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Incontinentia Pigmenti: A Case Report in a 1 Month Old Female Baby

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Abstract: ***Introduction: Incontinentia pigmenti, also known as Bloch- Sulzberger syndrome is a rare X linked dominant disorder that presents as skin lesions most commonly. This condition occurs due to mutation in NEMO (NF kB essential modulator) gene. It is a multisystemic disease that involves cutaneous tissues, dental, ocular and central nervous system besides other organs. Here, a case report in a 1 month old female baby is being discussed. Case Report: A female baby of 1 month presented to the dermatology OPD with features of hypertrophic, wart like lesion over the extremities (in a linear pattern), trunk and face. These lesions presented initially as vesicles and bullae during the first one week of life. These lesions followed blaschko's line. The baby also has patches of alopecia seen over the scalp. Clinical diagnosis of Incontinentia pigmenti was made. Conclusion: Incontinentia Pigmenti is a multisystemic disease, so it is crucial to examine the patient with a multidisciplinary approach. All the systems should be carefully examined, regular follow up to pediatric ophthalmologist is critical. Radiological evaluation is crucial for any dental abnormalities. Dermatological management is aimed at reducing the risk of infection of blisters by giving antibiotics and maintain proper hygiene.***

Keywords: Incontinentia Pigmenti

1. Introduction

Incontinentia Pigmenti (IP), also known as Bloch-Sulzberger syndromeis a rare X-linked dominant genodermatoses with cutaneous presentation being the most common finding. IP is a systemic disease presenting as skin lesions most commonly.Itinvolvestissues of both ectodermic and mesodermic origin, which includes cutaneous tissue, teeth, eyes and the central nervous system, amongst other organs.[1] This condition occurs due to mutation in NEMO (NF kB Essential Modulator) gene. NEMO stands for NF-KB essential modulator, which is located on the chromosome Xq28, a transcription factor involved in inflammatory and immune responses, and helps in protecting cells from tumour necrosis factor-induced apoptosis. Therefore, its mutation results in diminished NF-kB activity that results in increased cells susceptibility to apoptosis.[2,3] NEMO mutation is lethal to the male fetus. However, during early embryogenesis, as a result of lyonization phenomenon (or X chromosome inactivation), female baby survives.[4]

IP occur in 1 in 40,000 newborns approximately although its epidemiological data are not completely known[5]. A positive family history is noted in 50% cases and it is predominant in women, with female to male ratio being 37:1.In males, only less than 3% cases are known. Klinefelter's syndrome (47,XXY karyotype) were seen in many of them, where the second X chromosome resulted in survival of those male fetus from natural intrauterine death. Various genetic mutations were been seen in the other males, such as hypomorphic alleles or somatic mosaicism for the common IKBKG deletion.[6,7] Here, a case report in a 1 month old female baby is being discussed.

2. Case Report

A female baby of 1 month old had presented to our dermatology OPD with features of hypertrophic, wart like lesion involving the body.

On clinical examination, the child's anthropometric measurements were: 50 cm height and 3.5kg weight. Her blood pressure, pulse rate, breathing were normal. There was no abnormality detected in the ocular system. The musculoskeletal system was normal, except for a hypoplastic mandible. The parents did not gave any history of seizures of the baby.

On cutaneous examination, it was found that there were multiple hypertrophic, wart like lesion over the body. These lesions were present over the limbs, trunk and face and it were seen to involve along the Blaschko's lines. Linear warty lesions were observed on the extremities. Few hyperpigmented areas were noted over the trunk regions and intertriginous areas. On examination of her hair, it was found that there were alopecic patches about 4 in number.

Initially, the skin lesions appeared as vesicles and bullae in the first week of life with areas of hair loss over the scalp.

Gradually leading to the appearance of wart like areas in those previously involved. The mucosal surfaces were not involved.

Nail examination revealed normal except a few dystrophic nails.

She has been delivered by spontaneous vaginal delivery in a term pregnant mother. The mother was otherwise healthy and the rest of her pregnancy period was normal without any comorbidities or any complications. The mother's age was 33 years old at the time of delivery. There was no previous pregnancies or any miscarriages. During her childhood, the woman had suffered from varicella.

On examination of the mother, no any cutaneous, nail or hair abnormalities were noted. Maternal serology was negative for VDRL, HIV, HBV, HCV.

Routine blood tests was done for the baby and were found to be normal, however peripheral eosinophilia was noted.Test

for infections and autoimmune diseases were negative, C-reactive protein and was normal. Skin biopsy was performed and showed acanthosis, papillomatosis, foci of eosinophilic spongiosis and necrotic keratinocytes. In the dermis, there was an infiltrate of eosinophils. On the basis of history, clinical features, examination findings and investigations, diagnosis of in continentia pigmenti was made.

