wjpmr, 2018,4(4), 203 -205

SJIF Impact Factor: 4.639

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Case Report

ISSN 2455-3301

WJPMR

GENERALIZED MOTTLED PIGMENTATION WITH POSTNATAL SKIN BLISTERING IN THIRTY-FOUR PATIENTS

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Article Received on 11/02/2018 **Article Revised on 04/03/2018** **Article Accepted on 25/03/2018**

ABSTRACT

We describe thirty-four patients presented with a pigmentary disorder consisted of two phases, the first one expressed as a vesicular eruption, which appeared at birth mostly on the distal extremities and continued to have them at the site of trauma till age of 10 years when they disappeared completely, the second phase was mottled pigmentation of the skin which consisted of asymptomatic hyperpigmented and hypopigmented macules mainly on the trunk and the proximal extremities with relatively sparing of the sun-exposed skin. We think that molecular biological investigations would be required to characterized the phenotype of this disorder.

KEYWORDS: Blistering, Genetic diseases, Mottled pigmentation.

INTRODUCTION

In 1922, Siemens described a patient with diffuse mottled hypopigmentation and hyperpigmentation on the whole body, during a couple of weeks after birth, blisters developed on the wrists and ankles, but they disappeared and never returned later in life, on the dorsum of the hands and feet, warty hyperkeratosis were present, whereas the palms and soles showed diffuse callus formation and fissures. In 2004, Westerhof and Dingemans, described the same presentation in a family in three generations which presented with blisters on the distal extremities at birth associated with progressive mottled hypopigmentation and hyperpigmentation on the non-exposed parts of the body .[1] Now we mention thirty-four patients with symptoms that are very similar to those described by Siemens, Westerhof and Dingemans and also it resembles clinical features of epidermolysis bullosa simplex with mottled pigmentation [EBS-MP].

CASE REPORT

Thirty-four patients, nineteen females and fifteen males presented with generalized mottled pigmentation with or with history of postnatal blistering of the skin were studied in Al-Ramadi Teaching Hospital within four years period after obtaining a clearance from the institutional ethics committee and an informed consent was taken from all patients, their ages ranged from 7 months -56 years old with a mean age 21.3 years, their ages of onset ranged from birth to 6 years with a mean age of onset was 1.5 years with a female to male ratio was 1.2:1. From analysis of the family pedigrees, the inheritance was most probably autosomal recessive (AR) in about 51.5%, autosomal dominant (AD) about 42.4% while sporadic cases were 6%, consanguinity of patient's parents was found to be 91.2%.

Regarding the cutaneous manifestations of the patients, they consisted of two phases, the first one was the vesicular rash in which the vesicles were flaccid, easily ruptured and appeared at the extensor surfaces of the extremities in 82.3% on the sites subjected to trauma while they were generalized in 17.7% of patients, most patients had blisters at birth and continued to have them at the site of trauma till age of 10 years when they disappeared completely "Fig 1".

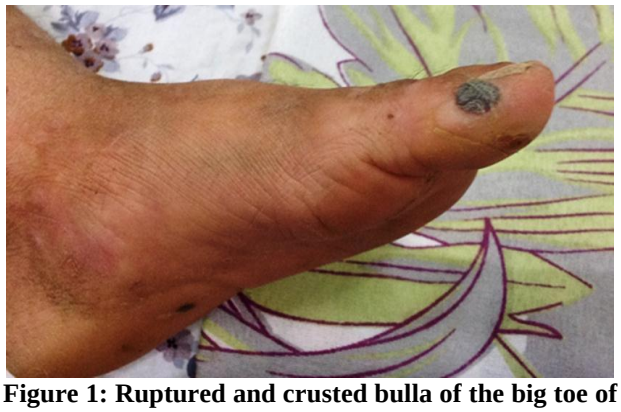
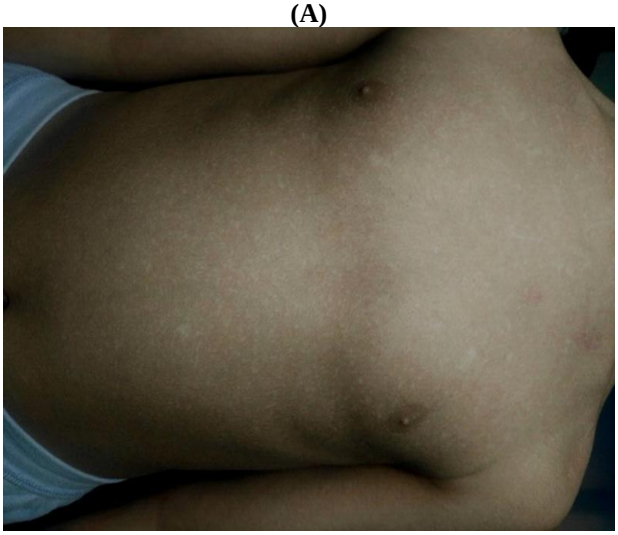


Figure 1: Ruptured and crusted bulla of the big toe of one affected patient.

