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Case Report

Dentistry Section

# Zinsser-Cole-Engman Syndrome: A Rare Case Report

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## ABSTRACT

Zinsser-Cole-Engmann syndrome also called Dyskeratosis Congenita (DKC) is a rare genodermatosis first described by Zinsser in 1906. Mutations in DKC1 gene is responsible for DKC. It is usually inherited as an X-linked recessive trait, resulting in a striking male predilection. It is characterized by a triad of reticular skin pigmentation, nail dystrophy and mucosal leukoplakia. Complications include predisposition to malignancy and bone marrow failure. Here, we report a case of DKC in a 9-year-old boy with classic triad of signs. Special investigations like endoscopy, barium swallow and bone-marrow aspiration study confirmed the diagnosis. There is no effective treatment for DKC. Some preventive measures can be adopted and the only long term cure for the haematological abnormalities is allogenic haemopoietic stem cell transplantation.

**Keywords:** Dyskeratosis congenita, Hyperpigmentation, Leukoplakia

## CASE REPORT

A 9-year-old boy reported to the Department of Pedodontics and Preventive Dentistry, with the complaint of difficulty in swallowing hot and spicy foods since one year. He was apparently asymptomatic four years back, then developed a small white patch on the left margin of the tongue. History and clinical features revealed other findings like ulceration of skin on even minor trauma, loss of appetite, nail changes since two years, photo sensitivity since one year, dengue haemorrhagic fever along with difficulty in swallowing. The dystrophic changes resulted in rudimentary nails without sharp demarcation between the nails and the skin [Table/Fig-1]. There was no history of consanguineous marriage, other siblings were normal and no other family members had similar complaint.

On general examination the child was thin built, ill-nourished and anaemic. On cutaneous examination a scaly patch of size 10x 4cm (approximately) was present on the scalp over the vertex. Reticulate pigmentation was present over the helix of the ears, concha, cheeks, neck, upper chest, upper limbs and lower limbs [Table/Fig-2]. Skin over the forearms and hands was shiny and with erythematous rash which showed blanching. Atropic macules were present over the elbows. Healing wounds were seen over the left medial malleous and right dorsum of foot [Table/Fig-3]. Excessive watering (epiphora) and redness was seen around right eye [Table/Fig-4].

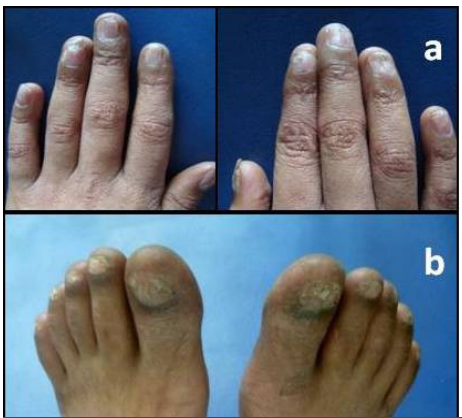
On intra-oral examination bilateral hyper pigmented plaques with erosion and ulcers were seen on the buccal mucosa [Table/Fig-5]. Tongue was eroded and white irregular patch was present over the dorsum [Table/Fig-6].