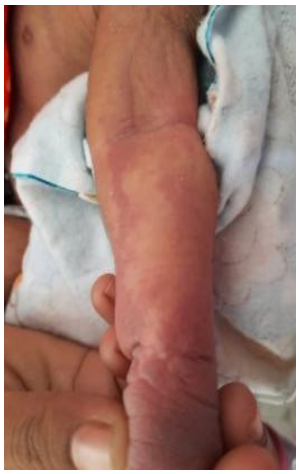

Figure A: Linear wart like lesions on limbs

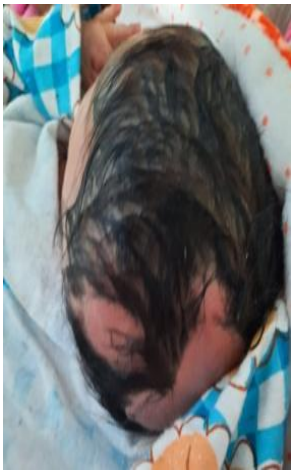

Figure B: Alopecic areas

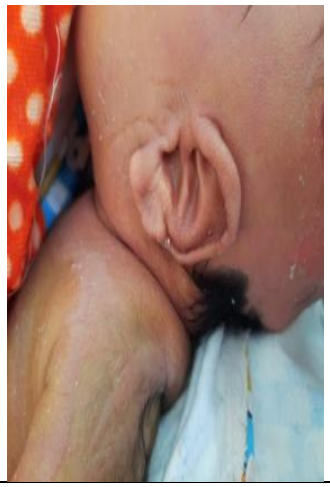

Figure C: Lesions along Blaschko's line seen

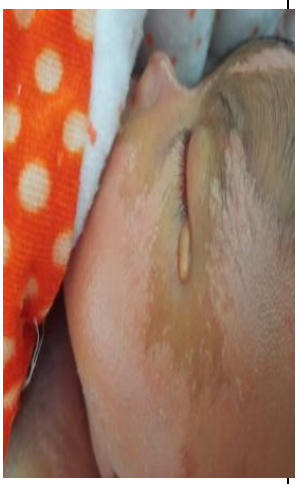

Figure D: Characteristic lesion on face

3. Discussion

Dermatological features are the most common presentation of IP, although can affect other organs. However, the clinical presentation of IP varies considerably, even among the affected family members of the same patient.[8]It can range from subtle cutaneous and dental involvement to a complex syndrome, sometimes deadly. The cutaneous lesions typically occur along the Blaschko's lines and evolve through four overlapping stages.[9,10]The first one is vesicobullous stage (stage1), which occurs during the first months of life and presents as recurrent crops of tense bullae in a linear pattern on the extremities mainly and aling Blashko's lines. Has been known to recur in childhood which may be associated with a febrile illness. The second stage is verrucous stage (stage 2) that occurs between 1 and 6 months of age, but can also occur in adolescence. Linear warty lesions are seen along the extremities. The third stage is the hyperpigmented stage (stage 3), which may be present from the outset of the diseaseor presents itself as the inflammatory stage of the disease starts resolving. Occurs mainly over the trunk and intertriginous areas from 3 months of age through adolescence. The fourth stage is the hypopigmented stage or atrophic stage that presents as atrophic, hypopigmented or depigmented bands or streaks, devoid of appendages that affect the calves. Occurs mainly in adolescents or adults[9,10].

There may be overlapping of stages and the onset and duration of each stage may varyamong individuals. In some, all the stages may not be seen. It has been observed that Stage 1 and 3 are more commonly than stage 2 and 4. Some of the affected child may show additional cutaneous manifestations such as palmoplantar hyperhidrosis, port wine stain, abnormalities of mammary tissue, hair abnormalities like alopecia, woolly hair and nails abnormalities like onychodystrophy, onychogryphosis, pitting, yellow discoloration, subungual and periungual keratotic tumours.[11,12]

Among the extracutaneous manifestations, dental abnormalities like delayed dentition, hypodontia, etc are the most commonly reported, occurring in more than 80% of all patients.[13,14]

Ocular defects occur in approximately one third of patients, which is characterized by retinal vascular abnormalities that can lead to visual loss during the first year of life. [9,10] Other ocular abnormalities that may be seen are strabismus, cataract, conjunctival pigmentosa uveitis, optic nerve atrophy, retinal vascular abnormalities, blue sclera, exudative chorioretinitis, retinal glioma.[15]

Neurological disorders, like seizures, spastic or paralytic quadriplegia, hemiparesis, cerebral atrophy, microcephaly and encephalopathy can be seen in about 25% of patients.[16,17] The incidence of mental retardation is about 25-35%.[4]

Musculoskeletal system can also be involved among other extracutaneous involvement. These include hemivertebra, hemiatrophy, syndactyly, congenital dislocation of the hip, club foot, dwarfism, scoliosis, supernumerary ribs. Cardiovascular involvement occurs in the form of atrial septal defects, acyanotic tetralogy of Fallot, ventricular endomyocardial fibrosis, tricuspid insufficiency, primary pulmonary hypertension.[18]

The diagnosis of incontinentia is mainly clinical, as there are no strict diagnostic criteria till date for IP. It is clinically diagnosed based on typical skin lesions and also the presence of dental, hair, nails and ocular, CNS involvement may support the diagnosis. Family history of X linked inheritance may also support the diagnosis.Lab

abnormalities of peripheral eosinophilia is a suggestive sign.[4]

Histopathological examination of the skin lesions and molecular genetic test (NEMO mutation) confirm the diagnosis.

4. Conclusion

Incontinentia Pigmenti is a multisystemic disease, so it is crucial to examine the patient with a multidisciplinary approach. Neurodevelopmental status should be monitored in all patients, and in case of any abnormalities, pediatric neurologist should be consulted. Dental abnormalities like delayed eruption, hypodontia, conical teeth can occur in 50-75% of patients.[19]Therfore, early dental intervention can help to minimize outcomes.

Paediatric ophthalmologist should be consulted and is crucial during the first year of life. For retinal vascular abnormalities, laser photocoagulation and vascular endothelial growth factor inhibitor appear to be good treatments.[20]

Regarding the dermatological part of management, it is mainly aimed at reducing the risk of infection. By prescribing antibiotics and adopting proper hygiene, risk of infection is reduced greatly. To decrease the rash, steroids can be prescribed. [21] In general, there is Spontaneous improvement and resolution of skin lesions. Laser therapies should be discouraged to treat the hyperpigmented lesions, as there are reports of an extensive vesicular-bullous eruption.[22]

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