CASE REPORT

PROTEUS SYNDROME: A RARE DISEASE OF DISPROPORTIONATE AND ASYMMETRIC OVERGROWTH OF CONNECTIVE TISSUE

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Proteus syndrome is a rare disease manifested by progressive segmental overgrowth involving the skeletal, Cutaneous, subcutaneous, and nervous systems. We report the case of a 24-year-old female who was born with no obvious abnormality at birth. From the age of 1 year, she developed asymmetric enlargement of her left upper limb and bilateral lower limbs leading to enlargement of the right-hand phalanges with radial deviation, enlargement of the right big toe, lateral deviation of left foot, and discrepancy in the length of lower extremities and kyphoscoliosis. She had become bed-bound for the last few years due to increasing disability. She was diagnosed with Proteus syndrome based on clinical features of progressive course, mosaic distribution, and sporadic occurrence of the lesions.

Keywords: Proteus Syndrome; Skeletal Overgrowth; Disfigurement; Disability

Citation: Qaisar F, Butt NI, Ghoauri MSA, Azhar M, Javed MU, Samad A. Proteus syndrome: A rare disease of disproportionate and asymmetric overgrowth of connective tissue. J Ayub Med Coll Abbottabad 2023;35(1):177–9.

DOI: 10.55519/JAMC-01-11210

INTRODUCTION

Proteus syndrome is a rare disease having an estimated prevalence of ≤1 in 1,000,000 live births.[1] It is characterized by disproportionate and asymmetric overgrowth of connective tissue including epidermal nevi, fat, or bones in a patchy or mosaic pattern leading to disfigurement and disability.[2] The histo-pathological findings of Proteus Syndrome include diffuse patchy overgrowth of cutaneous and subcutaneous tissue, defects in ossification, and plantar cerebriform connective tissue nevus.[2] Proteus syndrome has no or very few manifestations at birth in most patients. It manifests progressively in the toddler period and then progresses throughout childhood and adolescence which may lead to severe disfigurement by skeletal overgrowth and disability. The diagnosis of Proteus syndrome is based on clinical features including all 3 characteristics of progressive course of the disease, mosaic distribution, and sporadic occurrence of lesions.[3] If the clinical criteria are inconclusive, diagnosis can be established by using molecular genetic testing to identify the mosaic, somatic, heterozygous pathogenic variant in *AKT1*.[3] It is associated with various tumors including abdominal and pelvic malignancies, deep vein thrombosis, and pulmonary embolism.[4]

CASE REPORT

We report the case of a 24-year-old female who was born with no obvious abnormality at birth. At the age of 1-year, gradual onset of asymmetric enlargement of her left upper limb and bilateral lower limbs was noted by her parents, which gradually increased. She also developed enlargement of the right-hand phalanges with radial deviation as shown in Figure-1. She developed enlargement of the right big toe, lateral deviation of the left foot, and discrepancy in the length of lower extremities with time as shown in Figure-2. She had a delay in achieving developmental milestones. She started to crawl at 3 years of age and was able to walk by 4 years of age. At the age of 4 years, she developed abnormal curvature of the dorsal spine leading to kyphoscoliosis. X-Rays of the dorsal spine are shown in Figure-3. She was conscious, cooperative, and oriented in time, place, and person and had no gross neurological abnormality. Blood investigations revealed a mild hypochromic microcytic anemia with normal ESR and CRP. Other than showing skeletal abnormalities and kyphoscoliosis, her Echocardiography, HRCT scan of the chest, and CT scan of the abdomen & pelvis were normal. She had become bed-bound for the last few years due to increasing disability and was dependent on her family members for vocational, avocational, and self-care activities. She denied any history of trauma, respiratory complaints, joint pains, or skin abnormalities. There was no family history of a similar disease in any family member. However, her parents had a first cousin marriage. She was unmarried and did not use any illicit drugs. She was diagnosed with Proteus syndrome based on clinical features of progressive course, mosaic distribution, and sporadic occurrence of the lesions.