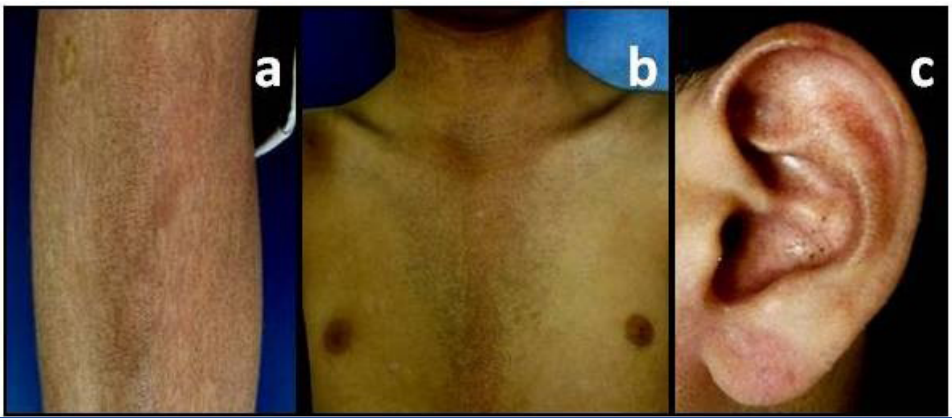
### Differential Diagnosis

The clinical findings were suggestive of Dyskeratosis Congenita (DKC) should be differentiated from other conditions that cause skin pigmentation such as Fanconi's anemia and Graft versus host disease. However, in Fanconis anemia, pigmentation of skin is more uniform and other than bone marrow failure, eye, renal and limb anomalies will also be present. In graft versus host disease similar skin pigmentation and nail features may be occasionally seen but these changes manifest after the transplantation of bone marrow. Skin lesions in Bloom's, Kindler's and Rothmund-Thomson syndromes may be similar to that seen in DKC, but are more sun sensitive and also differ in associated features [1].

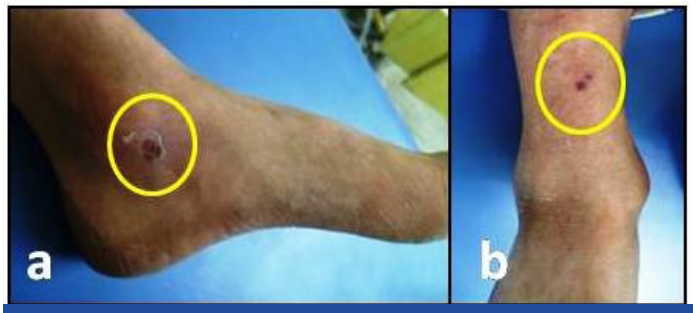
### Laboratory findings

Routine blood examinations were normal except mild hypochromic Red Blood Cells (RBC). But significantly lower levels of White Blood Cells (WBC: 58,000 cells/mm$^3$), and very high Erythrocyte Sedimentation Rate (ESR) values (1$^{st}$ hr – 65mm) were seen. Lipid profile was normal. Ultrasonography of abdomen revealed no abnormality. Endoscopy was not negotiable beyond the post-cricoid area due to the presence of a web [Table/Fig-7]. Patient was




**[Table/Fig-1]:** Rudimentary nails of (a) hands and (b) legs. **[Table/Fig-2]:** Reticulate pigmentation of skin on lower (a) limbs (b) upper chest and (c) concha.

