Case Report

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Hemihypertorphy and Cardiomegaly as Uncommon Findings Associated with Proteus Syndrome

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Abstract

A case of Proteus syndrome in a 10 year old male is reported. Asymmetric progressive enlargement started on left side of face, trunk, left hand and left leg as he grew up, hypertrophied left eyelid, cataract changes in left eye, missing teeth on left maxilla and extra teeth on left mandible, depressed chest and red patches on left side of chest. Cardiomegaly, delayed milestones, slowed scholastic performance, sluggish speech were present. There are only few reports of such cases in adults are reported in medical journals and this syndrome has rarely reported from India.

Key Words: Hemihypertorphy, Proteus syndrome, Disproportionate and asymmetric overgrowth, diagnostic criteria; misdiagnosis; evaluation and management.

Introduction

Proteus syndrome, also known as Wiedemann syndrome (named after the German paediatrician Hans-Rudolf Wiedemann), is a congenital disorder [1] that causes skin overgrowth and atypical bone development, often accompanied by tumors over half the body [2]. Proteus syndrome is highly variable [3]. It is a congenital complex disorder consisting of asymmetric overgrowth of skin, bones, muscles, fatty tissue, blood and lymphatic vessels which resulted change the shape. This condition is first described in the American Medical Literature by Dr. Samia Temtamy and Dr. Jhon Rogers in 1976 [4, 5]. Dr. Michael Cohen described it in 1979 [6].

The occurrence of Proteus syndrome is sporadic and till now very few cases were reported worldwide. Only few cases (about 200 cases) have been confirmed worldwide, with estimates that about 120 people are currently alive with the condition [7].

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In this case report, we report a case of Proteus syndrome of 10 year old male from Nanded district of Maharashtra. As attenuated forms of the disease may exist, there could be many people with Proteus syndrome who remain undiagnosed. Those most readily diagnosed are also the most severely disfigured.

Case Report

A 10 year old male, born full term following a normal delivery to no consanguineous parents was noticed to have asymmetric enlargements of the face, depressed chest and red patches on left side of chest (Fig 1).

Mother had no congenital anomalies. Father had neurofibromatosis since last 25 years. The other siblings are normal. The patient was thin built with 115 cm in height. There was progressive asymmetric enlargement, started on left side of face, trunk, left hand and left leg as he grew up.

His developmental milestones were delayed and scholastic performance was also slow. Patient while standing on both legs leans forwards. His speech was sluggish and not clears due to overgrowth of the tongue. Left palpebral conjunctiva showed a hypertrophied red mass (Fig 2). Left eye

showed cataract changes. Teeth were missing on the left side of the maxilla and extra teeth were seen on the left side of the mandible (Fig-3). Central part of the chest shows depression. Chest X-ray shows cardiomegaly (Fig-4).