The second phase of the disease was the mottled pigmentation of the skin which consisted of hyperpigmented and hypopigmented macules mainly on the trunk and the proximal extremities with relatively sparing of the sun-exposed skin in about 85.29%. “Fig 2”

(A)



(B)

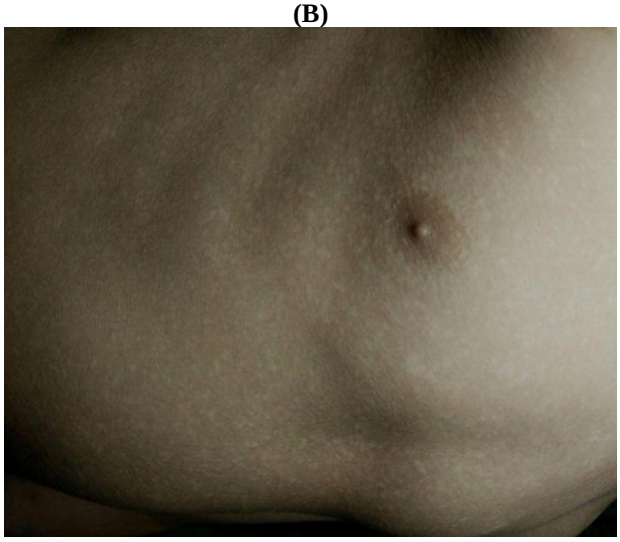
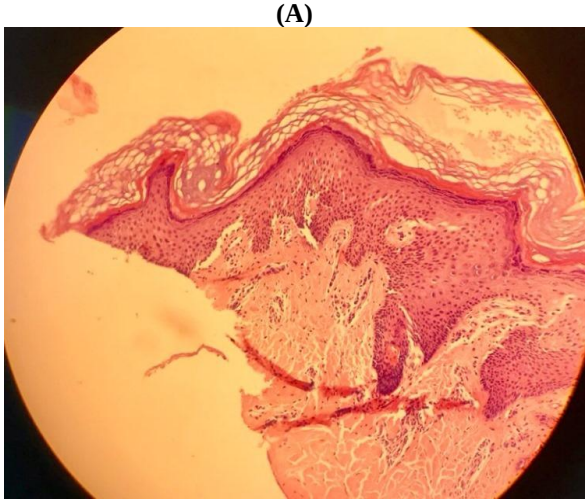


Figure 2: (A) Six years old male with mottled pigmentation of the skin, (B) Close up view of the patient.

The pigmentation appeared at age ranged from birth to 10 years with a mean age of onset was 1.6 years and it was not related to blisters formation, the pigmentation was stationary in 85.2%. Histopathological examination of a biopsy specimen from an intact blister demonstrated in “Fig3”, and of the hyperpigmented macules in “Fig 4”.

(A)



(B)

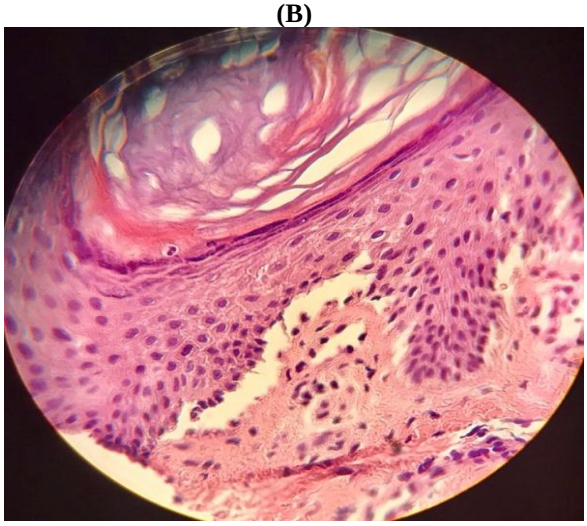
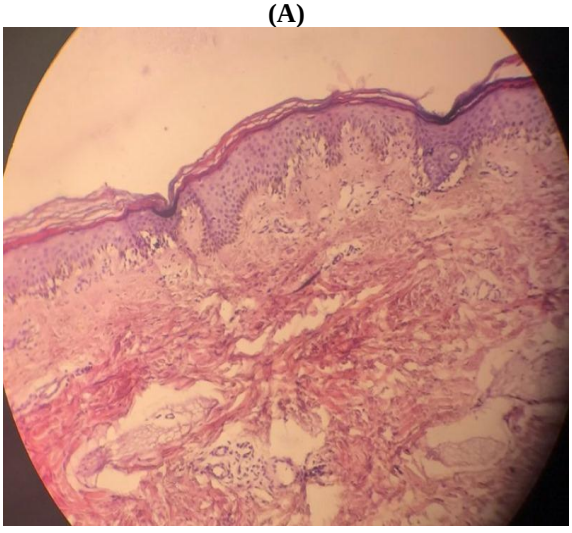