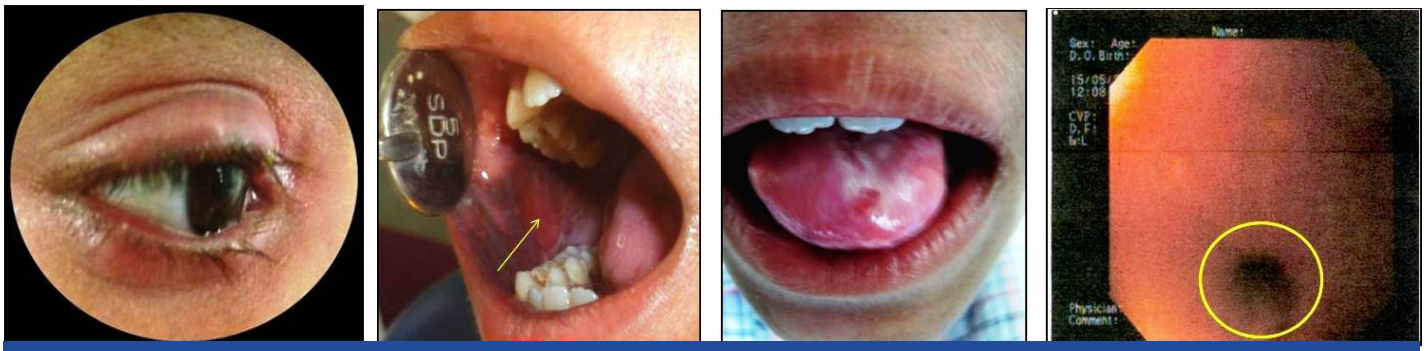



**[Table/Fig-3]:** Healing wounds over left medial (a) malleolus and (b) dorsum of foot.

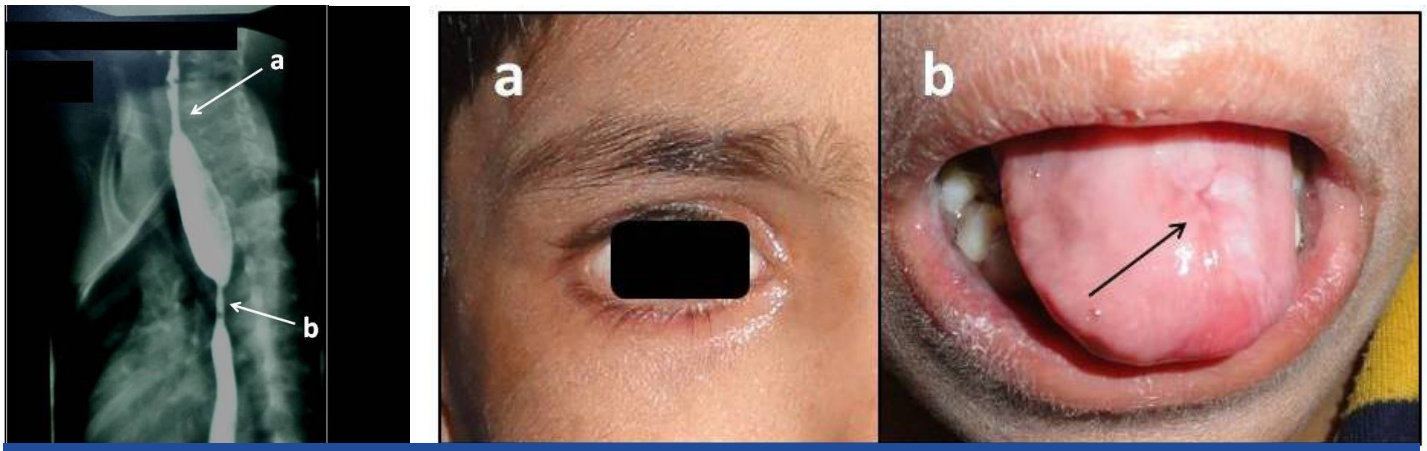
lesion over dorsum of the tongue reduced on follow-up [Table/Fig-9]. Patient was regularly monitored for any dermatological, hematological and malignant changes.

## DISCUSSION

Zinsser-Cole-Engman syndrome commonly called as Dyskeratosis Congenita (DKC) is a rare hereditary disease, which was first described by Zinsser in 1906. Later Engman (1926) and Cole et al., (1930) reported other cases in detail and hence it is known as Zinsser-Cole-Engman syndrome [1,2]. It is a rare genodermatosis that is usually inherited as an X-linked recessive trait, resulting in a



**[Table/Fig-4]:** Epiphora and redness around right eye. **[Table/Fig-5]:** Hyperpigmneted plaques with erosion and ulcer on the buccal mucosa. **[Table/Fig-6]:** White patch on dorsum of the tongue. **[Table/Fig-7]:** Endoscopy showing post-cricoid web.




**[Table/Fig-8]:** Barium radiography: Stricture in cervical oesophagus (a) at the level of C3-C4 vertebrae and (b) mid thoracic oesophagus showing stricture at the level of T4 vertebrae. **[Table/Fig-9a,b]:** (a) Reduced epiphora and redness around right eye and (b) reduced tongue lesion on follow up.

