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Proteus Syndrome

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Abstract This rare sporadic disease is named after the Greek god Proteus who could change shape. The syndrome has protean manifestations that include partial gigantism of the hands and feet, cerebriform plantar hyperplasia, hemangiomas, lipomas, lipohypoplasia, linear verrucous epidermal nevi, patchy dermal hypoplasia, macrocephaly, hyperostosis, muscular hypoplasia, and hypertrophy of the long bones.

Keywords: *dermatology, proteus syndrome*

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1. Case Report

Seven years old boy, he was the third child in his family, his parents are not relative and his brother and sister are both normal. As shown in the pictures below; There is disproportion of body length and in fingers growth (photo 1a, b), epidermal nevus on the dorsum hand as yellowish soft linear plaque (photo 2).

Photo1a

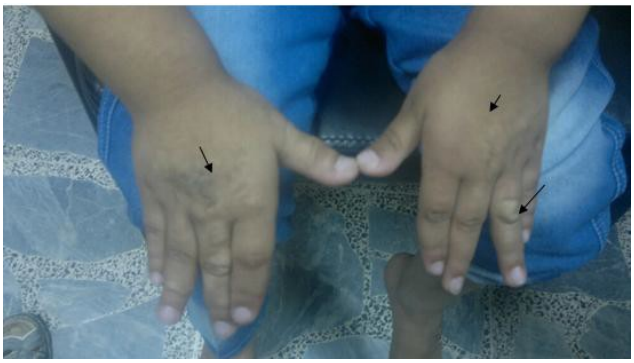

Photo1b.

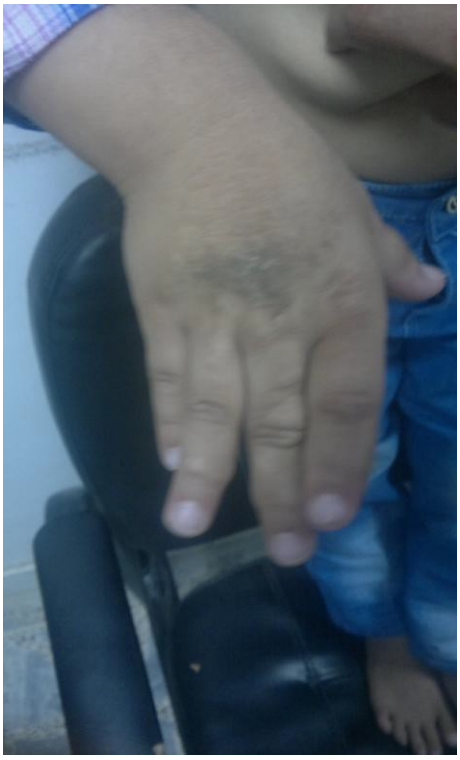

Photo 2a

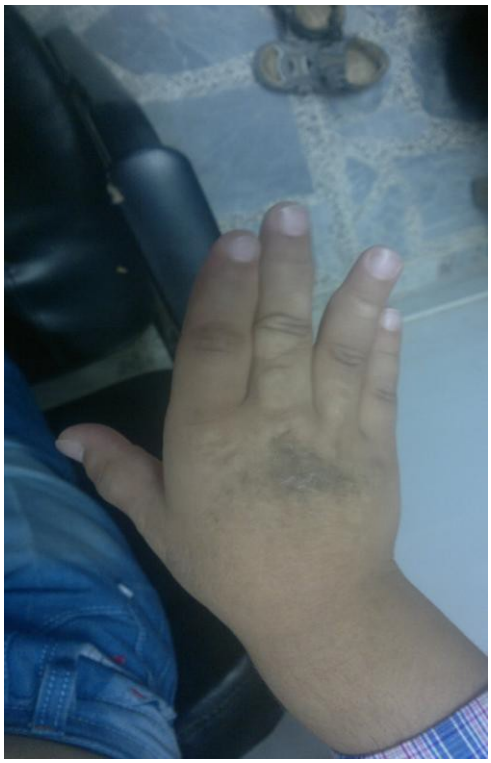

Photo 2b

Two soft tissue swellings on his anterior abdominal wall and lower anterior chest wall 10x10cm and 5x6 cm, imaging study for those soft tissue swelling revealed fatty tissue suggesting lipoma (photo 3). Left leg shows vascular abnormalities (tortuous veins) along the lateral aspect extended up word to the thigh (photo 4).

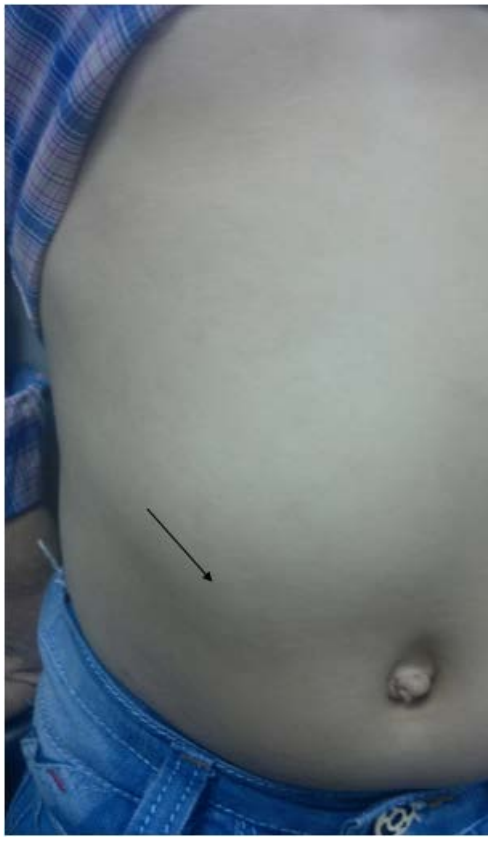

Photo 3.

