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Incontinentia Pigmenti, a rare genodermatosis - Two case reports

GEETHA
Department of Dermatology, Venerology & Leprosy, MADRAS MEDICAL COLLEGE AND GOVERNMENT GENERAL HOSPITAL

Abstract : Incontinentia Pigmenti (IP) or Bloch-Sulzberger syndrome is an uncommon genodermatosis that usually occurs in females and characterized by cutaneous, neurologic, ophthalmologic and dental manifestations. It is an X linked dominant neurocutaneous syndrome and is lethal in males. We report 2 cases of incontinentia pigmenti- one in a 19 year old female (case 1) with skin, dental and neurological manifestations and another in a 2 year old female child (case 2) with skin,ophthalmologic and neurological manifestations .Our patient (case 1) has demonstrated a rare clinical association of incontinentia pigmenti with hypoplasia of the breast.

Keyword : Incontinentia Pigmenti, Genodermatosis

Introduction:

Incontinentia pigmenti (Bloch-Sulzberger syndrome) is an X linked dominant neurocutaneous syndrome with cutaneous, neurologic, ophthalmologic and dental manifestations. Bloch and Sulzberger defined the condition in 1926 and 1928, respectively as a clinical syndrome with many unique features.1,2 Incontinentia pigmenti is characterized by abnormalities of the ectoderm derived organs. It is lethal for the hemizygous affected males.1,3,4In female patients lyonization results in functional mosaicism of X linked genes, which is manifested by the blaschkoid distribution of cutaneous lesions.6 The IP gene has been mapped to chromosome Xq28 which encodes the NEMO (Nuclear factor B essential modulator) gene, and contains 10 exons. About 80% of IP cases are due to deletion of these exons. 1,7 Mutations involving other alleles of the NEMO gene produce phenotypes different from IP, like anhidrotic ectodermal dysplasia with immunodeficiency.1,8 Carney in 1976 after analyzing 682 cases described in the world literature, found that the disorder is present in all races with a female to male ratio of 37:1. Later Landy and Donnai reported their experience of over 100 cases.1,4,9 The skin changes are often seen at birth and usually develop before the end of the first week or within first 2 months. Four distinct clinical stages are seen and they are as follows:1,3

Stage 1: Inflammatory macules, papules, vesicles and pustules.

Stage 2: Hyperkeratotic and verrucous lesions.

Stage 3: Grey brown pigmentation.

Stage 4: Atrophic, hypopigmented and depigmented bands or streaks that are hairless and anhidrotic and fail to tan on sun exposure.

The sequence of these stages are not regular and in some cases pigmentation may be the only abnormality present from the outset. Activity may rarely persist into adult life.2,10 The pigmentation may range in colour from blue grey to slate brown. The bizarre Chinese letter pattern of skin lesions along the blaschko's lines is diagnostic of this condition. The hair is usually normal, but in 25% of cases scarring alopecia may be seen near the vertex. The nails usually shows no changes.1 Other systemic manifestations may not be recognized until infancy or early childhood. They include neurological manifestations like microcephaly, mental retardation, ataxia and seizures, Ocular features like blindness, strabismus, cataract and retinal detachments, dental defects like hypodontia, anodontia, peg shaped teeth and delayed eruption, haematological changes like blood eosinophilia with altered immunological reactivity along with skeletal abnormalities like skull defects and palatal defects.1,3,11,12 Histopathological findings vary with the stage of clinical presentation. In the vesicular stage, spongiotic dermatitis with eosinophil filled intraepidermal vesicles are seen. The verrucous stage shows acanthosis, papillomatosis and hyperkeratosis whereas the hyperpigmented stage shows normal epidermis with melanin deposition and melanophages in the upper demis. In the atrophic stage there is an atrophic epidermis with a reduction in basal melanocytes.1,2 The prognosis is usually determined by the spectrum of clinical features present.4

Case Reports:

Case 1:

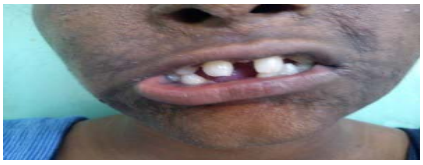
A 19 year old female born of third degree consanguineous marriage presented with asymptomatic fluid filled lesions over the face, arms and trunk at birth. Then she developed hyperpigmented lesions over the face, arms and trunk after a few months. There was history of two episodes of seizures at 10 years of age. There was no history of visual disturbances or heat intolerance. She had regular menstrual periods and fully developed secondary sexual characteristics. But she had hypoplasia of the right side of the breast. She had one elder sister who is normal. There was history of abortion in her mother. Examination showed multiple linear, streaky and bizarre hyperpigmented macules over the face, arms and trunk (Figure 1 & 2) with scarring alopecia over the frontal and vertex region of the scalp (Figure 3). She had widely spaced teeth and peg shaped lower incisors in the oral cavity (Figure 4). There was mild facial asymmetry and hypoplasia of the right breast (Figure 5). Her routine investigations like complete haemogram, renal

and liver function tests were all within normal limits. Histopathological examination revealed normal and slightly acanthotic epidermis with increased melanin deposits and melanophages in the upper dermis (Figure 6).

