

Approach in an adolescent Proteus male patient with megafoot

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Proteus syndrome is a rare overgrowth syndrome characterized by hemihypertrophy, lower limb asymmetry, hyperpigmentations, lipomas, and vascular malformation. In this paper, we present a new adolescent Proteus syndrome patient with bilateral megafoot. He was very successful in playing football and was very popular among his friends. We present this case for the psychological and surgical aspects of this very interesting entity. We also review the recent literature related with Proteus syndrome.

Key words: Proteus syndrome, adolescence, bilateral megafoot.

Proteus syndrome is a rare, sporadic, congenital hamartomatous syndrome (OMIM: 601728)¹ possibly due to somatic mosaicism and a germline mutation PTEN (10q23.31)². This syndrome is characterized by overgrowth of multiple tissues, hyperpigmented epidermal nevi, vascular malformations, lipomas, lipohypoplasia, cerebriiform connective tissue nevi, and dermal hypoplasia^{3,4}. Many of these abnormalities are seen in other hamartomatous syndromes, which leads to misdiagnosis. Proteus syndrome presents in many different clinical forms, which were proposed in an excellent guideline for diagnosis⁴. Unnecessary surgical operation should not be performed in these patients due to possible risk of pulmonary thromboembolism⁵. We present a 14-year-old male patient who was diagnosed as Proteus syndrome when he was first admitted to the hospital at 10 months of age because of overgrowth of both feet and abdominal soft tissue masses. The aim of presenting this case is to discuss the multidisciplinary approach to providing follow-up of an adolescent male patient with Proteus syndrome and megafoot.

Case Report

Our patient is the fourth living child of unrelated parents. He had three older healthy siblings. The mother was 38 years old and the father was 42 years old at the time of his birth. No significant family history was reported. He was admitted to our hospital at 10 months

of age due to disproportionate overgrowth of both feet. According to the anthropometric evaluation, his length was 73 cm (75 centile) and weight was 8,800 g (50 centile). His head circumference was 44 cm (3-10 centile) and chest circumference was 46 cm. Both feet were disproportionate to other parts of the body. Epidermal nevi were observed along the left leg and the penile shaft area. There was a soft tissue mass along pper epigastric region.

The patient was lost to follow-up due to the family's financial difficulties. He was readmitted to the Clinical Genetics Department at 14 years of age with the complaint of huge overgrowth of his feet and toes. Both feet had megafoot appearance. The right foot had four mega toes and the left foot had three mega toes. All toes of both feet, especially the first, second, and third, were macrodactylic (Fig. 1). At that time, his anthropometric parameters were: height 151 cm (3-10 centile), weight 44.1 kg (10-25 centile), head circumference 56 cm, and chest circumference 75.5 cm. In addition, body mass index (BMI) was 19.34 (75-90 centile). His vital signs were normal. There were epidermal nevi skin changes, which were more prominent on the medial surface of the left leg. His left leg also had some varicose vessels. Lower extremity arteriogram performed for evaluation of obstructive lesions was found within normal limits. The upper extremities were normal. There was no length

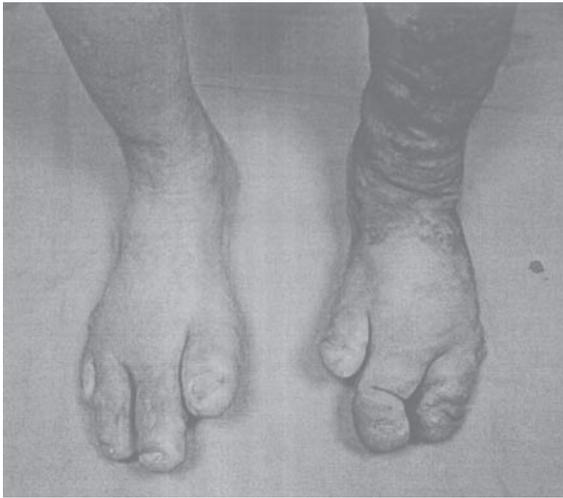


Fig. 1. Proteus syndrome with megafoot.

difference between the legs. He also had a mild compensatory scoliosis due to size difference of both feet. Scoliosis curved to the right and required no intervention.

The patient was diagnosed as Proteus syndrome because he had bilateral feet of abnormally increased size, mega toes with hypodactyly and epidermal nevi skin changes on the extremities and penile shaft area. He also had a soft tissue lipomatous mass on the abdominal area. The foot appearance had progressively increased since 10 months of age and his feet were surprisingly disproportionately huge compared to other parts of the body.

