

CHINESE MEDICAL SCIENCES JOURNAL

CASE REPORT

Tumor Susceptibility in Proteus Syndrome: a Case Report

Wei Ma and Wen Tian*

Department of Hand Surgery, Beijing Jishuitan Hospital, Beijing 100035, China

Key words: Proteus syndrome; somatic mutation; tumor susceptibility

Chin Med Sci J 2014; 29(2):120-121

PROTEUS syndrome is characterized by patchy and progressive overgrowth affecting multiple tissues, including bone, soft tissue, and skin, along with susceptibility to the development of tumors. It was originally described by Cohen and Hayden in 1979¹ and named by Wiedmann in 1983.² The cause of Proteus syndrome is proposed to be a somatic mutation that is lethal in non-mosaic state; cells derived from the mutated cell line carrying this mutation result in anomalies in multiple tissues.³ The clinical manifestations are variable, including partial gigantism of the hands or feet, hemihypertrophy, macrodactyly, plantar or palmar hyperplasia, hemangioma, lipoma, lymphangioma, varicosity, epidermal and connective tissue nevi, cranial exostosis, macrocephaly and skeletal anomalies.³ In this article, we report a case with typical clinical manifestations of Proteus syndrome and discuss about the tumor susceptibility in this medical condition.

CASE DESCRIPTION

A 3-year-old girl displayed rapid, progressive, postnatal macrodactyly involving four fingers and two toes, with multiple masses in the hands and feet, and cerebriform connective tissue nevus (CCTN) on the sole of left foot (Fig. 1). Physical and imaging examination, including X-ray, computed tomography, magnetic resonance

imaging, and color doppler ultrasonography, demonstrated discrepancy in arm length, linear verrucous epidermal nevus on her neck and waist, irregular adipose tissue on her chest, hand, and abdomen, bilateral ovarian cystadenoma, hemangioma in the spleen, and cyst in the liver.

The architecture of her hands and feet were significantly affected. Orthopedic lumpectomy was performed because of the loss of the joint mobility and cosmetic disfigurement.

The masses were located under tendons, with hard texture, unclear edge, and poor mobility. Most of them pinched on the tendons and invaded joint spaces. Specimens of the mass were pathologically examined, revealing abnormally calcified connective tissue.

Six months later, the patient was readmitted to our department with recurrence of masses on her hands and feet. The CCTN on the sole of left foot progressed, with expansion into previously uninvolved skin, increased thickness, and development of new lesions, frequently causing pain, pruritus, infection, and odor. We removed these masses and performed transplantation for the CCTN lesion with skin graft from the inguinal region. The specimens of the CCTN were pathologically examined, and the loss of fibroblasts with variable thick collagen bundles was discovered.

The patient was followed up for one year, and masses on her hand and feet recurred. The previous surgical regions were filled with pale firm nodules resembling keloid.



Figure 1. A 3-year-old girl with rapid, progressive, postnatal macrodactyly involved four fingers and two toes, sporadic masses in her left hand (A) and feet (B), and cerebriiform connective tissue nevus on the sole of left foot (C), which relapsed after skin graft surgery (D).

DISCUSSION

The diagnosis of Proteus syndrome for the patient in this case was reached based on the diagnostic criteria: conforming with three general criteria, plus category A (CCTN) and three criteria from category B in the specific criteria (linear epidermal nevus, asymmetric/disproportionate overgrowth of limbs, and tumors in the first decade of life). Her clinical manifestations are typical and various, some of which show tendency to the development of tumors, including relapsing CCTN, ovarian cystadenoma, liver cyst, spleen hemangioma and abnormally calcified masses.

It has been reported that patients with Proteus syndrome had mutations of phosphatase and tensin homolog deleted on chromosome ten (PTEN), which is a protein phosphatase with the ability to dephosphorylate both serine and threonine residues. PTEN signals down the PI3 kinase/AKT pro-apoptotic pathway.⁴ Lindhurst et al⁵ analyzed the DNA in 158 biopsy samples from 29 patients and unaffected tissues from the same patients with Proteus syndrome. The results showed that 26 of the 29 patients had a somatic activating mutations in the oncogene AKT1, which encodes an enzyme known to mediate processes such as cell proliferation and apoptosis, which are related to the formation of tumor.⁵

In conclusion, clinical manifestations in this case are typical and various, some of which show susceptibility to

tumor, including relapsing CCTN, ovarian cystadenoma, liver cyst, spleen hemangioma, and abnormally calcified masses. It is believed that Proteus syndrome is strongly associated with tumorigenesis, which is based on both clinical manifestations and genetic researches. Once this hypothesis is proven in the future, treatments for tumor, like radiotherapy, chemotherapy, and biotherapy, could be helpful for patients with Proteus syndrome.

REFERENCES

1. Cohen MM Jr, Hayden PW. A newly recognized hamartomatous syndrome. *Birth Defects Orig Artic Ser* 1979; 15:291-6.
2. Wiedemann HR, Burgio GR, Aldenhoff P, et al. 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.
3. Cohen MM Jr. Proteus syndrome: an update. *Am J Med Genet C Semin Med Genet* 2005; 137C:38-52.
4. Vazquez F, Ramaswamy D, Nakamura N, et al. Phosphorylation of the PTEN tail regulates protein stability and function. *Mol Cell Biol* 2000; 20:5010-8.
5. Lindhurst MJ, Sapp JC, Teer JK, et al. A mosaic activating mutation in AKT1 associated with the Proteus syndrome. *N Engl J Med* 2011; 365: 611-9.