

**CASE REPORT**

# Malrotation of Gut and Hiatus Hernia in a Child with Familial Dyskeratosis Congenita

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**Abstract**

Dyskeratosis congenita (DKC) is a rare inherited genodermatosis. We report familial occurrence of the disease. The index patient 12 years old had all classical features of DKC. There are 4 other siblings in the family suffering from similar disease. In additions to the features of DKC, the index patient presented with pain abdomen and vomiting. On investigation he had malrotation of gut and hiatus hernia. To the best of our knowledge this is being documented for the first time in association with DKC.

**Key Words**

Dyskeratosis Congenita, Malrotation of gut, Hiatus Hernia

**Introduction**

Dyskeratosis congenita (DKC) is a rare inherited bone marrow failure and cancer predisposition syndrome with a prevalence of 1 in 1 million people (1, 2). It is characterised by mucocutaneous triad of abnormal skin pigmentation, nail dystrophy and mucosal leukoplakia (2). It is caused by defects in telomere biology due to defective telomerase function (1, 3, 4). Gastrointestinal involvement is seen in form of esophageal stenosis, esophageal webs, enteropathy, peptic ulcerations, colitis, diarrhea, hepatosplenomegaly, and cirrhosis (3, 5). Bone marrow failure, malignancies and fatal pulmonary complication are the principal causes of early mortality (2). We encountered a classical case of DKC with familial occurrence. Malrotation of gut and hiatus hernia were responsible for chronic abdominal pain in our patient. This association have never been previously reported and prompted us to document.

**Case Report**

A 12 years boy presented with dull aching upper abdominal pain since early childhood. Pain was mild, usually encountered after the meals. There was no history of abdominal distension, constipation/obstipation though, he used to have off and on non-bilious vomiting. Also, since five years of age, child had nail changes in form of blackening, abnormal shape and loss of nails, first started in toes and then involved all nails. Black pigmentation of

dorsum of tongue and excessive sweating of palms and soles were also noted since 5 years of age. Younger sibling (9 years male) and 3 other male children (15 years, 11 years, and 9 years) on maternal side also had history of nail changes and black pigmentation of tongue. (*Fig 1*)

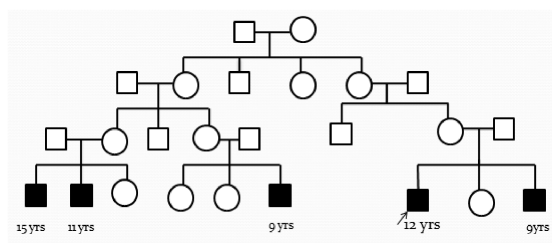
His height and weight was normal for age. Dorsum of tongue had leukoplakia and black pigmentation. Reticulate hyperpigmentation was noted over upper chest and neck. All nails were atrophied, thinned, distorted with loss of few nails. (*Fig 2*) Palms and soles were moist. Hepatomegaly was noted with liver span of 15 cm. Rest of systemic examination was normal. On basis of triad of nail dystrophy, reticulate skin hyperpigmentation and oral leukoplakia and pigmentation clinical diagnosis of DKC was made.

Laboratory investigations demonstrated hemoglobin of 12.6 gm/dl, total white cell count of 8700/mm<sup>3</sup>, platelet count of 2.5 lacs/mm<sup>3</sup>, and normocytic normochromic blood picture. Upper gastrointestinal endoscopy revealed hiatus hernia and normal stomach, first and second parts of duodenum. Barium meal follow through showed malrotation of midgut. (*Fig 3*) Liver and renal function tests were normal as were stool examination, chest radiograph, colonoscopic examination and karyotype.

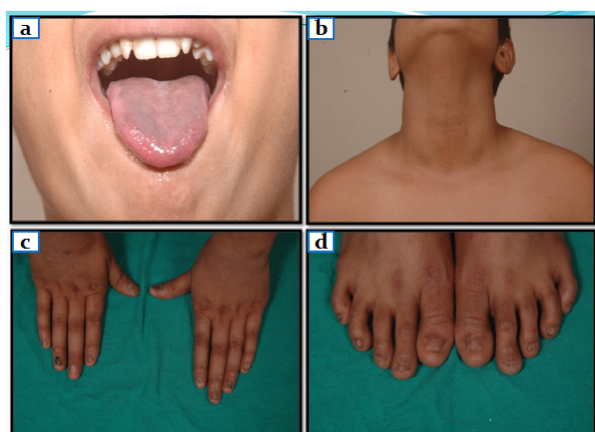
He was treated with rabeprazole and domperidone and his symptoms of pain abdomen and vomiting improved

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**Fig.1**



**Fig.2 Nail Changes & Black Pigmentation of Tongue & Nails Atrophied, Thinned, Distorted with Loss of Few Nails**

on follow up. About midgut malrotation, pediatric surgery consultation was taken; they suggested no active intervention is required at present since his symptoms are improved. But he was told to report in case of severe abdominal pain, vomiting or obstipation suggestive of SAIO.