Serum insulinlike growth factor (IGF)-1, IGF binding protein-3 (IGFBP-3) and growth hormone levels were within normal range. Abdominal sonography revealed lymphadenopathy on mesenteric region and minimal free fluid among bowel segments. On cardiac examination, a III/VI systolic murmur was best heard on mesocardium and an echocardiogram was normal. Intravenous pyelogram was within normal limits. Bone mineral density (BMD) of the L1-L4 region demonstrated osteoporosis with a Z score of (-2.91) (67%). Estimated bone mineral component and BMD, estimated area were 30.29 g, 0.601 g/cm² 50.37 cm², respectively, on L1, L2, L3 and L4 regions.

This adolescent boy with Proteus syndrome had normal intelligence based on interview. He was very popular among his friends. He

stated that he played football very well and his ability to shoot baskets was excellent, which he attributed to his large feet.

With respect to other than his soccer playing, we used the HEADSSS approach (Home, Education, Employment, Activities, Drug and alcohol use, Depression, Suicidality, Sexuality, Safety) to discuss the rest of his psychosocial functioning. We did not note any abnormalities on these issues. He showed a very good progress regarding social - cultural development.

Discussion

Proteus syndrome was first described in 1979 by Cohen and Hayden⁶. It was later termed Proteus from the Greek or Roman⁷. In mythology, Proteus was considered a god-like figure with prophetic powers, such as in our patient who was accepted as a hero for his soccer abilities. Proteus syndrome is a highly variable complex hamartomatous disorder including malformations and overgrowth of multiple tissues⁸. Klippel-Trenaunay-Weber syndrome, neurofibromatosis, and Milroy disease have to be kept in mind in the differential diagnosis⁴. Our patient met specific criteria for diagnosis such as disproportionate overgrowth of feet, vascular malformations including capillary and lymphatic malformations, and visceral overgrowth on the left hypochondrial region.

One of the important aims of describing management of a Proteus patient with megafoot is for surgical reasons. We know that many Proteus patients received surgical interventions before completing their growth. These patients experienced many complications due to excess overgrowth on their extremities^{15,16}. On the other hand, Muller et al.¹⁷ stated that surgical treatment at a young age in selected patients could be less invasive and less mutilating than in adulthood, when tumors have developed to excessive volumes. Kregel et al.¹⁸ suggested surgery should be postponed until growth is complete, such as in our case. Severe pulmonary abnormality as cystic lungs and lethal lung involvement were reported in Proteus syndrome patients⁹. Pulmonary thromboembolism was also reported to cause sudden death in Proteus syndrome⁵. These factors present a difficulty for Proteus syndrome patients who are candidates for any operation. We could not perform a biochemical study to determine the risk of thromboembolism in our patient.

A patient similar to our case who was operated before adolescence with multiple exostoses in the skull; facial, ear, and thoracic asymmetry; and unilateral macrodactyly was reported in 1982 by Balcı et al.¹⁰. This case was operated although surgical intervention was not advised before his growth was complete and he was followed for a period of 22 years. His outcome after operation was presented^{11,12}. His macrodactylic finger reached a huge size after plastic surgery was performed before adolescence, for which he underwent multiple corrective operations.

For many years, patients with Proteus syndrome were misdiagnosed as Klippel-Trenaunay syndrome or epidermal nevus syndrome^{4,13}, which have a variable clinical appearance and exhibit defined skin abnormalities. The presented patient with Proteus syndrome had epidermal nevi skin changes since birth but no cerebriform connective tissue nevi or facial anomaly was identified. Our patient complained of skin changes on the penile shaft area and the medial surface of the left leg, but this skin change was unlike the speckling type hyperpigmentation seen in Bannayan-Riley-Ruvalcaba syndrome (BRRS)¹⁴.

The psychological aspect of this patient with Proteus syndrome is interesting. The patient had overgrowth of the feet but had become accustomed to living with enlarged feet. He loved to play soccer and had considerable peer support. His only complaint was concerned with foot care. His parents encouraged him to be careful in avoiding injury and he wore special custom-made shoes. He was hesitant to obey rules although he was a very successful student. He had an excellent relationship with his peers and was a friendly adolescent, but he wished to live normally like his friends. His abnormality led to his attaining some type of leadership position among his friends.

He took advantage of this congenital abnormality as a secondary benefit during the adolescence period. When queried about his knowledge of the risk of acquiring infection due to his vascular problems, he replied that he did not take proper care of himself. We referred him to a psychiatric clinic to assist him in accepting his abnormal body image. Patients diagnosed with Proteus syndrome can benefit from a multidisciplinary approach (genetic, orthopedic, radiologic and plastic and reconstructive counseling) because they have a wide array of abnormalities.

