Proteus syndrome: a case report in Basra\ Iraq.

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Proteus syndrome is also known as elattoproteus syndrome and elephant man disease. The syndrome became widely recognized after the release of the movie "The Elephant Man", a screenplay depicting the life of Joseph Merrick (figure - 1) who was thought to have neurofibromatosis, but is now believed to actually have had severe Proteus syndrome.

A German paediatrician named the syndrome in 1983 after the Greek god Proteus, who had the ability to change his body into different shapes [(1)].

It Is a rare condition that can be loosely categorized as a congenital hamartomatous disorder[(1)], It is a complex disorder with multisystem involvement and great clinical variability and characterized by various cutaneous and subcutaneous lesions, including vascular malformations[(2)], lipomas, hyperpigmentation, and several types of nevi. Partial gigantism with limb or digital overgrowth is pathognomonic, with an unusual body habitus and, often, cerebriform thickening of the soles of the feet (figure 2).

[1]Figure -1) Joseph Merrick

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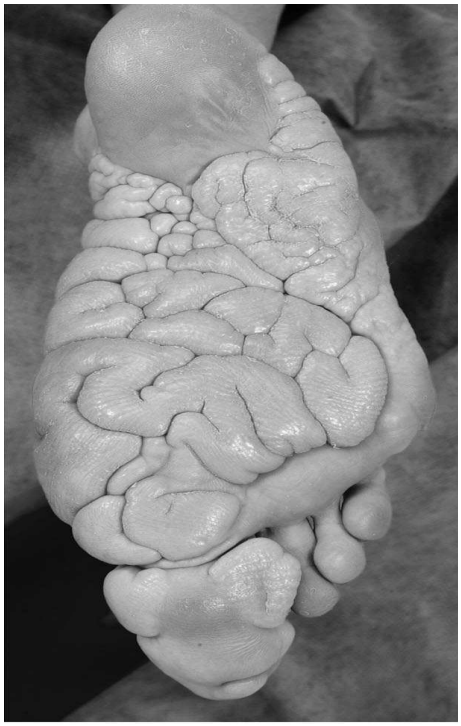
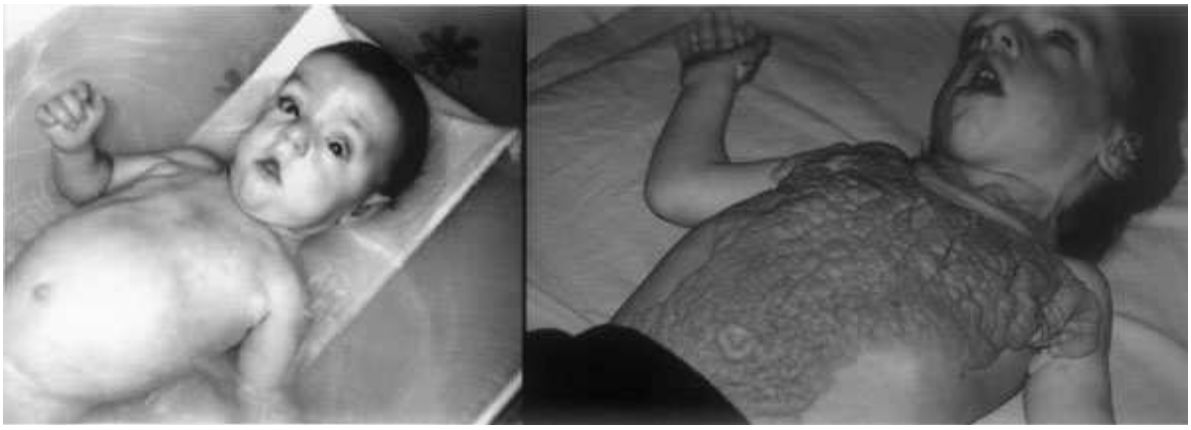


b.

(Figure 2) show cerebriform connective tissue navus of the sole[3] .

Because cutaneous lesions tend to appear over time, the diagnosis may be delayed until late infancy, childhood, or even adulthood (Figure -3).