advised barium swallow followed by dilatation. On barium swallow test a smooth short segment stricture was noted at cervical oesophagus. Mild thoracic oesophagus also showed smooth short segment stricture with proximal dilatation [Table/Fig-8]. Post cricoids stricture was dilated up to 12.8mm. Several biopsies were performed in different tissues and sent for histopathological examination. Punch biopsy of right forearm, duodenum etc., were not significant. Findings of the biopsy of the tongue mucosa were consistent with a non-specific ulcer. But, findings in the biopsy of right buccal mucosa were consistent with DKC. Biochemical report showed significantly high levels of vitamin B12 (1162 pg/ml against normal range of 211-911 pg/ml). Bone marrow aspiration study showed an increased number of erythroid cells with myeloblastic changes. The erythroid to myeloid ratio was found to be 2:1. These findings in correlation with thrombocytopenic changes were suggesting the possibility of myeloplastic syndrome.

The child was put on oral retinoid (Acitretin 10mg) for treatment of oral lesions. Clobetasol propionate topical steroid ointment (Temovate 0.05% cream) was prescribe for symptomatic relief of oral lesions and for application on extraoral wounds antibiotic ointment (Soframycin) was advised. Levofloxacin (Levobact drops 0.5%) and hydroxyl propyl methylcellulose (Lubrex 0.5%) eye drops were prescribed for the relief of eye symptoms. Patient was responding well to the treatment. Eye symptoms and the striking male predilection [3,4]. Its onset is reported in individuals ranging from 5 to 50 years of age. Prevalence is estimated to be one in one million [5,6]. Mutations in DKC 1 gene at Xq28 has been determined to cause the X-linked form of DKC [1,2,7]. The mutated gene appears to disrupt the normal maintenance of telomerase, an enzyme that is critical in determining normal cellular longevity. It is characterized by a triad of nail dystrophy, reticulated hyper pigmentation of skin and mucosal leukoplakia [2]. The syndrome often proves fatal due to progressive bone marrow failure or malignant change within areas of mucosal leukoplakia [8].

In general, the abnormalities are not neonatal in manifestation, but develop progressively at a variable rate. The primary defect has not been identified and none of the proposed theories is able to account for all of observed features.

The basic defect in DKC may be at the level of cell division. The abnormality in one of the enzymatic steps essential to normal cell division, for example DNA polymerase II whose activity correlates positively with the rate of tissue regeneration, can lead to hypo-proliferation or impaired regeneration of the skin, nails, bone marrow, and neurons in DKC [3]. Study of the haematological involvements showed the bone marrow failure to result from a defect of stem cells rather than suppression by any circulating factor [1].

Clinical manifestations of DKC often appear during childhood. Pedodontists should be aware of this disorder for many reasons: orofacial symptoms may be the first signs of the disorder and clinicians will have the opportunity to make the diagnosis. The patient should be referred for genetic counselling, as other family members may be affected.

Secondly, oral leukoplakia in patients with DKC has a high risk of malignant transformation. Regular follow up is necessary. Squamous cell carcinoma is the most common malignancy and often complicates leukoplakia [6].

Reticular hyperpigmented areas of the skin are associated with atrophy of epidermis, capillary hyperplasia and melanin pigment deposited near the blood vessels. Brittle nails result in longitudinal splitting and furrowing. Complete loss of nails may sometimes be present. Involvement of eye in DKC can lead to epiphora, inflammation of eyelids (blepharitis), growth in fundus, and loss of eye lashes [4].

Preventive measures should be taken to reduce damage to teeth and gums. Dental abnormalities that have been reported include defects in enamel, periodontitis, loss of alveolar bone, extensive caries, hypodontia and short blunt roots, taurodontism [6].

There is no effective treatment for DKC. Only preventive measures can be adopted [4]. The only long term cure for the blood abnormalities is allogenic haemopoietic stem cell transplantation [9].

## CONCLUSION

Dyskeratosis Congenita (DKC) is a severe multisystem disorder associated with premature mortality usually due to Bone Marrow (BM) failure/immuno-deficiency. Dentist should be able to recognize this fatal condition in its early stages and advice appropriate haematologic investigations. Dentists may be the first to see and diagnose DKC and have an important role in monitoring the oral malignant changes in the mucosa.

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