Figure 3: [A (X10) and B(X40)]: Specimen stained with Hematoxylen and Eosin (H/E) stain demonstrates intact stratum corneum and upper epidermis, with vesicle formation in the lower epidermis at the basal layer caused by degeneration of basal epidermal cells.

(A)



(B)

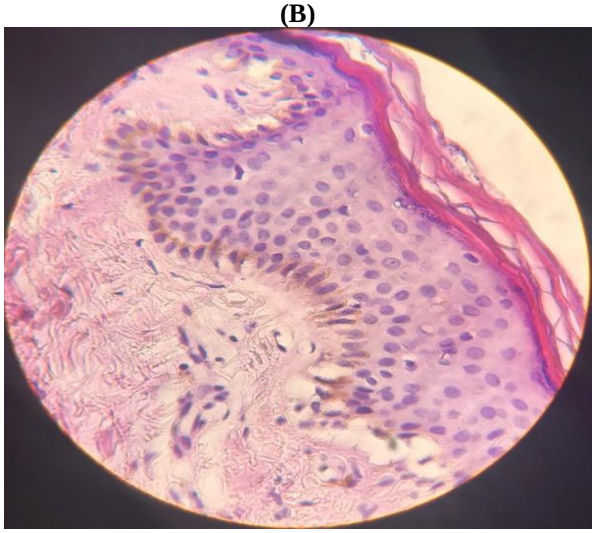


Figure 4 [A (X10) and B (X40)]: Histopathological examination of a skin of patient with mottled pigmentation stained with (H/E) stain demonstrates focal increased melanin pigment in the basal keratinocytes.

There was no pruritus, photosensitivity or photophobia, nails was affected in one patient and there was hyperkeratosis of the palms and soles in two patients. Hair, teeth and mucus membranes were not affected and no systemic involvement.

DISCUSSION

We have described a pigmentary disorder occurring in thirty-four patients characterized by mottled pigmentation of the skin associated with an episode of postnatal blistering, there are many genetic diseases has such manifestations, these may include dyschromatosis universalis hereditaria, amyloidosis cutis dyschromica ,dyskeratosis congenita and westerhof syndrome, all these can be ruled out because they have no episode of blistering.[2,3] Other vesicular diseases such as incontinentia pigmenti, characterized by pigmentation on the trunk preceded by vesicular and verrucous changes, the pigmentation follows the lines of Blaschko.[4]

Kindler syndrome is an (AR) disease characterized by acral skin blistering, photosensitivity and progressive poikiloderma, but without mottled pigmentation.[5] EBS-MP is an AD genodermatosis which distinguished from Other forms of epidermolysis bullosa simplex by the associated pigmentary changes .[1,6,7,8,9] In the evaluated patients, the inheritance was most probably AR, this may be related to increased rate of marriage among close relatives and this in contrast to EBS-MP which is inherited mostly as AD.[1,6,7,10,11] Most of patients developed blistering at birth and continue to have them till age of ten years when they disappeared completely but the blisters in EBS-MP decrease with age,[1,2,12] and this may be due to clinical heterogeneity.

The second phase of the disease, the mottled pigmentation of the skin, closely resembles that of EBS-MP.[7,12] which could be due to the presence of disease-causing mutation, P25L, of the keratin 5 gene, which has been suggested to play a role in melanosome transport, leading to abnormal pigmentation in EBS-MP.[5,6]

So the clinical presentation of the patients is similar to that of EBS-MP but with milder clinical features which could be due to low penetrance of the gene affected. In conclusion, generalized mottled pigmentation with postnatal blistering of the skin appears to be not rare disease and to reach an accurate diagnosis, molecular biological studies would be required to characterized the phenotype of this disorder.

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