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Incontinentia Pigmenti with Spastic Cerebral Palsy: A Case Report

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Abstract

Incontinentia Pigmenti (IP) or Bloch-Sulzberger syndrome is an uncommon X-linked dominant disorder that affects mostly females and is usually lethal in males. It is associated with skin (100%), dental (90%), skeletal (40%), central nervous system (40%), and ocular (35%) abnormalities. We report a florid case of a 9-year-old female who presented with convulsion and inflammatory vesicular skin lesion soon after birth which evolved into hyper-pigmented lesions along the lines of Blaschko over trunk, upper and lower extremities. Her teeth were peg-shaped and the skeletal examination confirmed scoliosis and hypoplastic mandible. She had quadriplegic spastic cerebral palsy, microcephaly with global developmental delay and mental retardation. Ocular examination revealed hypertelorism with micro-ophthalmia of left eye. She also had avascularity of left peripheral retina. On further investigation, MRI revealed gliotic areas in frontal and parietal region suggestive of microvascular vaso-occlusive insult. Histopathology of skin demonstrated pigment incontinence in upper dermis consistent with the diagnosis. Our patient had sporadic mutation as mother and sibling were normal. We report this case because of its rarity.

Key Words: *Genodermatoses, Incontinentia Pigmenti, Bloch-Sulzberger syndrome, Lines of Blaschko*

INTRODUCTION

Incontinentia pigmenti (IP) is a rare multi-systemic X-linked dominant genodermatoses with an estimated prevalence at birth of 0.7/100,000.[1] It is caused by mutation of nuclear factor kappa B essential modulator (NEMO) or gamma subunit of the inhibitor kappa B kinase (IKK-γ) gene located at Xq28. Over 80 percent of cases affect NEMO gene which results in defective activation of the transcription factor nuclear factor kappa B (NF-κB), essential for anti-apoptotic and proliferative cellular pathway.[2]

Garrod in 1906 first described this syndrome.[3] In 1926, Bloch further presented this case to swiss society for dermatology and named this new clinical condition as Incontinentia pigmenti.[4] In 1928, Sulzberger[5] also reported this syndrome and hence IP is also known as Bloch-Sulzberger syndrome.[6]

The name Incontinentia pigmenti originates from its histopathological characteristics (Stage 3) which shows melanin pigment incontinence from the epidermal basal cells to the upper dermis in the form of free pigment or aggregates of melanophages.[6]

IP essentially affects females with female to male ratio 35:1. Sporadic mutation exists in 45 percent of cases and only 55 percent have a positive family history.[7]

CASE REPORT

A nine-year-old female child born of non-consanguineous marriage was brought by her parents for vomiting since seven days. The child had global developmental delay with average developmental quotient (DQ) of 6.2 percent and refractory seizures. There was history of difficulty in feeding, drooling of saliva, bowel and bladder incontinence and recurrent respiratory tract infections since childhood. There was no history suggestive of cranial nerve involvement.

The antenatal period in mother was uneventful with no history of abortion. The child was born full-term by caesarean section, cried immediately after birth and weighed 3000 grams. Child developed vesicles all over the body at one month of age with hyper-pigmentation of the skin after three months. The parents and the other two siblings (one male and one female) were absolutely normal.

On examination, the child had decorticate rigidity with fixed contractures at elbow and ankle joint. Her vitals were stable with signs of some dehydration. She was under nourished and pale. The child also had microcephaly, hypertelorism, micrognathia, localised alopecia over scalp, conical teeth (Figure 1), thin nails, and scoliosis towards right. Hyperpigmented macular rash was present along the lines of Blaschko over trunk and limbs. (Figure 2 and 3)

Central nervous system examination revealed hypertonia in all four limbs. The child had absent superficial and brisk deep tendon reflexes with clonus. Sensory system examination was normal with no signs of meningeal irritation. Other systems examinations were within normal limits. The left eye showed sclerosis of vessels in superior and supero-temporal region with mild tortuosity and avascularity of peripheral retina

without any pigmentary deposits. The right eye was normal.

