

Incontinentia Pigmenti (Bloch Sulzberger Syndrome) (Bloch - Siemen's Syndrome)

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Summary and Introduction :

Incontinentia pigmenti (IP) is a syndrome with variable clinical presentation having dermatologic, neurologic, skeletal, developmental, ocular and dental defects. I.P is an x linked dominantly inherited disorder of skin pigmentation usually seen in females and is lethal to males. ⁽¹⁾

IP is transmitted through maternal lineage as shown in a pedigree where all affected members were females and transmission was only by females and affected members were only maternal female relatives. In the same pedigree there were two male abortions and no female ones. ⁽²⁾

I.P is associated with variable abnormalities that affect the skin in 100% of cases, dental 90%, skeletal 40%, central nervous system (CNS) 40% and ocular 35%. ⁽¹⁾ In this text we present a female infant who presented with the main manifestation of I.P simultaneously early in her infancy.

Case Report :

A.K.K. Full term baby, small for gestational age birth weight 2.24 kgs., female Qatari neonate was 14 days old when she presented with skin rash and hypoactivity of one week duration. Skin rash was more on the lower limbs and napkin area. The rash was vesicular and pustular in linear pattern, associated with hyperpigmented areas. New lesions appeared mainly on pressure areas while older lesions disappeared associated with hyperpigmentation. The infant was hypoactive but was feeding well. After two weeks verrucal wart like lesions were in linear pattern in addition to above rash (Fig 1 to 5). Father

and mother are first cousins, and the mother's first pregnancy was aborted at 3 months, and sex of the miscarriage was not determined. The present case is the first baby to the family.

Father and mother do not have any dermatological abnormality. On examination the infant had stable vital signs, good general condition, normal weight, height and head circumference, no fever, no convulsion and no change in bowel habit.

Cultures of the pustules on three occasions showed no growth.

WBCs showed 32000 cell/cu.mm, 23% eosinophil, 10% monocytes, 43% lymphocyte, 24% neutrophils, Hemoglobin 16.4 gram/dl, platelet 374000/cu.mm.

Cultures of blood, urine and cerebrospinal fluids showed no growth. Immunoglobulin IgG, IgA, IgM and IgE were all normal for her age, complements 3 and 4 were normal, T and B-cell sub-population were normal, her chromosomal study is 46 xx female.

Skin punch biopsy taken from left forearm showed slight hyperkeratosis. Perinuclear vacuolization is present in the upper and mid layer. There is mild exocytosis. The basal layer shows focal areas of vacuolization. No eosinophilic infiltration is present. Few melanophages are present in the upper dermis, but eosinophils were not seen.

Patient was discharged as a case of incontinentia pigmenti and followed in dermatology clinic.

Discussion :

I.P. is usually seen in females as an x linked dominantly inherited disease which is lethal in males. ⁽¹⁾ Female carriers of IP have high incidence of spontaneous abortions in males. It is emphasized that the disease expression is variable within an affected family as shown by the report of florid IP in a neonate while her mother had partial anodontia and history of a linear rash on her legs during her early childhood and the rash resolved spontaneously. ⁽³⁾ It is suggested that mosaicism is responsible for the variable clinical expression. ⁽⁴⁾

The gene of familial IP has been located on XP11.2 ⁽⁷⁾; or linked to the XP28 region. ^(3, 6)

The hallmark of IP is marked random X-inactivation of an X linked dominant gene. This pattern is found in peripheral blood leukocytes and in cultured fibroblasts in 98% of affected females. ⁽⁷⁾ This

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Fig. 1-Right hand and forearm showing warty lesions and hyperpigmentation.



Fig. 2-Right leg showing linear hyperpigmentation and warty lesion of right foot.



Fig. 3-Right thigh showing splashes of hyperpigmentation.



Fig. 4-Left foot showing warty lesions.



Fig. 5-Left thigh and leg showing splashes of hyperpigmentation.

finding provides a means for investigating uncertain cases of IP.⁽⁴⁾ Prenatal diagnosis could be done using trophoblast biopsy and finding the gene location chromosome XP28.⁽⁸⁾

More than 95% of cases of IP are females⁽⁹⁾ but IP may rarely affect boys who may have the IP in association with Klinefelter syndrome.^(10,11,12) The male affection is probably the result of spontaneous mutations and mosaicism of X chromosome.⁽¹⁰⁾

Statistical analysis showed that males with IP represent 2.6% of all IP cases.⁽¹³⁾ I.P. in males has to be differentiated from linear whorled nevoid hypermelanosis (LWNH)⁽¹⁴⁾ which is described to occur in early infancy and is characterized by multiple streaks of hyperpigmentation following Blaschko's lines and is not preceded by inflammatory eruptive lesions or any of the anomalies which characterize IP. (LWNH) histopathologically does not show pigment incontinence but one case of

