A CASE REPORT OF INCONTINENTIA PIGMENTI

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Abstract

Objective

Incontinentia Pigmenti (IP) (Bloch_Sulzberg syndrome) is a rare neurocutaneous syndrome characterized by multisystemic involvement that is prenatally lethal in the majority of affected males and shows great clinical variability when expressed in women. The diagnosis of IP is performed based on clinical features and the family history with the support of histological findings.

We report a 10-day-old female neonate with typical skin lesions and frequent seizure. Skin biopsy showed second stage IP.

Keywords: Incontinentia Pigmenti, Neonatal seizure, female neonate.

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Introduction

Incontinentia pigmenti (IP) is an X-linked neurocutaneous syndrome with neurologic, ophthalmologic and dental manifestations. Garrod reported the first probable case and described it as a peculiar pigmentation of skin in an infant (1).

His patient was a 2-year-old mentally retarded spastic diplegic girl who had a whorled pattern of brown skin pigmentation on her trunk and limbs (1,2)

Subsequently, Bloch and Sulzberger reported the condition in 1926 and 1928 as a clinical syndrome with constellation of features including typical cutaneous manifestation (1).

The disorder is a rare X-linked dominant genodermatosis (3,4,5,6).

Up until 1987, only 700 cases were reported in the literature (1).

Carney (1976) found 653 cases in the literature (593 females, 16 males and 44 of unspecified sex) (7).

IP has a worldwide distribution and appears to be more common among Caucasians (3).

IP is an X-linked dominant male lethal syndrome. More than 95% of the reported cases are females, the few male being probably the result of spontaneous mutations and mosaicism of the X chromosome (8).

IP is caused by mutations in the NEMO/IKK-gamma gene (1,2,3,4,5).

The skin changes are often present at birth, usually develop before the end of the first week and rarely appear after the first two months. Three clinical stages are recognized:

1) Bullae 2) Papular and warty lesions 3) Pigmentation (8)

In over half of the reported cases, organs other than skin have also been involved. Dental defects are frequent (8), up to 80%, and persist throughout the life (6).

Ocular defects are found in 30% of the cases. Many patients may become blind (7) but more than 90% have normal vision (6).

CNS manifestations occur in about 25% of the cases (8) and include mental retardation, slow motor development, spastic tetraplegia and diplegia, microcephaly and epilepsy (1). Microcephaly and hydrocephaly have been also reported (2). Skeletal abnormalities are less common and usually minor (8).

The diagnosis of IP is made based on clinical features and family the history with the support of histological findings (5).

Usually, no treatment is necessary other than the control of secondary infection. Family counseling should be offered (1,8).

Case report

A 10- day-old female neonate was admitted to the emergency ward of Ekbatan Hospital, Hamedan, because of skin lesions (Figure 1).

The skin lesions were erythematous linear streaks on the legs and trunk which appeared from three days before visiting. There were no more findings on physical examination. She was the first child and her parents were not consanguine. There were no similar cases in her family. On examination, the first episode of seizure occurred. She was admitted to the NICU and diagnostic evaluations and anti- convulsive therapy started. The most important laboratory finding was eosinophilia. Seizure occurred frequently in spite of treatment with Phenobarbital; therefore, phenytoin was added to the regimen.

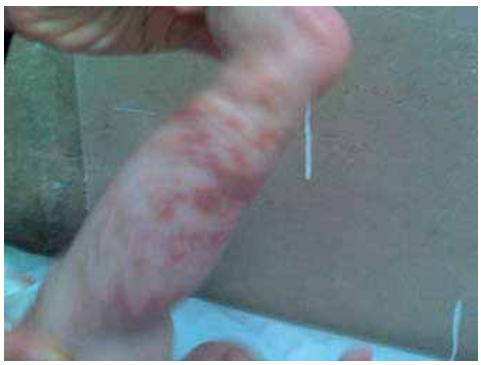

Figure 1. Erythematus lesions (on admission)

According to typical skin lesions and seizure, the diagnosis of IP was considered. Consultation with a dermatologist supported the diagnosis. Brain CT scan and ophthalmologic examinations were normal. EEG had a mild abnormal pattern. Finally, the patient was discharged with Phenobarbital. Skin biopsy was performed by a dermatologist after one month and was reported to be consistent with the second stage of Incontinentia Pigmenti. She was visited monthly for six months. Her skin lesions changed to warty lesions (figure 2) and then to hyperpigmented lesions (figure 3)