Magnetic resonance imaging of brain showed gliotic areas in the right frontal and bilateral parietal region suggestive of sequale to vascular insult or perinatal asphyxia.

Histopathology of hyperpigmented skin lesion demonstrated melanin pigment incontinence in the upper dermis consistent with IP stage III. (Figure 4)

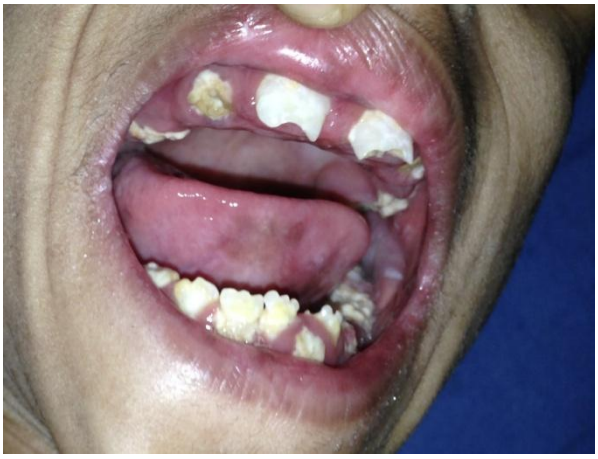

Figure 1- Conical teeth

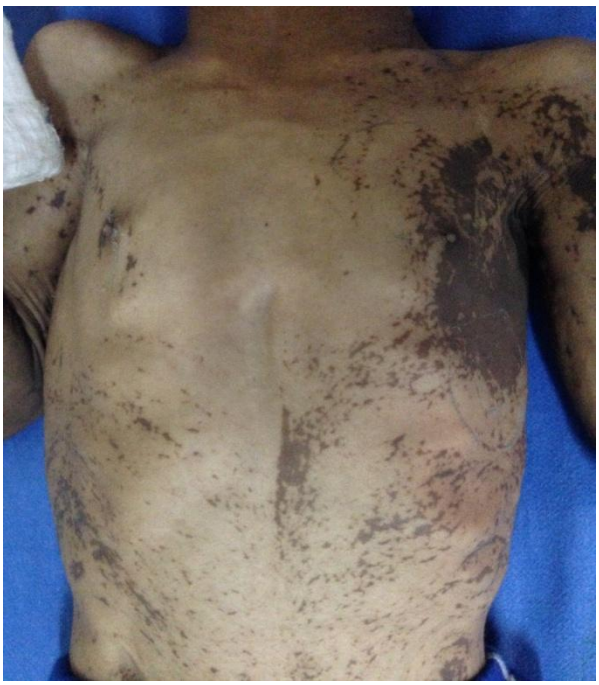

Figure 2- Hyperpigmented macular rash along the lines of Blaschko

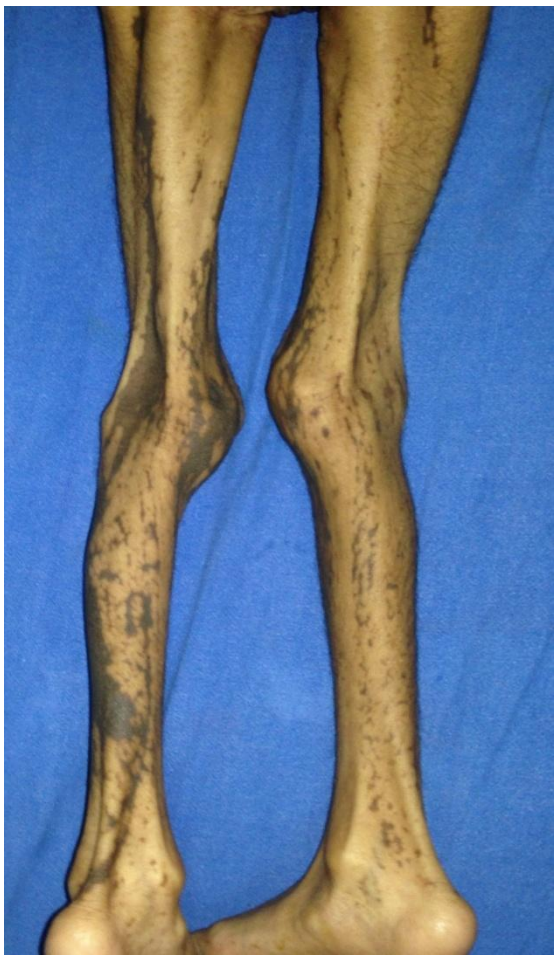

Figure 3- Hyperpigmented macular rash along the lines of Blaschko

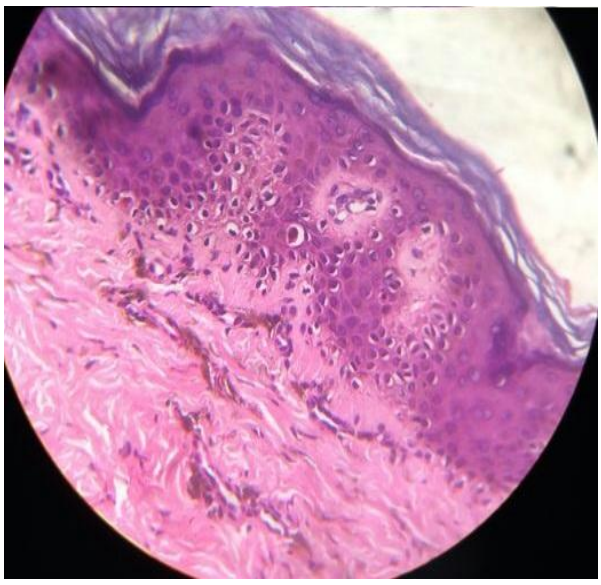

Figure 4- Histopathology of skin showing pigment incontinence in upper dermis

DISCUSSION

Incontinentia pigmenti involves organs and tissues of ectodermal and mesodermal origin. There are two genotypes of IP. IP type 1 is a sporadic form accounting for 85 percent of cases with gene locus on chromosome Xp11.21. Remaining 15 percent is IP type 2 which is a familial form with gene locus on chromosome Xq28.[6]

Cutaneous manifestation of IP is the main reason for detection of this condition. Classically, there are four phases of skin lesions which develop in succession with each having typical histopathological appearance. It is not necessary to have all the four stages in succession and several stages may overlap. Stage I has linear vesico-bullous lesion over trunk and extremities. Histologically, intraepidermal eosinophilic vesicles and vacuolized basal cells are present. Stage II has linear verrucous lesion affecting extremities with acanthosis