LWNH was reported to show incontinence of pigment.⁽¹⁴⁾ This histopathological finding is supposed to be conclusive of IP but in this case its presence did not exclude the diagnosis of LWNH.⁽¹⁴⁾

The cutaneous lesions occur in 100% of IP infants. Typical skin lesions appear at birth or shortly after. The lesions appear in three overlapping stages. An initial linear erythematous and clear vesicular and bullous eruption which often develop in crops on limbs and less often may be generalized and change within few weeks or a month or two into verrucous stage which appears as linear warty lesions on back of hands, feet, fingers and toes. The warty lesions resolve spontaneously within weeks or months and is followed by hyperpigmentation. The three stages of IP may be present simultaneously at birth.⁽⁸⁾ It has been estimated that 13.9% to 40% of patients with IP manifest the pigmentation without evidence of earlier stages.^(13,15,16) It is possible that the earlier inflammatory stages may occur in utero and do not progress after birth.⁽⁹⁾

The hyperpigmentation is described to have a pattern of fire work, fountain, splash, marble like or swirled appearance. The pigmentary disorder appears mainly on the torso and on the limbs to a lesser extent and rarely the inflammatory lesions may appear in already pigmented lesions. Inflammatory lesions are uncommon after the age of 6 months and it has been reported that vesiculation appeared after treating a pigmented macule in three years old girl

with limited Ruby laser therapy.⁽¹⁶⁾ The vesicles appeared in treated and untreated areas.⁽¹⁶⁾

Several authors describe a fourth stage if IP in which all the three stages fade especially the hyperpigmentations and the only remnant of IP in adults may be atrophy and depigmentation.⁽¹³⁾ Alopecia of the vertex diffuse or scarring⁽¹⁵⁾ was found in 37.8% of affected infants and usually occur since birth.⁽¹⁷⁾ Woolly hair nevus and agenesis of eye brows and eye lashes were reported in association with I.P.⁽²⁾ Nail dystrophy of unknown origin occur in 7.1% of patients⁽¹³⁾ and subungual keratotic tumors were described as a late manifestation of I.P associated with lytic deformities of distal phalanges.⁽¹⁸⁾

The histopathology of the vesicular lesions shows spongiotic epidermis with subcorneal vesicles containing eosinophils. The dermis shows inflammatory infiltrate which includes numerous eosinophils. The infiltrate invades the epidermis and many basal cells are oedematous and degenerate and the upper dermis shows pigment laden melanophages.

The warty lesions show hyperkeratosis, irregular acanthosis and individual dyskeratotic cells. The pigmented lesions show diminished pigmentation of basal cells with large quantities of melanin in melanophages in the upper dermis. The melanophages are present in all three stages.⁽⁹⁾ Over half of patients with IP have systemic manifestations.⁽⁹⁾ Leukocytosis with peripheral eosinophilia upto 50% in peripheral blood is usual when inflammatory changes are present.⁽⁹⁾ An immunologic defect may be part of IP. Defective leukocyte chemotaxis and impaired lymphocyte transformation are reported in I.P.⁽¹⁹⁾

About 80% of all patients with I.P appear to have had one or more anomalies of eyes, teeth, CNS and or structural development.⁽¹³⁾

Associated developmental defects do not regress and may result in a less favorable outcome. Dental anomalies are seen in 64.7% of cases⁽¹³⁾, mainly as partial anodontia, complete anodontia, late dentition, pegged or conical deformity of incisors or canines, enamel disorders with multiple caries and crumbly teeth.

Ocular anomalies are among the most severe systemic anomalies.

Progressive ischemia of the maculas of the eyes is characteristic of IP and occur as early as three months of age.⁽²⁰⁾ The mottled diffuse

hypopigmentations of the retina together with the retinal vessel abnormalities underly all other secondary ocular findings as cataract, leucocoria, optic atrophy, strabismus, nystagmus and microphthalmia, retrolental mass formation and exudative retinal detachment.⁽¹⁾ Visual loss and blindness was statistically reported to affect 20% of affected patients.^(1,3)

The CNS is affected in 30% of cases and the commonest manifestation is convulsive disorders, mental retardation, slow motor development, microcephalus, spastic paralysis, cerebral cortical atrophy, hydrocephalus, cerebellar ataxia, congenital hearing loss and abnormal EEG.^(8,13)

Other developmental anomalies include skull deformities, dwarfism, club foot, spinabifida, cleft pal-

ate or cleft lip or both, ear anomalies, hemiatrophy, congenital dislocated hip and chondrodystrophy.⁽¹³⁾

In our patient the three stages of vesicular, verrucous and pigmentation were present at the same time early in her infancy (2-4 weeks old) and her blood showed high leukocytosis and high eosinophilia (23%). Our patient might have got the disorder from mutation. Our patient is the

first child of her parent and follow up of this family pedigree may clarify more the mode of inheritance.

No satisfactory treatment is known for this case and follow up is necessary to detect any possible systemic association that may arise as a late manifestation of IP in this case.

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