Case Report

A Rare Case of Dyskeratosis Congenita: A Case Report from Tribal State of Arunachal Pradesh, Northeast India

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Abstract: Dyskeratosis congenita is a rare genodermatosis, which is characterized by triad of skin pigmentation, nail dystrophy and leukoplakic lesion in the oral cavity. The purpose of reporting this case with review of recent literature is to create better awareness about the multisystem manifestations of this fatal condition that can aid clinicians in early diagnosis. A case of 12 year old female is reported presenting with classical triad of lesions with briefly review of literature.

Keywords: Dyskeratosis congenita, Bone marrow failure, Nail dystrophy, Pediatrics, Telomere, leukoplakia, pigmentation.

INTRODUCTION

Dyskeratosis congenita (DC) first described as Zinsser Engman-Cole syndrome (also known as short telomere disease) is a rare inherited genetic and progressive multisystemic disease. It is prevalent among 1:1,000,000 individuals with a 13:1 male predominance and most cases occur between the ages of 5 and 10 years [1-2]. The syndrome shows a typical triad of oral leukoplakia, nail dystrophy and reticular hyperpigmentation. It can also present with other life-threatening complications involving the bone marrow, lungs and liver. Modes of inheritance in this disease include X-linked recessive, autosomal dominant and autosomal recessive patterns [3]. We report a case of 12-year-old patient with DC in department of Pediatrics at TRIHMS Hospital, in an attempt to increase awareness about this rare disease. The patient was duly informed and consent was obtained for publication of case report for medical benefit.

CASE REPORT

A 12 year old girl without any significant past medical history, was admitted with complaints of easy fatigability and poor appetite. At admission, vital signs were within normal limits, patient appeared pale. She had short stature and was underweight. Physical examination revealed reticular pigmentation of palms, soles, back, neck and trunk (fig 1, 2), dystrophy of nails (fig 3) and oral leukoplakia (fig 4). The onset of skin pigmentation had started since infancy and showed gradual progression. There was no similar family history. Respiratory and cardiovascular system was not remarkable. Patient had a normal development quotient. Ophthalmic evaluation was normal. Admission labs showed: hemoglobin - 12.6 g/dl, WBC- 2600 cells/ul, platelet count- 53000/ul, creatinine: 0.5 mg/dl, ALT: 43 U/L, ESR- 12 mm/hr. Peripheral smear showed normal study except for slight decrease in platelets, no atypical cells or blasts were seen. Chest X ray and echocardiography was normal. Further evaluation could not be done due to resource constraints. Patient received symptomatic management during the course of stay and is being followed up in our paediatric clinic.
Figure 1: Hyper-pigmentation of palms

Figure 2: Hyper-pigmentation of back

Figure 3: Nail dystrophy of fingers and toes

Figure 4: Leukoplakia
**DISCUSSION**

DC is caused by impaired telomere maintenance and affects the skin and bone marrow, which both have a high rate of cell proliferation. The following categories of individuals can be considered to have DC [4]:

1. Those with all three (abnormal skin pigmentation, nail dystrophy, and leukoplakia) mucocutaneous features.
2. Individuals with 1 out of 3 mucocutaneous features, bone marrow failure and other somatic features of DC.
3. Those presenting with aplastic anemia or myelodysplastic syndrome or pulmonary fibrosis associated with a pathogenic telomerase variant.
4. Individuals having four or more of features of the Hoyeraal–Hreidarsson syndrome (growth retardation, developmental delay, microcephaly, BM failure, immunodeficiency, and cerebellar hypoplasia).
5. Individuals with two or more features seen in DC associated with very short telomeres (< 1st centile)

The patient in our study presented with reticulate hyperpigmentation of the skin, nail dystrophy and leukoplakia on the tongue—that is, the three components of the classic triad. In addition to the symptoms described above, patients with DC can also present with a variety of other symptoms, including bone marrow failure, eye disorders, gastrointestinal and skeletal abnormalities [5, 6]. Clinical variants of DC are Hoyeraal Hreidarsson (HH) syndrome and Revesz syndrome (RS). HH is characterized by cerebellar hypoplasia, microcephaly, developmental delay, immunodeficiency, intrauterine growth retardation, and bone marrow failure. Features defining RS are bilateral exudative retinopathy, intrauterine growth retardation, BMF, sparse fine hair, and central nervous system (CNS) calcifications [7]. The bone marrow findings in DC are variable and range from normal to different severity of aplasia depending on the stage of the disease [8]. Peripheral blood cytopenias are common in DC, more frequently in children and in patients with multisystem disease. Our patient also had bicytopenia (leucopenia and thrombocytopenia). Although hematopoietic failure predominates, other causes of low blood counts in patients with DC needs to be evaluated. Bone marrow evaluation on presentation and serially is thus essential to evaluate for morphologic and cytogenetic changes to help distinguish aplasia versus transformation versus consumptive causes of cytopenias in DC [9]. The disease has a marked genetic heterogeneity, as at least 14 genes are responsible for the shortening of telomeres which is characteristic of this disease [10].

Diagnostic tests include flow cytometry and fluorescent in situ hybridization (FISH) measurement of leucocyte telomere length which is regarded as a good screening test for DC. Individuals with very short telomeres (< 1st centile) should further be directed for genetic sequencing for DC genes. DC genes include DKC1, TERC, TERT, NOP10, NHP2, TINF2, USB1, TCAB1, CTC1 and RTEL1 [11]. In about 50% of patients with the classic features of DC the pathogenic mutations have not yet been identified, suggesting that additional genes are involved in the same pathway of telomere maintenance [12]. Managing DC requires a comprehensive multidisciplinary approach including early genetic diagnostic facilities which are crucial for timely family genetic counseling. There is no definitive treatment available for DC. Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is the only curative treatment for bone marrow failure in patients with DC [13]. Other temporary options include androgens or androgen-derivative therapy. Systemic retinoids administered at low doses have determined some improvement in skin and nails in DC, but the side and long-term effects are uncertain [14, 15]. DC prognosis can vary considerably from death in infancy (usually due to BMF) to that in the seventh decade. The major causes of death relate to BMF, cancer, and lung disease, particularly pulmonary fibrosis [16]. Advances in diagnosing and treating DC are now being extensively researched and this case report can be beneficial not only to the health care professional but also to those suffering from this rare disease. Non-availability of diagnostic and advanced treatment facilities in our setting represents a big challenge in the management of such patients.

**CONCLUSION**

DC is a rare genetic disorder with variable clinical expressivity. The case of a 12 year old girl, who had all the major clinical features- hyperpigmentation of the skin, nail dystrophy, oral leukoplakia and early bone marrow involvement- which before now had not been documented in Arunachal Pradesh, Northeast India is reported.

**Conflict of interest:** None

**REFERENCES**


