Abstract

Dyskeratosis Congenita (DKC) is a rare progressive bone marrow disorder associated with multi-systemic involvement. It is also characterized by triad of abnormal skin pigmentation, nail dystrophy and mucosal leukoplakia. Liver cirrhosis and portal hypertension are said to be uncommon among these patients. We hereby report a case of an adult male who presented with pancytopenia, abnormal skin pigmentation, nail dystrophy and mucosal leukoplakia. Skin biopsies along with clinical features confirmed the case. Imaging studies were reported as suggestive of portal hypertension. Liver biopsy done but non-conclusive. Patient’s one son and one daughter also had similar skin pigmentation.

Dyskeratosis Congenita with Portal Hypertension of Unknown Etiology

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Introduction

Dyskeratosis Congenita, also known as a Zinsser Engman Cole syndrome, is a genetically heterogenous disorder characterized by progressive bone marrow failure and triad...
of abnormal skin pigmentation, nail dystrophy and mucosal leuoplakia. Here we report a case of adult male patient who presented with complaints of dyspnea on exertion, easy fatiguability, generalized weakness, pancytopenia over 3 years and pigmentation of skin, tongue, oral mucosa, nail deformities of both fingers and toes over 15 – 20 years with similar skin changes in son and daughter.

Case Report

A 33 year old male patient, non – addict, was admitted to the hospital with complaint of class II dyspnea, easy fatiguability and generalized weakness since 3 years. He also had pigmentation of skin of the chest, back and both lower limbs with both fingers and toe nails deformities since 10 years of age. There was no family history of skin and haematological disorders excepting his one son and one daughter who were having the same type of skin pigmentation. He was admitted 3 years back to peripheral hospital for malarial fever and on peripheral blood smear was found to have pancytopenia. He also had history of 4 units of blood transfusion.

On admission to our hospital, physical examination showed pallor, muddy sclera, epiphora with distorted eye – lashes and mild splenomegaly. Dermatologic findings were reticulated skin pigmentation affecting the face, chest, back, abdomen (Fig. 1) arms and legs. Dystrophic nail changes with longitudinal striations and deformities were present (Fig. 2, 3). Leuoplakia was present on the tongue (Fig. 4). Histopathology of the skin showed mild basket weave orthokeratosis with hpograulosis and thinned epidermis. The basal layer was pigmented. Dermis showed multiple melanophages and parivascular lymphocytic infiltrate. Thickened bundles of collagen and follicles filled with keratin were seen, all of which were consistent with the diagnosis of DKC. Complete blood count revealed pancytopenia.
with haemoglobin 9.4 g/dl, white blood cell count 2100 mm\(^3\) and platelet count 26000 mm\(^3\). Peripheral blood smear showed moderate anisocytosis, mild poikilocytosis, normocytic normochromic anaemia with feellipocytes seen along with macroplatelets. Routine blood biochemistry was normal. Bone marrow biopsy showed normocellularity and erythroid hyperplasia suggesting that pancytopenia might be due to a haemolytic process such as hypersplenism.

Abdominal ultrasound revealed splenomegaly, splenorenal shunts, dilated portal and splenic vein. Pertoovenous Doppler revealed portal hypertension, liver cirrhosis and mild splenomegaly. Upper gastrointestinal endoscopy showed grade II – III esophageal and gastric varices and severe portal hypertensive gastropathy in fundus. Liver scan showed liver function maintained with left lobe hepatomegaly, mild splenomegaly with colloid shift suggestive of early liver cirrhosis. Other causes of liver cirrhosis such as viral, autoimmune, Wilson disease and haemochromatosis were ruled out by investigations such as HBsAg, Anti – HCV, ANA, Anti – KLM, AMA, Anti – SMA, KF ring, serum ceruloplasin, 24 hours urinary copper level and serum iron studies. Finally liver biopsy was planned but in view of thrombocytopenia percutaneous approach was precluded in performing liver biopsy because of a vascular anomaly at the bifurcation of the internal jugular and subclavian veins but we found no difficulty in performing trans-jugular liver biopsy.

