Case Report :

1. Incontinentia Pigmenti

Yashank Yewale*, Pallavi Swami*, Vanshika Sharma*, Vikas Gupta Piyush Jain*****

* Junior resident, ** Sennior resident. *** Associate Professor Department of Paediatrics MGM Medical College hospital,Kamothe Navi Mumbai.
Corresponding Author: Dr Yashank Yewale Department of Paediatrics MGM Medical College Hospital, Kamothe Navi Mumbai,410209 Email: yashankyewale@gmail.com
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Abstract:

Incontinentia pigmenti (IP) is an X linked dominant genodermatosis that affects skin, eyes, CNS, teeth and skeletal system. Skin manifestations are most common and occur in four quite distinctive phases. Here, we present a female neonate with vesiculobullous lesions in the limbs and trunk which healed with hyperpigmentation. Skin biopsy revealed massive eosinophilia in the intraepidermal region. Also, eosinophil-filled intraepidermal vesicles were noted. The dermis showed spongiotic inflammation and infiltrates of lymphocytes in superficial dermis which confirmed the diagnosis of IP.

Keywords: *Incontinentia pigmenti, vesiculobullous lesion, Genodermatosis*.

Introduction:

Incontinentia pigmenti (IP), also known as Bloch-Sulzberger syndrome. This disorder was first reported by Dr. Bruno Bloch, a Swiss dermatologist in 1926 and Dr. Marion Sulzberger, an American dermatologist in 1928.It is a rare X-linked dominant, heritable genodermatosis. It is a multisystem, ectodermal and mesodermal disorder accompanied by dermatologic, neurologic, dental and ocular manifestations.1-4

Mutation of NEMO (NF-kappa-B essential modulator), also known as IKK-γ/IKBKG (inhibitor of nuclear factor kappa-B kinase subunit gamma) gene located on chromosome Xq28 is believed to play a role in the pathogenesis.5 NEMO/IKK-γ helps activate NF-κB, which controls the expression of multiple genes, including cytokines and chemokines, and protects cells against apoptosis.6-8

A lack of NEMO/IKK-γ therefore causes a lack of active NF-κB, which makes cells more prone to apoptosis. The paucity of affected males, the occurrence of female-to-female transmission, and an increased frequency of spontaneous abortions in carrier females (as seen in the reported case too) support this supposition. In this report, we describe a case of IP in a female infant with dermatologic lesions.

Case Report:

A full term (37.4 weeks) small for gestational age female baby was born to a G3 P1 L0 with two spontaneous abortions in the past 2 years. The delivery was via a caesarean section done in view of pregnancy induced hypertension and the baby weighing 2.245kg. The baby cried immediately after birth and did not have any significant birth or perinatal complications. (Photos on page No 69)

An HIV and VDRL test done in the mother was non-reactive. The mother aged 24yrs and failed to have any significant illnesses in the antenatal period. She did not have any skin, neurological or dental problems throughout her life till that point. It was noticed immediately after the delivery that the baby has skin lesions over both the upper and lower limbs and a few lesions over the chest. The baby was shifted to NICU. Basic laboratory investi-

gations sent. CBC, CRP and peripheral smear did not show abnormalities. Blood culture was sent showed no growth.

A dermatology reference was taken who were of the opinion that the skin lesions were suggestive of Incontinentia Pigmenti (IP)-Stage 1(vesicular stage). A skin biopsy was done for confirmation of the same. Histopathology showed massive eosinophilia in the intraepidermal region. Also, eosinophil-filled intraepidermal vesicles were noted. The dermis showed spongiotic inflammation and infiltrates of lymphocytes in superficial dermis which confirmed the diagnosis of IP.

Following this an ophthalmology reference was taken to rule to ocular manifestations of IP. After opinion of Pediatric Neurologist, MRI brain was done to rule out CNS manifestations of IP if any. Ocular examination as well as the MRI brain was normal. A dental examination was done which showed no abnormalities. The patient was started on fusidic acid cream and tacrolimusoinments as advised by the dermatologists.

As the baby did not have any other symptoms or signs pertaining to IP and its complications or otherwise, she was discharged after 5 days from the hospital and asked to regularly follow-up to watch for the complications of IP.