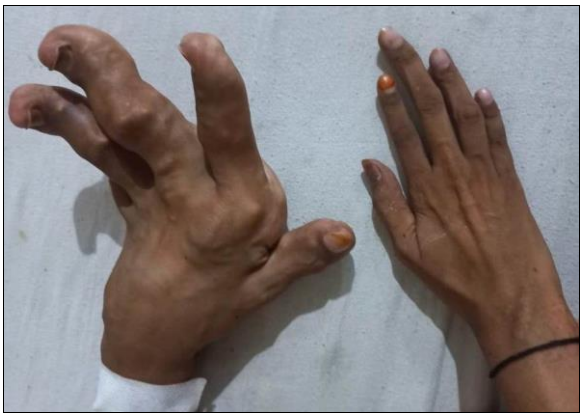

Figure-1: Image of both hands

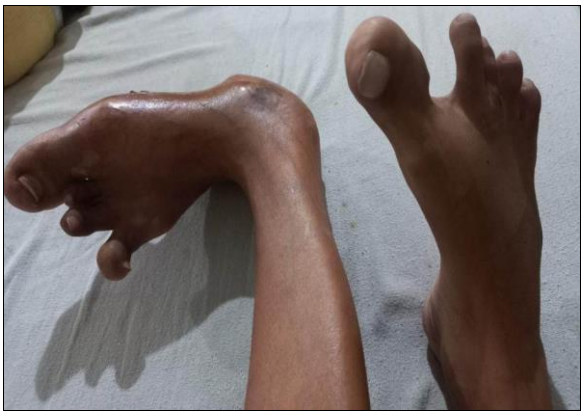

Figure-2: Image of both feet

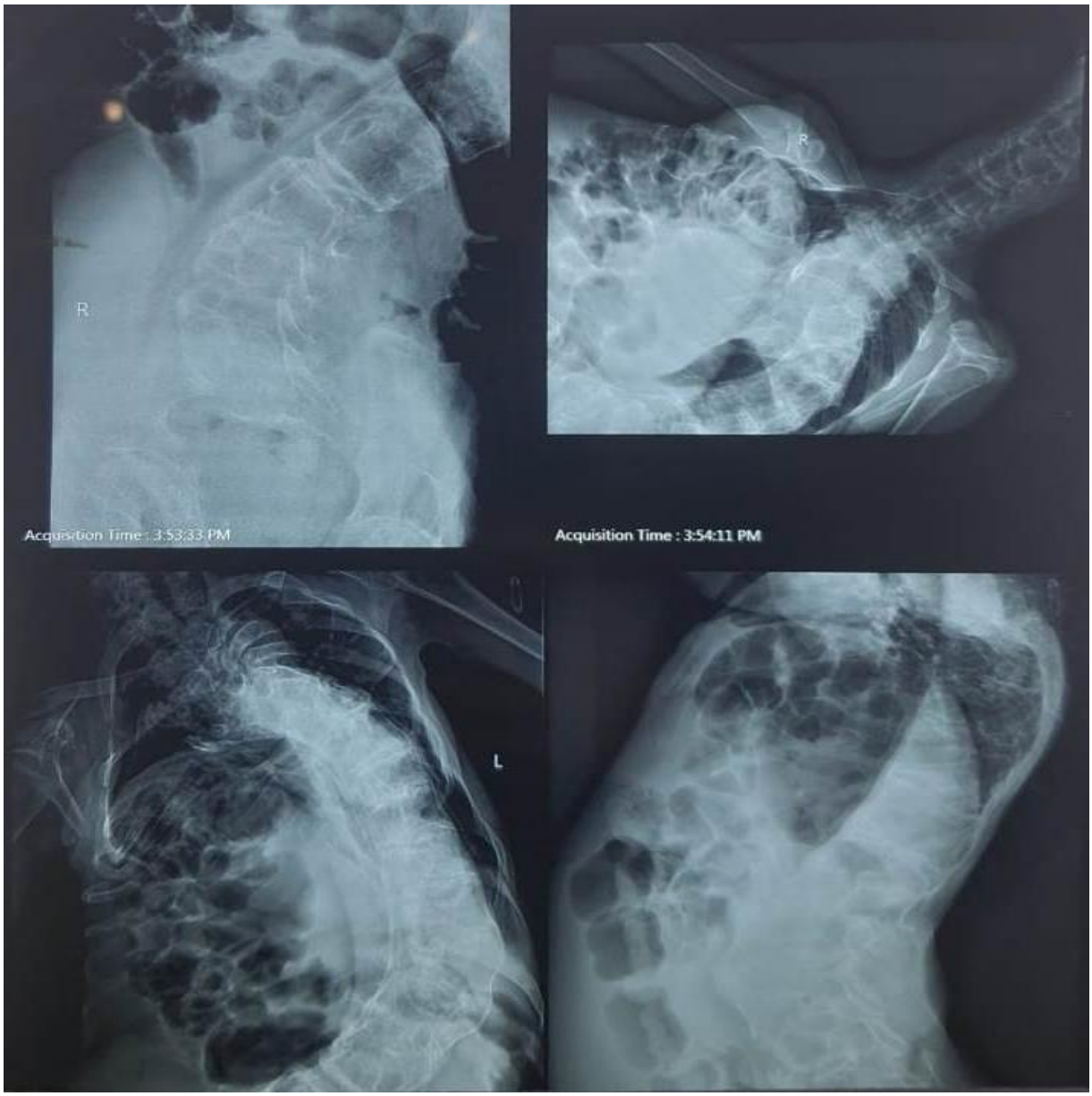

Figure-3: X-ray images of the dorsal spine

DISCUSSION

Proteus syndrome is manifested by malformations due to multi-focal excessive growth of connective tissue resulting in progressive abnormalities including vascular malformations, incomplete gigantism of limbs, and organomegaly.[5] Neuro-psychomotor development is normal in most patients with a life expectancy up to 29 years of age determined by the severity of the disease.[6] No or very few manifestations are apparent at birth.[1] Asymmetric disproportionate growth of feet and hands begins around the age of 6–18 months and full overgrowth will have occurred by age 6 years. Cerebriform connective tissue nevi presence is pathognomonic for Proteus Syndrome but is not seen in all patients.[7] Cutaneous capillary abnormalities and prominent varicosities (vascular malformations) develop in most patients. Therefore, patients with Proteus syndrome have a higher risk to develop deep vein thrombosis, pulmonary embolism, and respiratory failure which are the leading cause of death in these patients.

Proteus syndrome is essentially diagnosed clinically. There is no definite treatment and management is multi-disciplinary including psychological and clinical support.[2,4] Surgical intervention may be directed to improve functional status. Although difficult, it is pertinent to manage overgrowth in Proteus syndrome and requires orthopedic procedures over the years. Patients may still suffer extensive functional impairment and cosmetic disfigurement despite aggressive treatment.[7] The socioeconomic impact of having this syndrome creates numerous important psychological issues: affected patients and their parents commonly report feeling isolated due to the rarity of the disease and the social stigma associated with having a progressively disfiguring disorder. Depressive symptoms may be seen in up to 23% of parents with affected offspring.[8] Therefore it is necessary to provide psychological support to both the patients and their caregivers.

In conclusion, Proteus syndrome is a rare disorder that is characterized by asymmetric and disproportionate connective tissue overgrowth. It may be difficult to diagnose as it has a very mild feature in the initial stages and later on becomes progressive with variable phenotypes leading to disfigurement and disability. It is important to keep in mind various complications of Proteus syndrome so that prompt diagnosis and timely treatment may be initiated to limit disease morbidity.

Consent: Informed consent was taken from the patient.

Conflict of Interest: None declared.

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Submitted: August 06, 2022	*Revised: September 10, 2022*	*Accepted: September 14, 2022*

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