Our patient did not have any other abnormalities such as genitourinary, skeletal or vascular abnormalities as mentioned in the literature. Our patient has 2 children, one son and one daughter, both of them having the same type of skin pigmentation suggesting possibly the autosomal dominant mode of inheritance.

### Discussion

Dyskeratosis congenital is a rare progressive bone marrow failure disorder with multi-systemic involvement leading to increased predisposition to fatal pulmonary infection and malignancy leading to early morbidity and mortality.\(^{3,4}\) The mean age of diagnosis is approximately 20 years of age.\(^{6}\) Our patient was diagnosed by 33 years of age and he developed skin pigmentation and nail abnormalities by 10 years of age similar to other cases as mentioned in the literature.\(^{7}\)

The estimated incidence is about 1 in 1 million. Males are more affected than females with the ratio being 3:1 to 10:1. The principal causes of early morbidity and mortality and progressive bone marrow failure (pancytopenia in approx 90% of cases), predisposition to malignancy and fatal pulmonary infections.\(^{3,4}\)

DKC is genetically heterogenous, with X – linked recessive, autosomal dominant and autosomal recessive subtypes and is related to telomerase dysfunction. In the X-linked recessive form, the gene defect lies in the DKCI gene (located at Xq28), which encodes for the protein dyskerin. Dyskerin is composed of 514 amino acids and has a role in ribosomal RNA processing and telomere maintenance. In the autosomal dominant form, mutations in the RNA component of telomerase (TERC) or telomerase reverse transcriptase (TERT) are responsible for disease phenotype. Defects in the NOP10 gene were found in association with autosomal recessive DKC.\(^{3,4}\)

Along with skin, nail and oral mucosa, pulmonary, genitourinary, skeletal, neurological, ophthalmic, dental and gastrointestinal systems are affected.\(^{3,7}\) In gastrointestinal system, the findings such as esophageal strictures, webs, hepatosplenomegaly and cirrhosis are seen in 10% of cases.\(^{7}\)

Our patient had two major system affections such as skin and liver along with ocular involvement in form of epiphora and distorted eye – lashes out of various system affection as mentioned in the literature. Incidentally bilateral moderate sensorineural hearing loss was also noted. Dental abnormalities in form of tooth decay were also present.

Gastrointestinal findings such as esophageal strictures, hepatomegaly or cirrhosis are seen in 10% of cases.\(^{9}\) Other abnormalities such as anal strictures, esophageal diverticula, gastroduodenitis, duodenal ulcers and chronic diarrhea have also been reported.\(^{10}\) Association of portal hypertension with DKC has been extremely uncommon and if present is either due to cirrhotic and non cirrhotic mechanisms.

Brown et al\(^{9}\) and Kawaguchi et al\(^{11}\) have suggested a possible association with non cirrhotic portal hypertension in their article. Yusuf YAZGAN et al mentioned in his article difficulty in performing liver biopsy because of a vascular anomaly at the bifurcation of the internal jugular and subclavian veins but we found no difficulty in performing trans-jugular liver biopsy.\(^{12}\)

Our patient did not have any other abnormalities such as genitourinary, skeletal or vascular abnormalities as mentioned in the literature.\(^{7}\) Our patient has 2 children, one son and one daughter, both of them having the same type of skin pigmentation suggesting possibly the autosomal dominant mode of inheritance.

### Conclusions

Dyskeratosis congenital, though a rare multisystemic disease, should be considered in the differential diagnosis of any patient presenting with reticulated skin pigmentation, dystrophic nail changes, mucosal leucoplaikia and pancytopenia. Thorough portal hypertention is said to be extremely uncommon with DKC, seeing the case report and study by Brown et al,\(^{9}\) Kawaguchi et al,\(^{11}\) Yusuf YAZGAN et al\(^{12}\) and our case one should look for it in a case of DKC. Any patient diagnosed to have Dyskeratosis congenital family screening should be done.

### References

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