Fig 1: Showing hypertrophy on left side with depressed chest

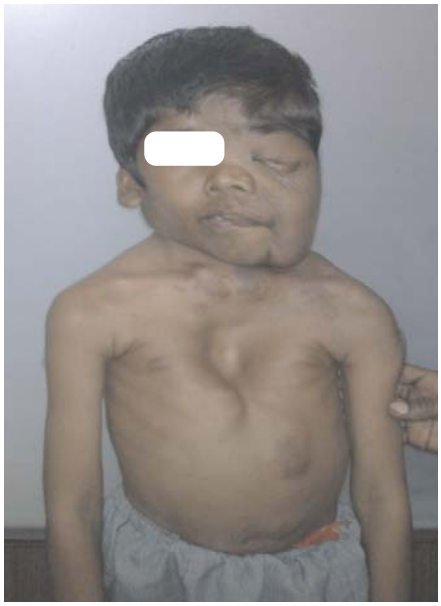


Fig 2: Showing hypertrophied left eyelid

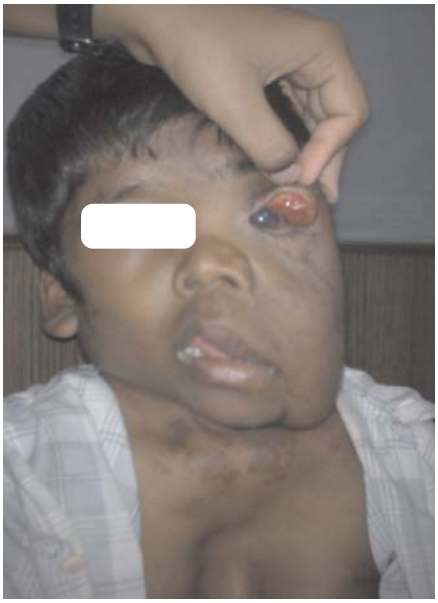


Fig 3: Showing missing left maxillary teeth

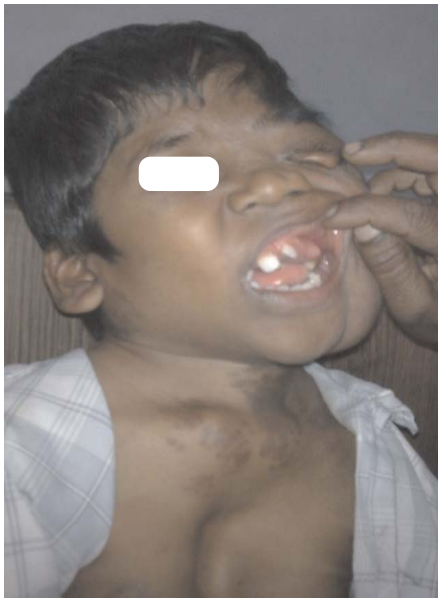
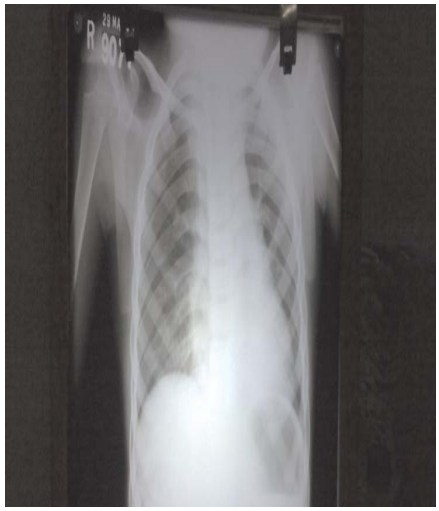


Fig 4: PA View of chest x-ray Showing Cardiomegaly



Discussion

Proteus syndrome is a complex disorder with multisystem involvement and great clinical variability. It is a rare condition which can be categorized as a harmartomatous disorder. This condition is characterized by various cutaneous and subcutaneous lesions including vascular malformations, lipomas, hyperpigmentation and several types of naevi. As lesions appear over time due to which diagnosis may be delayed in late infancy or childhood. Orthopaedic complications often

pose the most challenging medical problems, although vascular complications also contribute to overall morbidity. Severe disfigurement and social stigmatization are additional challenges that must be addressed. It is a hamartomatous disorder described by Wiedemann et al 1983 [1]. Since then about 50 cases have been reported in World literature, only 4 being in adults [2]. The typical clinical features include progressive and asymmetric megalodactyly, hemihypertrophy, subcutaneous masses, and localized cerebroid thickening of the palms and soles and linear skin lesions.

Proteus syndrome is a progressive condition wherein children are born without any deformities, but tumours, skin and bone growths appear as the age advances. A team of doctors in Australia has trial tested the drug Rapamycin in the treatment of a patient said to have Proteus syndrome and have found it to be an effective remedy [8].

Molecular basis

Genetic Relation

Researchers determined the cause of Proteus syndrome. In 26 of 29 patients who met strict clinical criteria for the disorder Lindhurst *et al.* identified an activating mutation in the AKT1 kinase in a mosaic state gene [9]. A mosaic gene alteration is a change in the genetic code that is present in some of the body's cells but not others. This mutation was not present in more than 1,000 persons who were unaffected by this disorder. Previous research had suggested the condition linked to PTEN to chromosome 10, [10] while other research pointed to chromosome 16 [11]. Prior to the determination of the cause of the disease in, other researchers expressed doubt regarding the involvement of PTEN or GPC3 [12].

Embryological Relation

The post zygotic event that results clinical manifestations is embryonic somatic recombination leading to at least three subsets of cells. These subsets include normal, overgrowth (Pleioproteus), and atrophy (Elattoproteus) cells. The discordance for Proteus syndrome is monozygotic twins suggest that the condition arises postzygotically [13]. Bony overgrowth in Proteus syndrome is secondary to mesenchymal changes during embryonic life with formation of extra large cartilage precursors.

Associated Anomalies

Hemi hyperplasia and soft tissue overgrowth are the more significant medical complications. Lesions are identified at birth in more than 17% of cases. Soft tissue and bone overgrowth may slow after puberty. Facial involvement may be associated with not only asymmetric mandibular growth, maxillary growth but also with premature dental eruption and idiopathic root resorption. Eye findings may include strabismus, epibalbar dermoids and cysts. Ocular findings are seen in 40% of cases [14]. Scoliosis or kyphoscoliosis may be severe and progressive, leading to respiratory compromise in some cases. Neck and trunk elongation with upper body wasting and leg muscle hypertrophy may contribute to abnormal body habitus and functional abnormalities. Kidney or bladder involvement is in 10% of cases in which hydronephrosis, renal cysts, asymmetry of kidney or bladder is seen. Cutaneous and subcutaneous lesions create cosmetic and functional problems. Benign growths such as lipomas, connective tissue nevi, epidermal nevi and vascular malformations are locally invasive and contribute greatly. Cystic lung malformations are seen in 10% of cases and are common in a young female patient. Either deep vein thrombosis or pulmonary embolism contributes to morbidity and mortality even in children's. Learning disabilities or mental retardation occurs in facial phenotype patients with or without CNS malformations and seizures [14].

Conclusion

The present case report showing the Proteus syndrome, aims at highlighting the uncertain anatomy and possible genetic and embryological explanation of this rare syndrome. Depressed chest is one of the rare signs associated with this case.

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