Proteus Syndrome: Case Report And Review Of The Literature

Poster No.: R-0011
Congress: RANZCR-AOCR 2012
Type: Educational Exhibit
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Keywords: Tissue characterisation, Genetic defects, Structured reporting, Education, Digital radiography, Conventional radiography, CT, Musculoskeletal system, Musculoskeletal soft tissue
DOI: 10.1594/ranzcraocr2012/R-0011

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Learning Objectives

Report a very rare syndrome, which is estimated to exist about 200 cases worldwide.
Background

Congenital syndrome described by Cohen and Hayden (1) in 1979, being called Proteus syndrome (also known as Wiedmann Syndrome) in 1983 by Wiedmann (2) because of the multiple variations with which can present (Proteus in greek means polymorph), is an extremely rare disease: 200 cases are described worldwide (23), with about 120 alive.

Proteus Syndrome has a mosaicism genetic etiology. The reported cases are sporadic, with no association by sex, race, national origin, parents age at conception and chromosomal examinations of both normal by current methods (9). With these data in mind, it is suggested as a cause an autosomal mutation that would affect the production and/or local growth factors regulation, resulting in overgrowth of some structures (14,20). It was later proposed the etiology of this syndrome as a genetic defect, secondary to an autosomal dominant lethal mutation and only mosaicism allow the survival (15). In the literature, there is a description of a mosaic abnormality in the long arm of chromosome 1 (16).

Characterized by verrucous pigmented nevus and skin thickening, lipomas, hemangiomas, hemihypertrophy, gigantism of the extremities (hands and feet), visceral abnormalities and rapid growth rate of the patient in the first year of life (2). Most patients have normal psychomotor development, with life expectancy between 9 months and 29 years, according to the severity and location of anomalies (9).

Other abnormalities were included as part of this syndrome and the most frequent are: hemihypertrophy partial or complete, macrodactyly, macrocephaly, asymmetries and exostosis, palmar or plantar giriform mass representing nevus or lipoma conjunctive, linear epidermal nevi, subcutaneous tumors composed by vascular tissue of blood, lymphatic or mixed, pronounced longitudinal growth in the first years of life and skeletal deformities such as scoliosis, bone hypertrophy and hyperostosis (4).

The partial gigantism of the hands and/or toes is the most important Proteus Syndrome manifestation, which may be of the fingers, and not always located on the same side of hemihypertrophy (9). Other common manifestations are syndactyly, polydactyly and clinodactyly, but there is no sufficient reports to define the treatment (1,17,18).

The subcutaneous tumors may be lipomas, hemangiomas, lymphangiomas, or any combinations of these, highly variable developing including complete regression (2,9,17). They occur anywhere in the body and can grow to such an extent that infiltrate tissues sites, hindering their resection (9,11,17). Rarely associated with malignant or benign tumors (23). Treatment includes emptying and liposuction, but the results are unsatisfactory for tumor recurrence and hypertrophic scarring at the site (9,17).
Some of these changes are also part of other syndromes such as Klippel-Trenaunay Syndrome, Maffucci Syndrome, neurofibromatosis and other, but the mesodermal abnormalities and asymmetric distinguish from Proteus Syndrome. At birth, the lesions are already present and it is possible to recognize the polymorphic nature of the syndrome. The changes are severe, deforming a little the patient, causing an stigma, involving social skills since childhood (21).

Regarding the major manifestations, there is knowledge that the hemihypertrophy is usually mild or absent at birth (in most cases), progressing rapidly in the first year of life, being slowed at childhood and stopping at puberty. It may be partial, complete or crossed, causing the destruction of the affected limb and making it difficult to walk (9). Treatment involves epiphysiodesis, limb shortening, reduce disparities, stretching bony, arthrodeses, arterial ligation and amputations, which are often progressive. However, the recurrence of deformities is common (1,17,18).

Surgical treatment involves resection of soft tissue tumors, partial amputation of the hypertrophy extremities. Every effort should be made to minimize patient discomfort, improve the quality of life and allow him to social life (21).
Imaging Findings OR Procedure Details

Male patient, 3 years old, mulatto, Brazilian, born in Santos (SP) and living in São Vicente (SP), referred to the Santa Casa da Misericordia de Santos Orthopedics and Traumatology, with the genetic diagnosis of Proteus Syndrome made by AACD, because the change in the growth of the right foot at birth. His mother was at the time of pregnancy, 31 years and the father 33 years, both full healthy. There isn’t report of problems during the prenatal period, including ultrasound examinations. There is no report of consanguinity between parents and grandparents, maternal and paternal. The father has another child, from another marriage, healthy.

