Case Report

A Rare Case Report of Garcia Hafner Happle Syndrome

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Abstract

Garcia Hafner Happle Syndrome is a rare type of epidermal nevus syndrome. It is caused by mutations to the fibroblast growth factor receptor 3 (FGFR) gene and is also called FGFR3 epidermal nevus syndrome. It is clinically characterized by keratinocytic epidermal naevii with cerebral and skeletal involvement.

Keywords:Garcia Hafner Happle Syndrome,disorder

Introduction

Garcia-Hafner-Happle syndrome, was identified by Garcı'a-Vargas et al in 2008. The disorder is caused by a mosaic R248C mutation of the FGFR3 gene. It is a rare subtype of epidermal nevus syndrome (ENS). This form of ENS is characterized by keratinocytic epidermal nevus along with neurological abnormalities like seizures, intellectual impairment, cortical atrophy and underdevelopment of corpus callosum[1]. ENS is a rare neurocutaneous syndrome presenting as epidermal nevus along with symptoms of any other system of body like neurological, cardiovascular or skeletal[2]. Here we present the case of a seven year old boy with rare diagnosis of Garcia-Hafner-Happle syndrome.

Case History

A seven year old boy presented with history of seizures for one year. It was focal seizures with secondary generalization with semiology consisting of transient giddiness followed by vacant blank stare, loss of contact with surrounding, associated with deviation of eyes to the left side and tonic clonic movements in left upper and lower limbs. This was followed by loss of consciousness for 3-4 minutes and then amnesia about the event.

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He had three such episodes of focal dyscognitive seizures with secondary generalization prior to visiting the OPD.

He had multiple hyperpigmented hyperkeratotic verrucous plaques over face, arms, neck, abdomen, legs and back as shown in figure 1, 2 and 3, since birth. These were distributed in a blaschkoid pattern over the left segment. He also had acanthosis nigricans over the nape of neck. These lesions were progressive in nature and had become more pigmented and hyperkeratotic over the last 3-4 years. Lesions were not preceded by blistering or inflammatory changes.

Dilated veins were noticed on right side of the lower limb and hallus varrus noticed bilaterally. Hypertrophy of left side of the body along with segmental macroglossia was also present.

He was born out of non-consanguineous marriage with normal vaginal delivery, no perinatal insult and normal developmental milestones. There was no history of any endocrinal, dermatological or systemic disorders in any of the family members. He had normal skeletal and mental development appropriate to his age. His systemic examination was normal. He was not hirsute or obese, had no hair or nail abnormality. His echocardiography and ultrasonography of abdomen were normal. Electroencephalography revealed focal right temporal sharp and slow wave discharges and MRI of brain was not completed as patient was uncooperative. All other routine blood investigations were normal

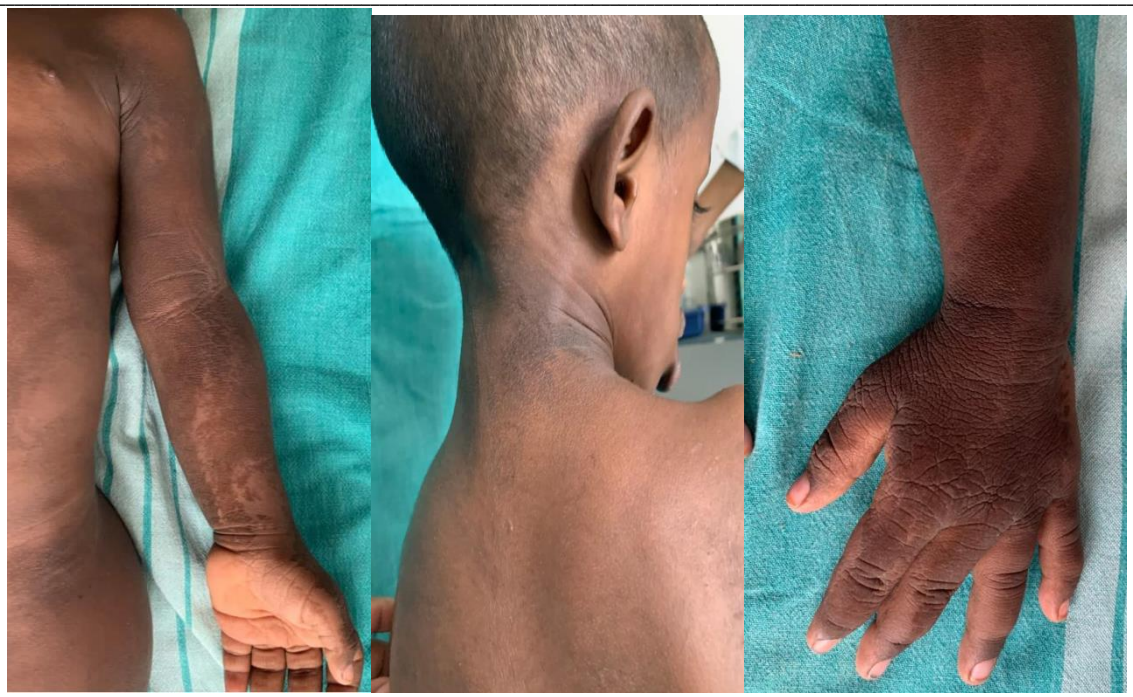

Fig 1,2,3 : multiple hyperpigmented hyperkeratotic verrucous plaques over arms, neck, hands

Discussion

Epidermal nevii are organoid nevii arising from the basal layer of embryonic epidermis. These are overgrowths of structures and tissue of the epidermis of skin. The original description of "epidermal nevus syndrome"(ENS) given by Solomon et al in 1968 included a epidermal nevii with systemic findings. ENS is a neurocutaneous disorder with an incidence of 1 in 1000 live births without gender or ethnic predominance[3].ENS has been classified, on the basis of type of epidermal nevus, histopathologic findings, presence or absence of heritability and on the basis of well-defined common associations of a particular type. Recently, 9 well-defined and 7 less well-defined subtypes of ENS, each with specific clinical phenotype has been described. It has been proposed that one of the factor responsible for the pathogenesis of this syndrome is the occurrence of gene mosaicism in which an autosomal dominant lethal gene survives by mosaicism[4].

Garcia Hafner Happle Syndrome is caused by a mosaic R248C mutation of the FGFR3 gene[5]. In Garcia Hafner Happle Syndrome, patient presents with soft velvety keratinocytic epidermal nevus along with manifestations of central nervous system (CNS). Around 50% of patients of ENS show CNS manifestations and with involvement increases upto 66% in case of keratinocytic nevus syndrome[6]. Nevus lesions involving the face or scalp are usually associated with seizures, cognitive defects and mental retardation[7].

Skeletal, ophthalmologic, cardiovascular and nephrologic abnormalities are also associated with various types of ENS. Our patient had multiple hyperpigmented hyperkeratotic verrucous plaques distributed in a blaschkoid pattern and also acanthosis nigricans. He had CNS involvement in the form of focal seizures. The differential diagnosis include other ENS like Proteus syndrome, type 2 segmental Cowden disease, CHILD syndrome and Fibroblast growth factor receptor 3 ENS i.e. Garcıa-Hafner-Happle syndrome[8]. Treatment of ENS involves ablative CO2 laser and surgery. Topical therapies like retinoids, intralesional steroids, 5-fluorouracil are being tried. CNS manifestations and can be treated by antiepileptic therapy.

Conclusion

Extensive literature and good treatment modalities along with strong clinical and histopathological evidences are needed for more detailed study of Epidermal nevi syndrome and its various types for the benefit of the patients.

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