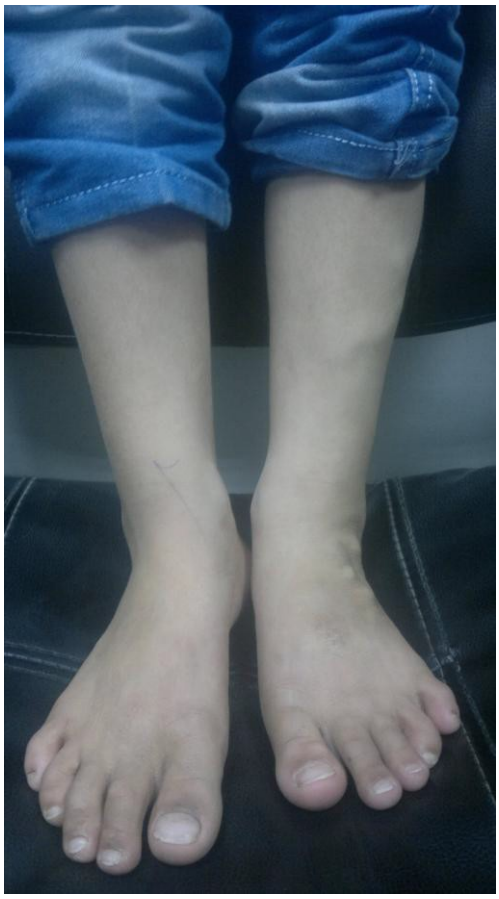

Photo 4

2. Discussion

This syndrome, named after the Greek god of many forms, is a mosaic disorder characterized by asymmetric overgrowth of a variety of tissues.

Before Proteus syndrome was defined in 1983, patients with this condition were often classified as having Klippel–Trenaunay syndrome or Neurofibromatosis1.

Diagnostic criteria for Proteus syndrome were established in 1999, emphasizing the mosaic distribution of lesions, progressive course (particularly during childhood), and disproportionate nature of the overgrowth (Turner et al., 2014).

2.1. Genetics

Proteus syndrome occurs sporadically and is caused by mosaic activating mutations in the AKT1 gene (Johnston et al., 2011).

2.2. Pathogenesis

The involvement of multiple organ systems in Proteus syndrome is consistent with the expression of AKT1, a serine-threonine protein kinase that promotes cell growth and survival, in many tissues. Although PTEN mutations have not been identified in patients with classic Proteus syndrome, some patients with Proteus-like phenotypes have a type 2 segmental form of PTEN hamartoma tumor syndrome (Loffeld et al., 2006; Loffeld et al., 2008; Happle, 2010).

This is not surprising considering that PTEN negatively regulates the growth-promoting PIK3CA/AKT pathway that is activated in affected tissues of Proteus syndrome patients.

2.3. Clinical Features

Epidermal nevi in Proteus patients tend to be relatively thin and "soft" (Sapp et al., 2007).

Other cutaneous manifestations include slow-flow vascular malformations (particularly port-wine stains), cerebriform palmar or plantar connective tissue nevi, patchy dermal hypoplasia resulting in prominent subcutaneous veins, and abnormal fat deposition producing lipomas and lipoatrophy.

Disproportionate overgrowth typically results in asymmetric macrodactyly or limb gigantism, usually with abnormal bones and deficient soft tissue, and scoliosis related to megaspondylodysplasia. Visceral overgrowth, especially of the spleen, can also occur.

2.4. Differential Diagnosis

Several other disorders feature epidermal nevi and vascular malformations together with asymmetric overgrowth. However the latter to be relatively proportionate, leading to a "ballooning" effect but normal structure, and less progressive than that of Proteus syndrome. Type 2 segmental PTEN hamartoma tumor syndrome (also known as SOLAMEN syndrome) is characterized by macrocephaly, thicker and more verrucous epidermal nevi, vascular array. with a fast-flow component, and a lack of truly "cerebriform" palmoplantar connective tissue nevi(Caux et al., 2007).

Another entity in the differential diagnosis is CLOVE(S) syndrome – congenital lipomatous overgrowth, vascular anomalies, epidermal nevi and scoliosis/other skeletal abnormalities (especially broad hands and feet) (Sapp et al., 2007).

Epidermal nevi are an occasional feature of macrocephaly–capillary malformation syndrome.

Although the association of an epidermal nevus with a port-wine stain was originally included as a form of phakomatosis plexiform neurofibromas of Neurofibromatosis1 can be distinguished from Proteus syndrome by the clinicopathologic features and presence of café-au-lait macules and other stigmata of Neurofibromatosis1. Unlike Proteus syndrome, the overgrowth in Klippel–Trenaunay syndrome (KTS) is spatially associated with a vascular malformation.

2.6. Treatment

Management is symptomatic and organ-specific. Individual hamartomas and localized overgrowth can sometimes be treated surgically. Limb gigantism usually requires vascular imaging, with selective embolization sometimes providing an alternative or adjunct to surgery.

Patients with Proteus syndrome (like those with KTS) are susceptible to deep venous thrombosis and pulmonary em.bolism.

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