(Figure-2) ***Normal chest and abdomen of an infant. By 4½ years of age, he developed an extensive cerebriform connective tissue nevus of his chest and abdomen.from*** **Cohen [2002a].**

Although the cause of PS is, as yet, unknown ,it is thought to arise from a postzygotic mutation [4,5] based on (1) mosaic distribution of lesions, (2) sporadic occurrence, (3) exclusively unaffected offspring born to affected individuals, and (4) discordant identical twins [6-8].

Proteus syndrome is believed to be exceedingly rare, with less than 100 confirmed affected individuals reported worldwide [2] . This suggests that prevalence is less than 1 case per 1,000,000 live births. No racial or ethnic differences in disease occurrence are apparent. Males are almost twice as likely to be affected as females and also appear to be at greater risk for thrombosis than females [9].

Orthopedic complications often pose the most challenging medical problems, although vascular complications also contribute to overall morbidity. In addition to that some patients developed mild, moderate and massive pulmonary embolism[10]. And other complicated by malignant changes[11]. Ophthalmologic complications were common (42%) [12]. Severe disfigurement and social stigmatization are additional challenges that must be addressed.

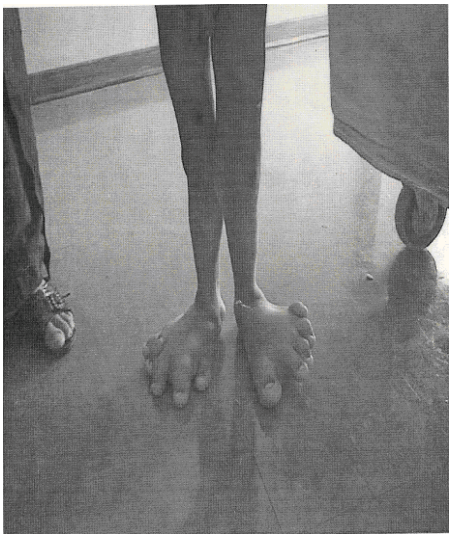
And here we will present and discuss a patient with Proteus syndrome admitted in Basra teaching hospital (Iraq- Basra).

Case presentation

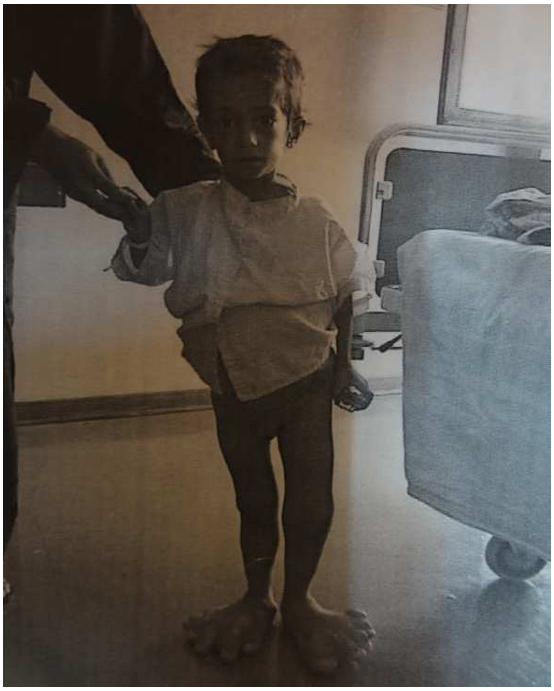
A 3.5 years old male presented with huge progressive irregular swelling of the right chest and abdominal walls since birth with weight loss and difficulty in walking because of deformities of both lower limbs.

On examination:

1- The patient is alert and mentally retarded, the tendon jerk and muscles tone are reduced.
2- Dolichocephaly, long eyelashes, low set ears (the length of right ear is 4.5 cm and the left is 4 cm.).
3- Sever macrodactyly of the fingers, thickened deeply rugated skin on soles of his feet and over growth of both feet and soles (Figure -3).
4- Irregular over growth of thorax and large lymphangiomas on right chest and abdominal walls.
5- Abdomen: is distended and soft, the spleen is just palpable below the costal margin, and umbilical hernia is present (figure 4).
6- The external genitilia are well developed, but the right testicle was absent from the scrotum.
7- The skin: multiple different size purple\maroon macules overall the body with multiple small subcutaneous soft tissue masses (lipomas) with visible dilated veins on chest, abdomen and both lower limbs, with epidermal nevi on left chest wall.



