Cibtech Journal of Bio-Protocols ISSN: 2319–3840 (Online)
An Open Access, Online International Journal Available at http://www.cibtech.org/cjbp.htm
2015 Vol. 4 (2) May-August, pp.1-4/Agale et al.
Case Report

DYSKERATOSIS CONGENITA – A CASE REPORT

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ABSTRACT
Dyskeratosis congenita is a systemic disorder involving various body organs characterised by mucocutaneous pigmentation and bone marrow failure. It has various modes of transmission. Several genes have been mapped to the cause of this disease. Aplastic anemia is the most common cause of morbidity and mortality in these patients.

Keywords: *Dyskeratosis Congenital, Dyskerin Gene, Aplastic Anemia, Mucocuteous Pigmentation*

INTRODUCTION
Dyskeratosis congenita (DKC) is defined by presence of mucocutaneous pigmentation, nail dystrophy and leukoplakia. It is a genetic disorder with three modes of inheritance, i.e. X linked recessive, autosomal dominant, autosomal recessive. The X-linked variety is most common due to defective DKC1 (dyskerin) gene on chromosome Xq28. It was identified by Heiss *et al.*, (1998). Dyskerin gene has a role in cell cycle regulation and nucleolar function. Autosomal dominant type is due to mutation in hTERC, which encodes an RNA template, hTERT, which encodes the catalytic reverse transcriptase, telomerase. Telomerase mutation leads to inability in maintaining telomere length affecting the proliferative capacity of cells. Autosomal recessive inheritance is due to mutation in NOP10, NHP2, which have a important role in telomere maintenance leading to production of defective telomerase. Few patients show mutations in the shelterin component TIN2, a TRF1-interacting protein, clinically a severe phenotype and presence of very short telomeres despite normal telomerase activity (Beier *et al.*, 2012). Hoyeraal-Hreidarsson syndrome (HHS) is a severe variant of mutation in DKC1 gene, resembling DKC and is characterized by intrauterine growth retardation, microcephaly, delayed development, and bone marrow failure (Walne *et al*., 2013).

CASES
An 18 year old male presented with generalised weakness and yellowish discolouration of eyes and urine since one and half year.

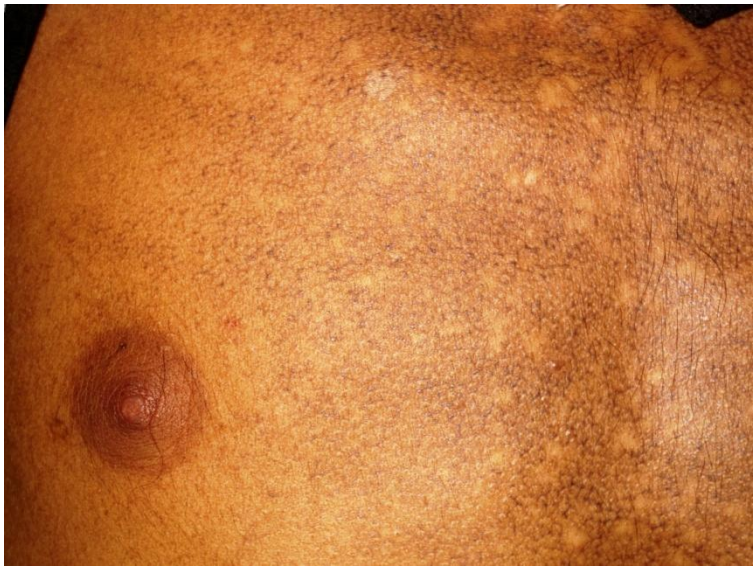

Figure 1: Clinical picture showing reticular skin pigmentation.

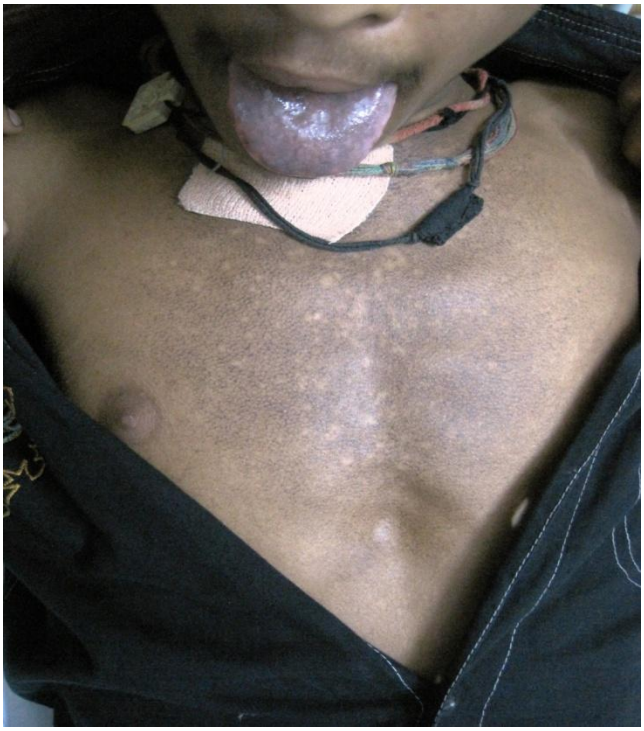

Figure 2: Oral leukoplakia with black pigmentation.

