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PROTEUS PARADIGM : A RARE CASE REPORT OF 1 IN MILLION BIRTH

Dermatology

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ABSTRACT

Proteus syndrome (PS) is a hamartomatous disorder characterized by various cutaneous and subcutaneous lesions, including vascular malformations, soft tissue tumors, lipomas and several types of nevi. Partial gigantism with limb or digital overgrowth is pathognomonic. Mosaic disorder with mutation in AKT1 gene. The patient was a 8 year-old child with clinical features that were indicative of the Proteus syndrome, such as mosaic distribution of lesions, sporadic incidence, progressive path, disproportionate overgrowth of the legs, verrucous epidermal nevi and venous malformations .

Only a few cases of PS have been reported in the literature so far.We report a case of PS in a 8 year-old child with classic cerebriform plantar hyperplasia and macrodactyly of the bilateral foot and right finger was reported in the current study. PS is a difficult and contentious condition to diagnose clinically and manage owing to the aggressive and disproportionate postnatal overgrowth. They have a higher chance of dying prematurely and also risk of tumors . Therefore prenatal diagnosis is crucial and proper counselling and regular followup is needed.

KEYWORDS

Proteus syndrome, macrodactyly, cerebriform connective tissue nevi, disproportionate overgrowth

INTRODUCTION

Proteus syndrome (PS) is a rare syndrome named after the Greek God Proteus who was able to change his shape at his will. It is an etiologically unexplained condition characterised by patchy or mosaic postnatal overgrowth. Overgrowth usually begins in childhood and can affect any organ or tissue in the body. Connective tissue , bone, skin, adipose tissues, the central nervous system are among the most commonly affected tissues, although it appears to affect any tissue. Its approximate incidence is one per 1 million [1]. So far, about 100 cases of PS have been identified, with a male-to-female ratio of 1.9:1[2,3]. Macrodactyly deformities, unilateral hypertrophy, palmar or plantar cerebriform hyperplasia, subcutaneous tumours, verrucous nevus, exostosis, and vessel hamartomas are all thought to be diacritic clinical manifestations [4,]. PS is caused by a serine/threonine protein kinase 1 (AKT-1) activating mutation in chimeric cells, according to research published in 2011[5]. Due to certain overlapping features with other overgrowth syndromes, diagnosis is usually delayed. In the present report, a rare case of PS that presented with disproportionate overgrowth and cerebriform plantar hyperplasia of the left foot was documented.

CASE REPORT

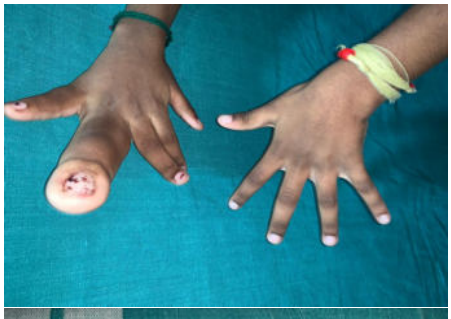
An 8 year old male child born out of a consanguineous marriage presented to our OPD with complaints of disproportionate overgrowth of right upper limb and lower limb and left foot present since birth and progressive in nature. Child had difficulty in walking due to the asymmetric limb overgrowth.

On detailed history, prenatal scan (3rd trimester) showed thoracoabdominal wall cystic lesion extending in to right lower limb and adequate liquor .Birth was uneventful. Postnatal MRI abdomen and right lower limb showed extensive lymphovascular malformation. At the age of 1 year, child was operated for anterior abdominal wall swelling ,the intraoperative findings showed multicystic lesions which had features of lymphangioma. At 2 years of age, he was operated for right hydrocele .

The patient's vitals were stable. Height and weight were appropriate for age. Developmental milestones and intelligence were normal. Examination revealed disproportionate overgrowth of the right upper limb with macrodactyly of right finger. Right lower limb gigantism and multiple angiokeratoma, pyogenic granuloma verrucous epidermal nevi of right foot and macrodactyly were present. Left foot disproportionate overgrowth and macrodactyly were present. Cerebriform connective tissue nevi(CCTN) of bilateral foot was present . There were no port-wine stains, hemangiomas, or purpura Histopathology of skin lesions showed features of angiokeratoma and pyogenic granuloma.