Discussion:

Incontinentia pigmenti(IP) is inherited in an X-linked dominant manner. Therefore, more than 95% of the patients are female infants.9 In males, it is usually lethal and most of the affected male fetuses result in miscarriage or stillbirth.4 Rarely affected surviving males are attributed to the presence of an extra X chromosome (eg. Klinefelter's syndrome/XXY syndrome) or as a result of a mutation in some of the body's cells (somatic mosaicism) with relatively mild effects.10In our case, although there was no information on the fetus's sex, the history of miscarriages might be a result of IP. IP is hereditary in 10%-25% of cases.11

Dermatologic findings are often the first observed sign of IP and are present in nearly all patients.7In most cases, the onset of skin changes is before 6 weeks of age as seen in this case too.4 Progressive cutaneous manifestations are the main clinical feature of the disease and classically evolve through 4 stages. However, their sequence is irregular and some of them may overlap with others or not appear at all. Stage 1 (vesicular stage) is presented at birth or within the first 2 weeks in 90% of patients and is characterized by a rash of erythematous blisters, which often appear to be grouped along the lines of Blaschko. Biopsy characteristically exhibits spongiotic dermatitis with massive intraepidermal and intradermal eosinophilia.7

Stage 2 (verrucous stage) occurs in about 70% of patients. Eruption of hyper keratotic-verrucous papules and plaques develops over the healing blisters. It usually appears within 2 months and disappears within 6 months. Hyperkeratosis, dyskeratosis, acanthosis and papillomatosis are present in this stage.11, 12

Stage 3 (hyperpigmented stage) is classically the hallmark of IP. Nearly 98% of patients experience stage 3. Pigmentation ranges from blue-grey or slate to brown, and occurs in streaks or whorls. It generally develops within the first few months of life and tends to fade by adolescence. Melanophages in the dermis and vacuolization of basal cells is the most common finding.4, 13

Stage 4 (atrophic/hypopigmented stage) occurs in adolescence and persists into adulthood. Pale, hairless patches or streaks, sometimes scar-like lesions are mostly found on lower legs. Such changes are mostly permanent and often the only sign of skin involvement in adult patients. It presents as atrophy and thinning of the epidermis with the absence of skin appendages.4, 14-16

The vesicular stage is most often observed at birth or within the first two weeks of life in IP, which coincides with our case. The patient presented with stage 1 at birth. Cutaneous lesions

may also be accompanied by defects of cutaneous appendages in the form of vertex alopecia, ridged, pitted, or dystrophic nails.17 (Refered to image section)

Extracutaneous manifestations occur in various ways in about 70%-80% of IP patients. Dental abnormalities are the most common types and affect more than 80% of patients with delayed dentition, partial anodontia, cone or peg shaped teeth or absence of teeth. Some 30%-50% of patients exhibit neurologic deficiency, identified as seizures, mental retardation, developmental delays, spastic paralysis, ataxia and motor dysfunction.18-20 Ocular abnormalities are also observed in around 30% of patients including strabismus, cataracts, optic atrophy, retinal dysfunction, uveitis, nystagmus and blindness. Skeletal and structural anomalies have occasionally been reported as well, such as somatic asymmetry, skull deformities, spina bifida, dwarfism, syndactyly, extra ribs, primary pulmonary hypertension, and cardiopulmonary failure.

Keratotictumors in late adolescence may involute spontaneously. Several cases of IP have been associated with cancer in childhood.21,22In our case, skin lesions was the first manifestation of the disease but no other signs were present. Anomalies may not appear at the initial evaluation but may appear later on. Therefore, longterm follow-up with dermatology, paediatrics, neurology, ophthalmology and dentistry is crucial.

Archan Sil 23et al also reported a similar case and concluded that IP is a very rare genodermatosis, so it is difficult (important) to exclude other more common causes. But one should be aware of the typical manifestation to diagnose it early and help patient's family to convey information regarding subsequent course of the disease and thus ensuring regular follow up at later age.

Conclusion:

The diagnosis relies mostly on the characteristic skin lesions and other clinical findings. Therefore, timely recognition of IP by pediatricians and dermatologists is crucial. Skin biopsy and molecular genetic testing of the NEMO gene may help confirm the disease. Although skin lesions are the most common manifestations and one of the most important aspects of the diagnosis, they are actually less damaging to the patients and tend to heal spontaneously. The management of systemic abnormalities is based on sympto-matology. Support and corrective treatment should be used whenever and wherever needed. Family history or a history of multiple miscarriages also supports the diagnosis of IP as seen in this case.

Contribution: PJ- Revising manuscript, VG-Checking Reports, histopathology, YY-Collection & analysis of literature,writing manuscript, PS,VS-Manageing case, counseling and follow up ,

concept of study,

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Neonate with vesiculobullous lesions in the limbs and trunk which healed with hyperpigmentation should raise suspicion of IP.

Skin biopsy revealed massive eosinophilia in the intraepidermal region, spongiotic inflammation and infiltrates of lymphocytes in superficial dermis which confirmed the diagnosis of IP.