaneous lesions was referred to our clinic. She presented with inflammatory linear vesiculopustular lesions on her acral extremities, especially on the left side, since 3 days of age.

Two weeks later, the eruption extended over her legs, chest and abdomen and then some papillomatous verrucous plaques appeared on these areas (Fig.1). The patient had been treated with systemic antibiotics for 20 days without any improvement. Careful examination revealed a patch of congenital scarring alopecia on the vertex.

Review of CNS, ophthalmological and skeletal systems did not reveal any abnormality.

The infant was born at term by cesarean section with a birth weight of 2600 grams to consanguineous parents. The mother had a streaky, atrophic and hypopigmented lesion on her right leg in addition to partial anodontia.

She had no history of spontaneous abortion, however, one of her children, a female, had died soon after birth due to bacterial pneumonia. The other sister and brother of the infant were in good health.

Laboratory data revealed leukocytosis (37300/mm³), eosinophilia (15666/mm³) and also lymphocytosis (12700/mm³) with no atypical cells detected in her peripheral blood. Routine serum biochemistry was within normal

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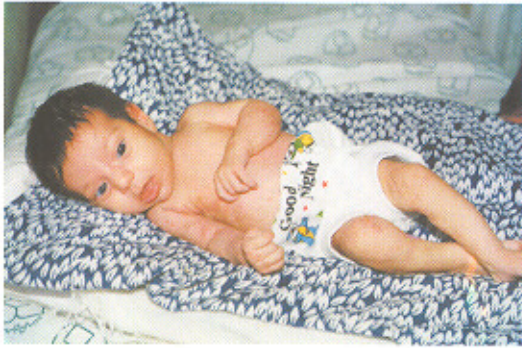


Figure 1: Vesicles, bullae and scattered verrucous papillomatous lesions on the upper and lower extremities, especially the left side.

range.

Scraping and culture of vesicles were also negative for bacteria or fungi.

A skin biopsy from an intact vesicle, showed acanthosis, spongiosis and exocytosis of a large number of eosinophils infiltrated into the epidermis. A few scattered dyskeratotic cells were seen throughout the epidermis, in addition to a relatively dense dermal infiltrate composed of eosinophils and mononuclear cells (Fig. 2).

Discussion

Incontinentia pigmenti (IP) is an uncommon neurocutaneous syndrome which is believed to represent a dominant X-linked inherited disorder. The locus for its gene has been linked to markers in Xq28.²⁻⁴

A recurrent deletion in the ubiquitously expressed NEMO (IKK-gamma) gene accounts for the vast majority of Incontinentia pigmenti mutations.⁵

The few cases reported in male patients were hypothesized to have occurred by spontaneous half-chromatid mutation. So, a female/male predominance of greater than 35:1 has been estimated from large statistical

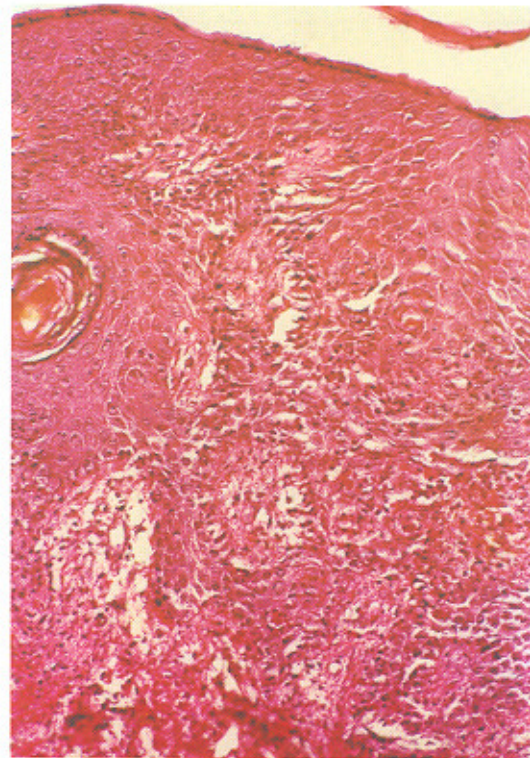


Figure 2: Epidermis showing acanthosis, spongiosis with abundant eosinophilic infiltration and a few dyskeratotic cells. Dermal infiltrate contains some eosinophils beside mononuclear cells. (H&E stain, magnification X40).

analyses. Several cases of IP have been reported in males with Klinefelter's syndrome.⁶

IP is suggested by Roberts et al. as a chromosomal instability syndrome, hence there may be an increased incidence of certain childhood neoplasms such as Wilms' tumor, retinoblastoma and rhabdomyosarcoma.⁷ Basophils may play a role in attraction of eosinophils through the release of eosinophil chemotactic factor. In addition to basophil mediators, leukotriene B₄ (derived from keratinocytes) induces accumulation of eosinophils within the epidermis. There is also evidence of lymphocyte dysfunction in patients

with IP.^{8,9} Our patient also had lymphocytosis, an observation not previously reported in the literature.

Four overlapping cutaneous stages (vesicular, verrucous, hyperpigmented and atrophic) and associated extracutaneous findings are relatively common, while constitutional symptoms are absent.¹⁰

The first stage of cutaneous involvement usually begins within 2 weeks after birth. It consists of linear erythematous vesicles or pustules most often located on extremities. Stage 2 usually begins between the second and sixth weeks of life and consists of verrucous, papillomatous plaques arranged linearly in the same areas.¹¹

In one recent report, a patient with IP had continuing development of new warty lesions of which one had resulted in squamous cell carcinoma in situ.¹² Stage 3 is characterized by whorled, slate-brown hyperpigmented macules and patches on the trunk which start to occur at the age of 12 to 26 weeks of life.¹¹ Stage 4, if present, causes streaky atrophy and hypomelanosis especially on the lower extremities¹⁰ (as was seen in the patient's mother), indicating that the late cutaneous manifestations of IP are not always hypermelanotic bizarre streaks.¹³

Ocular anomalies have been reported in about one third of cases. While strabismus is the most common (18%), a nearly consistent and pathognomonic finding is pigment retinopathy or diffuse mottled hyperpigmentation. These individuals should be clinically observed at regular intervals because of the risk of exudative retinal detachment which usually occurs in very early childhood.¹⁴ Laser photocoagulation used at the onset of retinopathy results in subsequent resolution of the vasculopathy.¹⁵

Major dental abnormalities occur in 65% to 90% of patients; the most common being partial anodontia or hypodontia (43%) and pegged teeth (30%),^{16,17} as were seen in our patient's mother. The central nervous system

is affected in up to 33% of patients with convulsive disorders occurring in 13% of cases. Typical cranial MRI findings of the disorder include hypoplasia of the corpus callosum, enlargement of the lateral ventricles and periventricular white-matter lesions.³

Familial cases of IP are sometimes missed due to lack of recognition of such late cutaneous manifestations. This emphasizes the variable disease gene expression and the importance of recognizing this condition.¹⁸

It is suggested that all patients with IP should have dental examination by the age of 2 years. Ocular examination should be done within 1 month of birth and repeated at 3-month intervals until 1 year of age (as done for the patient reported above), to prevent complete blindness.¹⁰

Acknowledgement

We give thanks to Dr. M.R. Radan for his help in preparing this manuscript.

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