We wish to publish this case because symmetrical huge feet were present before adolescence and any attempt at reconstructive surgery would have caused additional problems. The presented case is different from the previously described cases of Proteus syndrome. This case showed fully penetrant expression of congenital hamartomatous pathology. Molecular studies of similar cases will clarify whether the presented case is a separate entity or a genetic heterogeneity.

REFERENCES

1. Jones KL. Smith's Recognizable Pattern of Human Malformation (6th ed). Philadelphia: WB Saunders; 2006: 514-515.
2. Zhou XP, Marsh DJ, Hampel H, Mulliken JB, Gimm O, Eng C. Germline and germline mosaic PTEN mutations associated with a Proteus-like syndrome of hemihypertrophy, lower limb asymmetry, arteriovenous malformations and lipomatosis. *Hum Mol Genet* 2000; 22: 765-768.
3. Samlaska CP, Levin SW, James WD, Benson PM, Walker JC, Perlik PC. Proteus syndrome. *Arch Dermatol* 1989; 125: 1109-1114.
4. Biesecker LG, Happle R, Mulliken JB, et al. Proteus syndrome: diagnostic criteria, differential diagnosis, and patient evaluation. *Am J Med Genet* 1999; 84: 389-395.
5. Slavotinek AM, Vacha SJ, Peters KF, Biesecker LG. Sudden death caused by pulmonary thromboembolism in Proteus syndrome. *Clin Genet* 2000; 58: 386-389.
6. Cohen MM Jr, Hayden PW. A new recognizable hamartomatous syndrome. *Birth Defect* 1979; 15: 291-296.
7. Wiedemann HR, Burgio GR, Aldenhoff P, Kunze J, Kaufmann HJ, Schirg E. The proteus syndrome. Partial gigantism of the hands and/or feet, nevi, hemihypertrophy, subcutaneous tumors, macrocephaly or other skull anomalies and possible accelerated growth and visceral affections. *Eur J Pediatr* 1983; 140: 5-12.
8. Lacombe D, Taieb A, Vergnes P, et al. Proteus syndrome in 7 patients: clinical and genetic considerations. *Genet Couns* 1991; 2: 93-101.
9. Newman B, Urbach AH, Orenstein D, Dickman PS. Proteus syndrome: emphasis on the pulmonary manifestations. *Pediatr Radiol* 1994; 24: 189-193.
10. Balcı S, Önel B, Erben A, Hazarlı G. Multiple exostosis in skull, facial, ear, and thoracic asymmetry, unilateral macrodactyly (possible chondromatous lesion?). Is it new entity? Identification of genetic syndrome in pediatrics. International Postgraduate Course 1982 Abstract book poster 1 October 14-17, Firenze, Italy.
11. Balcı S, Önel B, Erben A. Kafada multipl osteomlar, yüz, kulak ve toraks asimetrisi makrodaktili bulguları ile giden yeni sendrom. *Çocuk Sağlıklı ve Hastalıkları Dergisi* 1990; 33: 239-249.
12. Balcı S, Kayıkcioglu A. A new hamartomatous syndrome characterized by facial-thoracic asymmetry, multiple osteomas, left sided hemihypertrophy, café au lait spot: a 22 year follow up. 10th International Congress of Human Genetics 2001 Abstract book poster 185 May 15-19, Vienna, Austria.

13. Roma P, Murlidharn R, Kumar B. Proteus syndrome. *J Dermatol* 2002; 29: 238-241.
14. Ekinçi S, Karnak I, Balcı S, Tanyel FC, Büyükpamukçu NB. Bannayan-Riley- Ruvalcaba syndrome from the point of view of pediatric surgeon. *Eur J Ped* 2006; 16: 209-213.
15. Vaughn RY, Selinger AD, Howell CG, Parrish RA, Edgerton MT. Proteus syndrome: diagnosis and surgical management. *J Pediatr Surg* 1993; 28: 5-10.
16. Guidera KJ, Brinker MR, Kousseff BC, et al. Overgrowth management in Klippel-Trenaunay-Weber and Proteus syndromes. *J Pediatr Orthop* 1993; 13: 459-466.
17. Muller E, Lichtendahl DH, Hofer SO. Proteus syndrome in adulthood. *Ann Plast Surg* 2002; 48: 197-201.
18. Krengel S, Fustes-Morales A, Carrasco D, Vázquez M, Durán-McKinster C, Ruiz- Maldonado R. Macrodactyly: report of eight cases and review of the literature. *Pediatr Dermatol* 2000; 17: 270-276.