On examination, he had reticulate pigmentation all over the body including tongue (Figure 1-2). There was evidence of nail dystrophy (Figure 3-4).

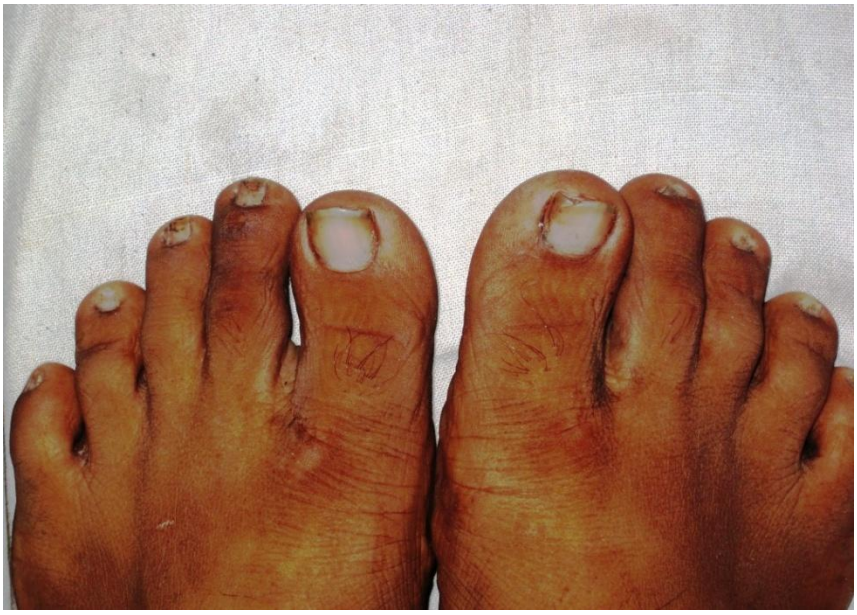

Figure 3: Nail dystrophy

Laboratory investigations showed haemoglobin-6gm%, total cell count- 1970/cmm with neutrophilia of 85%, reticulocyte count- 1.2%, red blood cell- 1.6million/cmm, random blood sugar-82gm/dl. Peripheral blood smear examination revealed pancytopenia with anemia of dimorphic type. USG abdomen showed mild splenomegaly and multiple collateral at splenic hilum, mildly prominent splenic vein with minimal

interbowel free fluid. Bone marrow examination showed a hypocellular marrow. Liver and kidney function tests were unremarkable. Skin biopsy showed mild hyperkeratosis and increased melanin pigment in basal layer of epidermis with melanin incontinence and collagenisation of dermis (Figure 5).