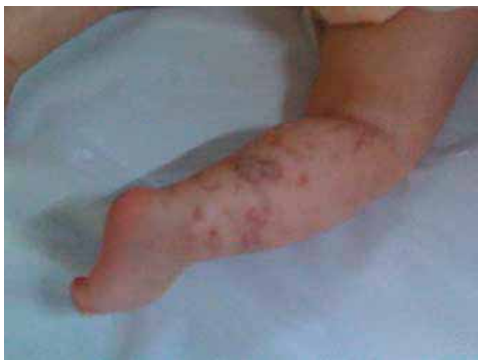

Figure 2. warty lesions (at one month of age)

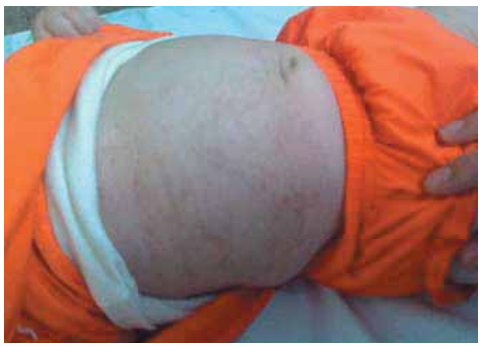

Figure 3. Hyperpigmented lesions (at six month of age)

The neurologic development was good until 6 months of age.

Discussion

Incontinentia pigmenti (IP) is one of the group of gene-linked diseases known as neurocutaneous disorders. This rare hereditary multisystem ectodermal disorder features dermatologic, dental and ocular abnormalities (6).

We report this case to emphasize that in neonates with seizure and skin lesions, this diagnosis should be

considered although it is a rare syndrome.

Most pedigrees are small, but from the accumulated genetic data it appears that this syndrome is due to an X-linked dominate trait that is usually lethal in males.

More than 95% of the reported cases are females (8). Our case was a female, too.

Familial IP is caused by mutations in the NEMO gene and is referred to as IP2 or classical IP. Sporadic IP, the so called IP1, which maps to XP11, is categorized as hypomelanosis of Ito (7).

Histologically, the deposits of melanin pigment are seen in the corium. The designation was based on the idea that the basal layer of the epidermis is incontinent of melanin (7,9).

IP is divided into 4 stages, which frequently overlap or appear together. During the first stage, which is between birth and 6 months of age, there is inflammation accompanied by skin redness and spiral lines of small fluid-filled blisters.

The second stage gradually develops with rough warty skin growths which appear on the arms or legs and sometimes on the head or trunk. These growths, which are often arranged in the same spiral or linear pattern as in the first stage, usually resolve during infancy or early childhood. The third stage begins between 3 months and 3 years of age and is characterized by discoloration appearing in unusual patterns. The third stage is the hallmark of IP. The fourth stage consists of diminished pigmentation or atrophy in areas of previous discoloration (1,2,3,4,5,6,7). The skin changes are often present at birth, usually develop before the end of the first week and rarely appear after the first two months (7).

Our patient was a 10-day-old girl with erythematous skin lesions from 3-4 days before admission.

The pigmentation, ranging in color from blue-gray to slate brown, is characteristic of the syndrome and its bizarre splashed linear or Chinese figure and its distribution are diagnostic (8).

We referred the patient to a dermatologist and skin biopsy from the lesion was done. The result was reported as the second stage of Incontinentia Pigmenti.

Peripheral eosinophilia, up to 50%, is usual when acute inflammatory skin changes are present. There is evidence of both neutrophil and lymphocyte dysfunction, and altered immunological reactivity is observed in some patients (8).

In the first CBC of our patient, eosinophilia (12%) was detected.

Involvement of other organs in over half of the reported cases are seen including dental and ocular defects, and CNS and skeletal abnormalities (1,2,3,5,6,7,8).

Neurologic complications occur in up to 30% of the patients (10). Seizure are the most common neurologic complication (1,8). MRI discloses a variety of abnormalities. These include hypoplasia of the corpous callosum, neuronal heterotopias and small or large vessel occlusion (10).

Our patient had refractory seizures that were finally controlled with phenobarbital and phenytoin. Neurologic complications may result in part from vaso-occlusive ischemic events (1). Other neuro-developmental manifestations include neurodevelopmental delay, spastic paralysis, microcephaly, and cerebral edema (1,7).

The brain CT scan of our patient was normal and development up to 6 month of life was also intact. Skin lesions were hyperpigmented at 6 months of age (Figure 3). Ophthalmologic examination was normal. No treatment is usually necessary other than the control of secondary infection (2,7,8,11). Systemic therapy with corticosteroid or sulfapyridine is usually unsuccessful (7).

Morbidity and mortality are related to neurologic and ophthalmologic sequelae (1).

The prognosis of IP is generally good (1).

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