Right Upper Limb- disproportionate overgrowth with macrodactyly of right ring finger and little fingers. FIGURE 1 A and B

A



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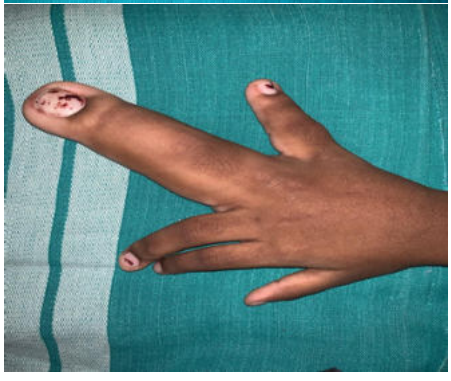
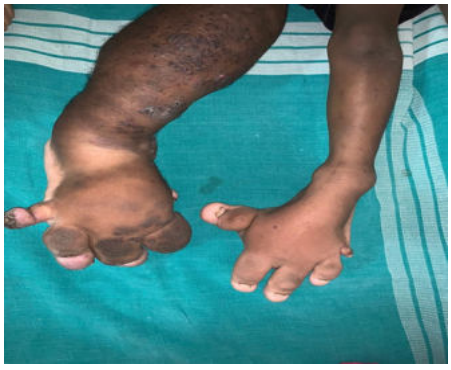


Right Lower Limb- gigantism and multiple angiokeratoma – FIGURE 2 A and B

A



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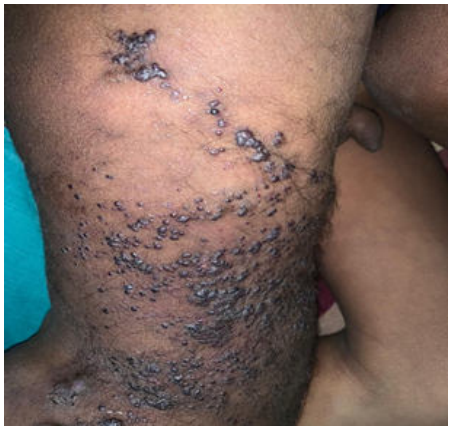
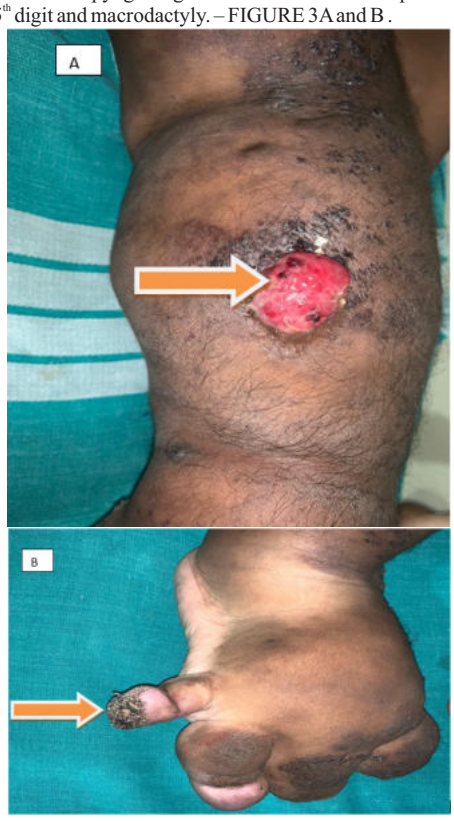
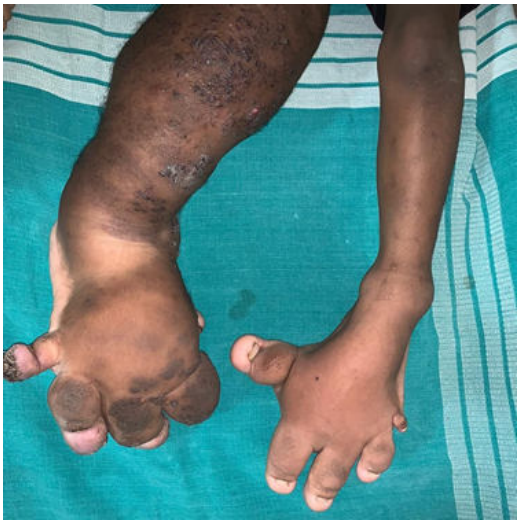


Right lower limb - pyogenic granuloma and verrucous epidermal nevi of right 5th digit and macrodactyly. – FIGURE 3A and B .

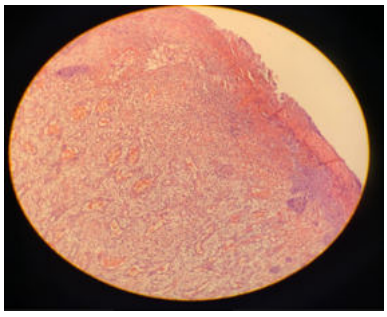


Left Foot- Disproportionate Overgrowth And Macrodactyly – **Figure 4**

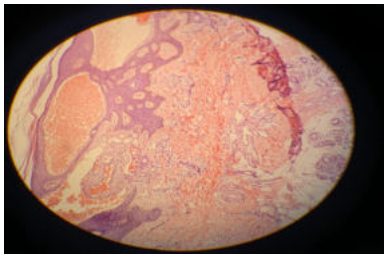


Cerebriform Connective Tissue Nevi Of Sole - **Figure 5**

Biopsy Done From The Left Lower Limb Lesions ,showed Features Of Pyogenic Granuloma- FIGURE 6 – Histopathology shows Epidermis ulceration , subepithelial anastomosing, proliferating blood vessels with edema and mixed inflammatory infiltrate.