At birth the patient presented with gigantism right foot, medianized right hallux and completely lateralized fifth toe, with the remainder of the physical examination without changes (Figure 1).

Performed radiographic exams, it was noted the absence of the middle phalanx in the fifth right toe (Figure 2). Rest of the X-rays were normal.

Over the years there is a clear perception of diseases evolution, as well as the right foot and right leg become worse, the right knee and right thigh started to be affected. Finally, growth is being noticed on right buttock. However, corroborating the literature on the disease, his psychomotor development still normal.

Patient already operated in three opportunities. The first surgery was in 2007 with 3 months of life in which the right forefoot was amputated (Figure 3). The second surgery was performed at 2 years of age for removal local lipomas. Finally, the third surgery, held on 26/11/2010, one year after previous surgery, for an amputation on the right foot due to osteomyelitis site (Figures 4 and 5).

2 days before the third surgery, CT scans were performed of head, abdomen and lower limbs of the patient, based on existing literature on the subject.

CT scans were performed in regions where there are changes caused by the syndrome. We used CT scans because it has an easy access and to be a test that performs extensive analysis of the human body, reporting changes that have not yet caused symptoms, an attempt to trace the changes since, so far, it is not possible predict which organ will occur the next change. All scans were examined by two radiologists.

In head CT scans, changes were not seen in any structure (Figure 6).
In abdomen CT scans due to hyperdense appearance of the liver, led to suspect of a storage disease. The tests performed for hemochromatosis detection were not conclusive for this (Figures 7 and 8).

Lower limbs CT scans showed the presence of a mass with attenuation equal to the fatty tissue, featuring lipoma, extending from the thigh posterior surface to the pelvis (Figures 9, 10, 11, 12).
Fig. 3: Postoperative forefoot amputation. References: Department of Radiology, Santa Casa da Misericórdia de Santos, Brazil. 2011.

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**Fig. 4:** Postoperative midfoot amputation for osteomyelitis. References: Department of Radiology, Santa Casa da Misericórdia de Santos, Brazil. 2011.

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**Fig. 8:** In abdomen CT scans due to hyperdense appearance of the liver, led to suspect of a storage disease. The tests performed for hemochromatosis detection were not
**Fig. 9:** Lower limbs CT scans showed the presence of a mass with attenuation equal to the fatty tissue, featuring lipoma, extending from the thigh posterior surface to the pelvis. References: Department of Radiology, Santa Casa da Misericórdia de Santos, Brazil. 2011.

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**Fig. 11:** Lower limbs CT scans showed the presence of a mass with attenuation equal to the fatty tissue, featuring lipoma, extending from the thigh posterior surface to the pelvis. References: Department of Radiology, Santa Casa da Misericórdia de Santos, Brazil. 2011.

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**Fig. 1:** At birth the patient presented with gigantism right foot, medianized right hallux and completely lateralized fifth toe, with the remainder of the physical examination without changes. References: Department of Radiology, Santa Casa da Misericórdia de Santos, Brazil 2011.

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Fig. 2: Right foot deformation with soft tissue swelling, partial syndactyly and the absence of the middle phalanx in the fifth right toe. References: Department of Radiology, Santa Casa da Misericórdia de Santos, Brazil. 2011.

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Fig. 5: Soft tissue swelling of heterogeneous aspect associated with partial amputation of the right foot. References: Department of Radiology, Santa Casa da Misericórdia de Santos, Brazil. 2011.
Fig. 10: Lower limbs CT scans showed the presence of a mass with attenuation equal to the fatty tissue, featuring lipoma, extending from the thigh posterior surface to the pelvis. References: Department of Radiology, Santa Casa da Misericórdia de Santos, Brazil. 2011.
Fig. 6: In head CT scans, changes were not seen in any structure. References: Department of Radiology, Santa Casa da Misericórdia de Santos, Brazil. 2011.

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Fig. 7: In abdomen CT scans due to hyperdense appearance of the liver, led to suspect of a storage disease. The tests performed for hemochromatosis detection were not conclusive for this. References: Department of Radiology, Santa Casa da Misericórdia de Santos, Brazil. 2011.

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Fig. 12: Lower limbs CT scans showed the presence of a mass with attenuation equal to the fatty tissue, featuring lipoma, extending from the thigh posterior surface to the pelvis. References: Department of Radiology, Santa Casa da Misericórdia de Santos, Brazil. 2011.

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Conclusion

We conclude that these patients need further clinically detailed and complementary evaluation, due to the amount and variety of possible changes and diagnosable with armed propaedeutics, looking to the constant progression of the disease.
References