and hyperkeratosis present on histology. Stage III is characterised by whorls of hyperpigmentation along lines of Blaschko most commonly on the trunk showing melanophages and pigmentary incontinence on histology. Stage four has areas of hypopigmentation and or atrophic streaks with histology showing atrophy and fibrous scarring of all layers and absence of skin appendages. Our case presented to us in stage III, however there is also a history of stage I lesions.

Extracutaneous manifestations are present in 70-80 percent of cases and involves the central nervous system (seizures, spastic paresis, motor retardation, mental retardation, microcephaly, ischemic cerebrovascular accidents); Teeth and Jaws (cone/peg shaped teeth, hypodontia, partial anodontia, delayed dentition, Impactions, Prognathia, Micrognathia); Eyes (strabismus, cataracts, Retinal vascular abnormalities, Retinal pigmentary changes, anophthalmia, micro-phthalmia); Hair (Localised or generalised alopecia, woolly hair nevus, eyelash and eyebrow hypogenesis); Nails (Onychodystrophy, pitting, ridging); Bone and musculoskeletal structure (syndactyly, skull deformities, scoliosis, congenital hip dislocation, supernumerary ribs, hemiatrophy and shortening of the legs and arms).[2,6,7]

Our patient was a sporadic case with conical teeth, scoliosis, spastic quadriplegic cerebral palsy, avascularity of peripheral retina in the left eye with hyperpigmentation along lines of Blaschko corresponding to histopathological finding of melanin pigment incontinence in the upper dermis.

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