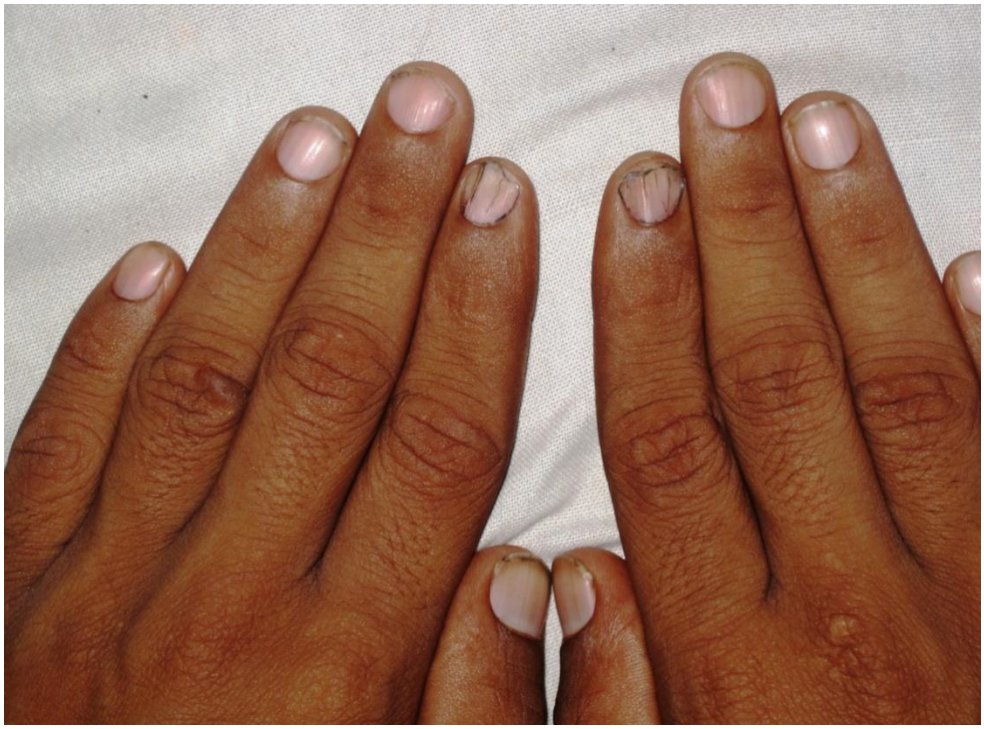

Figure 4: Nail dystrophy

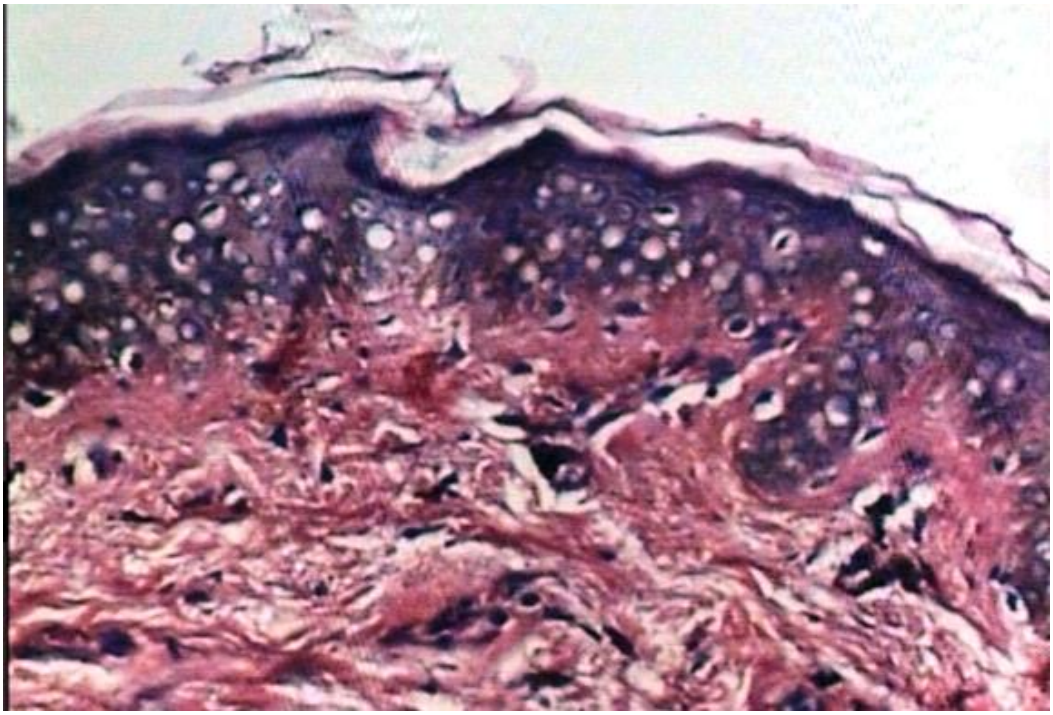

Figure 5: Skin histology showing mild hyperkeratosis, increase basal layer pigmentation, melanin incontinence and collagenisation in dermis

DISCUSSION

Dyskeratosis congenita (DC) is a rare, inherited bone marrow failure syndrome characterised by defective telomerase and hence, inability to maintain telomere length. Dyskeratosis is Latin word signifying irreversible degeneration of skin tissue, and congenita means inborn. DC was first described in 1906 by Zinsser. It is also known as Zinsser-Cole-Engman syndrome.

The clinical manifestations of DC include abnormal skin pigmentation, nail dystrophy, oral leukoplakia and bone marrow failure (Vulliamy *et al*., 2006). Symptoms may appear at birth or in childhood, adolescence, or adulthood. The minimal clinical criteria (Inderjeet, 2009) for diagnosis of DC include the presence of at least 2 of the 4 major features (abnormal skin pigmentation, nail dystrophy, leukoplakia, and BM failure) and 2 or more of the other somatic features (epiphora, learning difficulties/developmental delay, mental retardation, pulmonary disease, short stature, extensive dental caries/loss, esophageal stricture, premature hair loss/greying/sparse eyelashes, hyperhiderosis, malignancy, intrauterine growth retardation, liver disease/peptic ulceration/enteropathy, ataxia/cerebellar hypoplasia, hypogonadism/undescended testes, microcephaly, urethral stricture/phimosis, osteoporosis/aseptic necrosis/scoliosis and deafness. Our patient had skin pigmentation and nail dystrophy as described in literature along with deranged liver functions, thus presenting with yellowness of sclera. DC predisposes to early onset of variety of malignancies like myelodysplastic syndrome (MDS), acute myeloid leukemia (AML), esophageal or head and neck cancer (Alter *et al*., 2009).

These patients are treated with anabolic steroids, granulocyte colony stimulating factor and erythropoietin; however, definitive treatment is bone marrow transplantation only (Sinha *et al.,* 2013). Unfortunately, prognosis remains poor in full blown case and most of the patient's die of some or the other complication. We lost our patient for follow up.

Conclusion

The better understanding of clinical symptomatology and pathogenesis with our enhanced knowledge about genetic mechanisms help in diagnosis and planning treatment approach for the patients of DC. Genetic counselling in a family with known case is of prime importance.

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