Diffuse Mesangial Sclerosis in a Child With Dyskeratosis Congenita Leading to End-stage Renal Disease

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Keywords. dyskeratosis congenital, end-stage renal disease, nephrotic syndrome

Dyskeratosis congenita (DC) is a very rare inherited disorder. It is caused by dysfunction of telomere maintenance. It involves RNA telomerase components relevant to various mutations leading to a classic triad of physical findings consisting of nail dystrophy of the hands and feet, mucosal leukoplakia, and reticular pigmentation of the skin, most commonly on the head, neck, and trunk. Bone marrow failure along with pulmonary complications and malignancies are all common causes of premature death in patients with DC as well as other abnormalities. We report a new case of DC with impure nephrotic syndrome relevant to histopathologic signs of a diffuse mesangial sclerosis, leading to an early end-stage renal disease. Challenges remain to understand the diverse spectrum of DC especially in children. To the best of our knowledge this is the first case of DC associated to diffuse mesangial sclerosis.

IJKD 2016;10:416-8
www.ijkd.org

Case Report

INTRODUCTION

Dyskeratosis congenita (DC) is an inherited ectodermal disease first described in 1960 as Zinsser-Engmann-Cole syndrome.[1] It is a rare disease caused by telomere shortening related to a dysfunction in a regulatory protein "shelterin" by mutation of one of its components, dyskerin causing a wide spectrum of diseases apostrophized commonly by mucocutaneous signs, which are nail dystrophy, reticulate skin pigmentation over the trunk and neck, leukoplakia, and hematological signs mainly cytopenia or multivisceral abnormalities.[2,3]

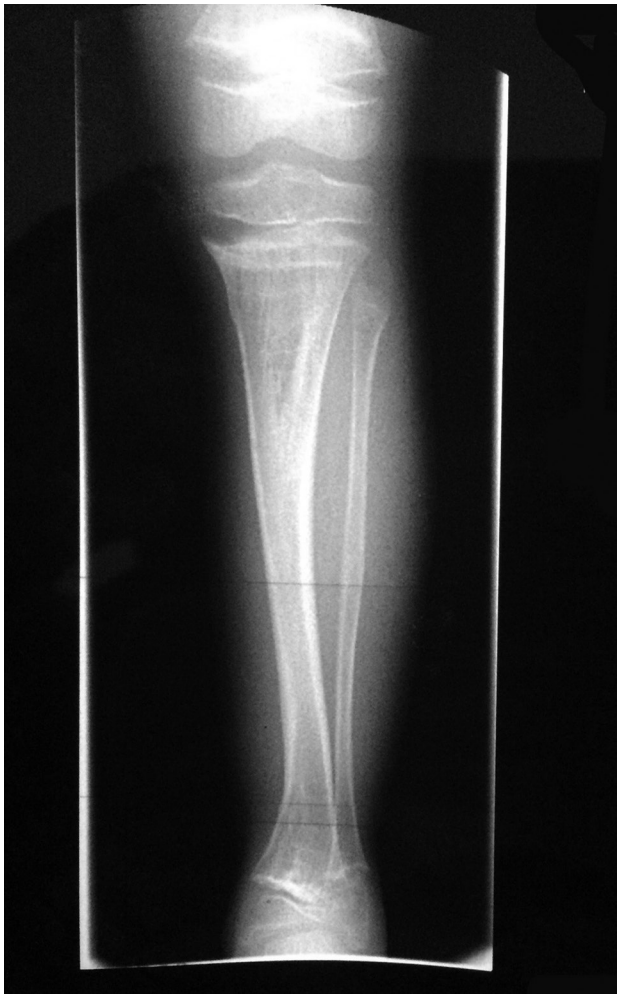
Life expectancy ranges from infancy to well into the 7th decade. Up to 40% of patients will have bone marrow failure by the age of 40.[4] Major causes of morbidity include bone marrow failure, cancer, and visceral complications, mainly pulmonary fibrosis. We report a case of DC with impure nephrotic syndrome relevant to histopathologic signs of a diffuse mesangial sclerosis, leading to an early end-stage renal disease.

CASE REPORT

An 8-year-old boy, originally from Tunisia, born at term from consanguine parents of the second degree, with a personal history of cow's milk protein allergy (immunoglobulin E mediated) and lymphocytic meningitis at 5 months and bullous impetigo at 8 months. He was referred to pediatric department for nephrotic syndrome. Hypochromic cutaneous spots have been noticed and reported to be lasting since the age of 9 months. Dysmorphic features were noted, including broad and bulging forehead, low implanted ears, hypertelorism, dental malposition with multiple caries, a bilateral genuvalgum, deviation of the radial axis, skin xerosis, photosensitivity, hyperpigmentation balled with healthy skin areas of the face and trunk, a reticulated appearance in the limbs, erythrocyanosis of both feet, diffuse alopecia of the scalp, and longitudinal hyperstriation of fingernails. We noted edema of the lower limbs. Routine blood tests showed a normal blood cell count, a total serum

protein level of 50 g/L and a serum albumin level of 19 g/L with severe kidney failure (glomerular filtration rate of 16.7 mL/min and proteinuria at 143 mg/kg/24 h).

Plan radiography showed abnormalities of the radial axis of the upper limb, irregular and widened metaphysis, shortening of the ulna and fibula, and tibia in italic S (Figure). Renal ultrasonography showed normal-sized dedifferentiated kidneys with hyperechoic cortex. Laboratory tests of immunity were normal. Kidney biopsy showed diffuse mesangial sclerosis. The diagnosis of DC was considered. The patient received conservative treatment for the end-stage renal disease, including an angiotensin-converting enzyme inhibitors. After 10 months, despite a slight regression of the proteinuria, the patient reached the end-stage renal disease and underwent automated peritoneal dialysis.



Tibia in italic S with irregular and widened metaphysis.

DISCUSSION

Dyskeratosis congenita is a rare ectodermic dysplasia characterized by the classic triad of pigmentary abnormalities with incontinencia pigmenti and skin atrophy, nail dysplasia, and oral leukokeratosis.[1] Transmissions have been reported to be autosomal dominant, autosomal recessive, or X-linked with mutations in genes which code for proteins whose role is telomere maintenance and affecting telomere length.[2] Dyskeratosis congenita has a wide phenotypic spectrum and age onset. Patients show an increased risk for progressive bone marrow failure and may develop myelodysplastic syndrome or acute myelogenous leukemia.[3,4] Various additional clinical findings have been reported and may include developmental delay, short stature, microcephaly, blepharitis, epiphora, peridontal disease, decreased teeth-root ratio, esophageal stenosis, liver disease, urethral stenosis, osteoporosis, avascular necrosis of femur and humerus, premature hair greying or alopecia, and abnormal eyelashes.[5] Individuals with DC are at a high risk of pulmonary fibrosis.[6]

A chromosomal analysis revealed a normal male karyotype and cytogenetic tests revealed an unidentified mutation in Xq27; molecular biology, sequencing and telomere length measurement were not performed. Otherwise, diffuse mesangial sclerosis was at the forefront with clinically a nephrotic syndrome with a severe kidney failure. The kidney biopsy showed a diffuse mesangial sclerosis. The spectrum of the DC is very broad and enriched every time, but renal impairment described in our patient to the best of our knowledge has not been reported in the literature.

Like other telomere shortening syndromes, various unusual symptoms may occur in dyskeratosis congenita in addition to typical signs. That is why a detailed clinical examination is required to identify each specific or nonspecific complication and a particular care may be considered in time.

CONFLICT OF INTEREST

None declared.

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Received April 2016
Revised July 2016
Accepted July 2016