(Figure-3) ***overgrowth and deformities of feet.***



(***Figure 4) deformed pelvis, and normal external genitilia***

Laboratory investigations and imaging study:

1- Blood test within normal .
2- Chest X-ray: right chest wall soft tissue mass, with right side scoliosis.
3- Pelvic X-ray: left side of pelvic bone is higher than the right side by about one cm.
4- X-ray of both feet: hyperplasia of soft tissues with hypertrophied bones.
5- ECG, and ECHO. are normal.
6- U/S for chest and abdomen shows huge hypoechoic multi- cystic mass at the right chest and upper abdominal walls.

7- Genetic study: done in Italy "Milano": karyotype from peripheral lymphocytes that was result normal ((46 XY)).

On basis of this phenotype this patient affected by Proteus syndrome.

Treatment:

Total excision of the swelling with its overlying skin and muscular attachments from chest and abdominal walls and send for histopathological examination that reveals lymphangiomas and hemangiomas. The postoperative period pass smoothly apart from simple wound infection treated by antibiotics.

Excision of forefeet by metatarsal osteotomies, excision in Toto of the 5^{th} ray, transfer of the peroneus tendon and insertion to the base of the 4^{th} metatarsal bone and fixation with 2 K- wires and resection of the hypertrophic tissues. Postoperatively removal of the cast and K-wires after one month, appropriate sized blocks under the short right leg and adequate shoes.

Discussion.

Proteus syndrome is a congenital disorder with varied clinical manifestations - Happle(1987)[13] hypothesized that the syndrome resulted from a somatic alteration of a gene leading to mosaic effects that would be lethal if the mutation were carried in a non mosaic fashion. This potentially explains the variability among and within patients, but has led to diagnostic confusion. The first National conference on Proteus syndrome for parents was held at the national Institute of Health in Bethesda, Maryland from March18-20, 1998 and recommendations were given on diagnostic criteria, differential diagnosis and guidelines for evaluating patients [14]. The general characteristics of mosaic distribution of lesions, progressive course and sporadic occurrence are considered mandatory, regardless of specific manifestations in a given patient. Connective tissue nevi are common and are facultative but not obligatory i.e. they may or may not be present. When present, a connective tissue nevus is almost pathognomonic for Proteus syndrome and kept in specific criteria (Category A). Category B includes (1) Epidermal nevus;(2) Disproportionate overgrowth in one or more limbs (arms/legs/hands/feet/digits), skull (hyperostosis), external auditory meatus (hyperostosis), vertebrae (Megaspondylodysplasia), visceral enlargement (spleen, thymus) and (3) Specific tumours before end of second decade (either one), bilateral ovarian cystadenomas, parotid monomorphic adenoma. Category C includes : (1) Dysregulated adipose tissue (either one) - lipomas, regional absence of fat ;(2) Vascular malformations (one or more)- Capillary malformations, venous malformation, lymphatic malformation; (3) Fascial phenotype- dolichocephaly, long face, minor down slanting of palpebral fissures and/or minor ptosis, low nasal bridge, wide or anteverted nares, open mouth at rest. Our patient fulfilled the general criteria and had features from category A,B and C.

The principle differential diagnosis are diseases producing hypertrophy of limbs , macrodactyly and skin lesions. Klipplel-Trenaunay syndrome is the first differential diagnosis, it produce hemihypertrophy usually monomelic with vascular abnormalities. Neurofibromatosis (von Recklinghausen's Disease) which may produce asymmetrical hypertrophy , macrodactyly and skin lesion was not considered due to lack of axillary freckling, neurofibromas and iris nodules. And also Maffucci syndrome is another possible rare differential diagnosis.

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