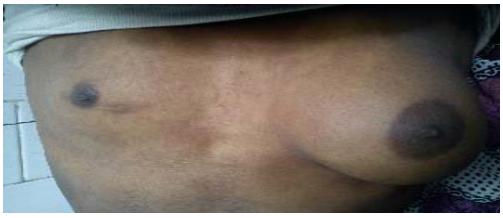
IP facial lesion (case 1) Fig 1

IP over trunk (case 1) Figure 2

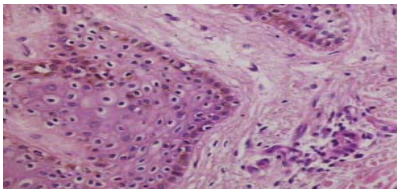
Scarring alopecia (case 1) Fig 3



Widely spaced teeth (case 1) Fig 4



Hypo plastic breast (case 1) Fig 5

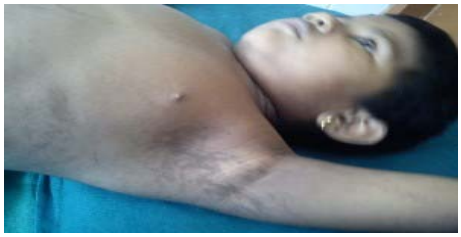


IP HPE (case 1) Fig 6

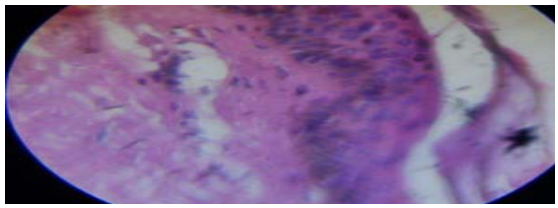
Case 2:

A 2 year old female child born of non consanguineous marriage presented with hyperpigmented macules over the trunk, axilla and both thighs since birth. There was history of recurrent episodes of seizures for the past one year and she is on treatment with antiepileptics. There was history of delayed mile stones with hyperactive behavior. On examination multiple linear and streaky hyperpigmented macules were seen over the trunk, both thighs and axilla with distribution along the lines of blaschko (Figure 7 & 8). There was a focal patchy hairless atrophic area over the vertex. The teeth and nails were normal. On neurological examination, global developmental delay was noted and the motor, adaptive, language and social development were at one year age level. There was subnormal intelligence and hyperactive behaviour. On ophthalmological examination, there was strabismus with retinal pigment alteration. Her routine investigations were normal. CT scan, MRI brain and EEG were normal. Video EEG showed focal sharp waves in right fronto-temporal regions. Histopathological examination was consistent with the pigmentary stage of IP and revealed hyperpigmentation of the basal cells with mild melanin incontinence in the dermis (Figure 9).

IP Child (case 2) Fig 7



IP Pigmentation along Blaschko's lines (case 2) Fig 8



IP Child HPE (case 2) Fig 9

Discussion:

The diagnosis of Incontinentia pigmenti in the 2 cases were based on the description of vesiculobullous lesion at birth followed by hyperpigmented lesions (case 1), associated neurological involvement in both cases, typical morphology of the skin lesions with scarring alopecia in both cases, dental anomalies (case 1), ophthalmologic findings (case 2), and the histological evidence in both cases. Our patient (case 1) demonstrated rare clinical association of IP with hypoplasia of the breast. In our cases, for case 1 dental opinion regarding oral hygiene and plastic surgical correction was done for the hypoplastic breast and for case 2 , neurological and ophthalmological management were done.

Although Linear and whorled nevoid hypermelanosis can be observed as similar pigmented lesions, it is not associated with blistering phase in the neonatal period and there are no extra cutaneous findings seen. Naegeli- Franceschetti syndrome a rare entity similar to IP, does not have blistering phase and is associated with keratoderma of the palms and soles, hypohidrosis and dystrophic nails. In Focal dermal hypoplasia there may be associated papillomatous lesions, telangiectasias, adnexal changes, skeletal and ocular abnormalities.1,2,14

Conclusion:

The prognosis in IP is based the spectrum of clinical features. The pigmentary changes may diminish with age. The early inflammatory lesions may require topical tacrolimus or steroids. Proper oral hygiene and regular dental care is necessary. Treatment of neurological features like seizures with anticonvulsants should be done. Routine neuro-developmental assessments and frequent opthalmologic evaluations are required, with long term follow up to prevent complications.

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