Histopathology Of The Left Lower Limb Lesions- Angiokeratoma - **Figure 7** - Dermis Shows Congested Blood Vessels With Perivascular lymphocytic infiltrate.



Based on Turner *et al* revised the diagnostic criteria for the syndrome [6], which comprise three general and three specific criteria categories .For a confirmed diagnosis, the patient should fulfill all the general criteria, namely mosaic distribution of the phenotype, sporadic emergence, and progressive course. Subsequently, an additional single sign from category A, two signs from category B, or three signs from category C are sufficient to establish the diagnosis of PS.

In this patient General criteria Plus 4 specific criteria was fulfilled such as Cerebriform Connective tissue nevi (CCTN)of soles from category A, Epidermal nevi and Disproportionate overgrowth from category B, Capillary, venous or lymphatic malformation from category C was present.

Radiography of the affected lower limb showed soft tissue masses around the phalanxes , and irregular bone structure of the phalanxes. CT thorax and abdomen was normal . Xray spine ,Skull xray was normal.

Symptomatic treatment was given .Radiofrequency ablation was done for the pyogenic granuloma. Regular dressing for the wound was done .Psychosocial counselling was advised. Developmental paediatrician consultation was taken and special education for the child was given.The child is being followed up to monitor for tumors and associated complications.

DISCUSSION

PS is a rare congenital condition in which overgrowth of various tissues is seen. It may affect any of the three germinal layer

tissues[1,8]. The spontaneous or mosaic distribution of symptoms across the body is a defining feature of this condition. The most common entities that are confused with PS are Klippel-Trénaunay syndrome and Hemi hyperplasia-multiple lipomatosis (HHML) syndrome[9]. PS exhibits more features of reticular connective tissue naevi, which are not manifested in Klippel-Trenaunay-Weber syndrome[10].Other differential diagnosis of overgrowth syndromes like CLOVE, SOLAMEN , PTEN mutation syndromes are excluded based on the criteria. In those patients, the prognosis is good as they do not appear to suffer from the aggressive overgrowth of PS and do not appear to be as susceptible to thrombosis as the above conditions. Dermatological manifestations of PS as reported by Beachkofsky *et al*, CCTN was present among 94% of their 36 patients[7]. CCTN, a hallmark of the disease, was seen in our case . The lesion progresses slowly in some patients, and it can last well into puberty. It starts as a localised thickening of the subcutaneous tissue that progresses to a significant thickening that can be a centimetre or more deep over time [1]. Other dermatological manifestation reported are epidermal nevi, cutaneous vascular malformations including capillary, venous, lymphatic or combined malformation, lipoma, partial lipohypoplasia and patchy dermal hyperplasia[8].Hence dermatologists have an important role in diagnosing PS and misdiagnosis can be avoided.

PS is difficult to treat because of its many clinical characteristics. Patients should be monitored for the occurrence of complications on a regular basis [11]. Surgical therapy is used to remove symptomatic lesions in most cases. Early surgical procedures are critical to minimise extra malformations, physical defects, and complications, given the rising operative complexity and rate of complications over time [12]. In addition, it is necessary to monitor the patients for potential tumor development. The seriousness of the complications affects the prognosis. About 20% of PS patients die too soon, most often from venous thromboembolism or pulmonary embolism, pneumonia, or surgical complications [9,13].

Management should be directed towards functional improvement. Patients with limb length discrepancy, joint immobility and macrodactyly are best managed by team consisting of pediatrician, orthopedic surgeon, plastic surgeon and occupational therapy[13]

PS is a tissue overgrowth condition that is extremely rare, highly variable, and progressive. The precise pathogenesis and etiology of this disease are unknown. Given the complications and early mortality seen in patients, we stress the importance of early PS diagnosis and the need for multidisciplinary approaches [14].

CONCLUSION

Paediatric overgrowth syndrome is quite distressing for growing child and the family causing financial burden and psychological disturbance. Given the complications and early mortality seen in patients, we stress the importance of early PS diagnosis and the need for a multidisciplinary approach.Prenatal diagnosis is crucial and proper counselling has to be done.Considering the severe complications ,it is necessary for regular follow up , to remain alert regarding potential tumor development in such patients, in order to improve their quality of life.

Conflict Of Interest

None

Consent

Informed consent has been obtained from the parents of the child for this publication.

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