### Discussion

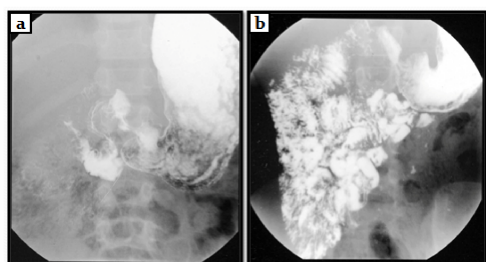
The name, dyskeratosis congenita (DKC), was derived after the description by Zinsser, in 1910, of two brothers who had nail dystrophy, oral leukoplakia, and skin pigmentation and later by Engman and Cole leading to the designation Zinsser-Engman-Cole syndrome (6). Early reports focused on the dermatologic features. As more cases were described with other medical complications, it became clear that DKC is a complex, multisystem disorder and affects all systems of the body (6, 7). More than 500 cases have been reported in the literature (8).

DKC is a genetically heterogeneous, with X-linked recessive, autosomal dominant and autosomal recessive subtypes. DKC is related to telomerase dysfunction (4, 9). All genes associated with this syndrome (i.e. DKC1, TERT, TERC, and NOP10) encode proteins for the

telomerase complex (3, 10, 11). Telomeres are repeat structures found at the end of chromosomes that function to stabilize chromosomes with each round of cell division, they have critical role in preventing cellular senescence and cancer progression. Rapidly proliferating tissues with the greatest need for telomere maintenance (e.g., haematological and dermatological system) are at greatest risk of failure (12). The present patient had X-linked disease as 3 male cousins on maternal side and one brother had features of DKC.

The triad of reticular hyper-pigmentation of the skin, nail dystrophy, and leukoplakia are the characteristics DKC. Patient, usually present during first decade of life, with the skin hyper-pigmentation and nail changes typically appeared first. The mucocutaneous features typically develop between ages of 5 and 15 years. Male to female ratio is approximately 13:1 (3). Abnormal skin pigmentation noted in 90% patients in form of lacy, reticular pigmentation, primarily of the neck and chest; may be subtle or diffuse hyper- or hypopigmentation (2, 3). Nail dystrophy occur in 88% cases in form of abnormal fingernails and toe nails, with ridging, flaking, or poor growth, or more diffuse with nearly complete loss of nails. Finger nails involvement often preceding toe nail involvement. Mucosal involvement occurs in around 80% cases in form of leukoplakia typically involves oral mucosa, tongue and oropharynx. All these characteristic findings are there in present patient. Early greying of hairs or hair loss (16%) and hyperhidrosis (15%) also seen in DKC. Other mucosal sites may be involved (e.g. oesophagus, urethral meatus, glans penis, lacrimal duct, conjunctiva, vagina, and anus). Constriction and stenosis at these sites leads to dysphagia, dysuria, phimosis, and epiphora. Ophthalmic manifestations reported in 80% patients in form of epiphora (30%) due to stenosis of the lacrimal drainage system, blepharitis, sparse eyelashes, ectropion, entropion, trichiasis, and exudative retinopathy (Revesz syndrome). Pulmonary fibrosis and pulmonary vascular abnormalities are seen in 20% cases.

Gastrointestinal finding include oesophageal stenosis/webs (17%), enteropathy, hepatosplenomegaly and liver fibrosis and cirrhosis. We noted hepatomegaly in present patient. In addition he also had malrotation of gut and hiatus hernia which has not been documented with DKC earlier. Musculoskeletal problems include osteoporosis (5%), avascular necrosis of the hips and shoulders, scoliosis, and mandibular hypoplasia. Neurologic involvement occurs as developmental delay, mental retardation (25%), microcephaly (5.9%), cerebellar hypoplasia (Hoyeraal-Hreidarsson syndrome), intracranial



**Fig 3. Barium Meal Follow Through Showed Malrotation of Midgut**

calcifications (Revesz syndrome), learning disabilities, and ataxia (6.8%). Hypogonadism/undescended testes (5.9%), short stature (19.5%) and intrauterine growth retardation (7.6%) also reported with DKC.

Bone marrow failure (BMF) occurs in 85-90% of patients. It is major cause of death with approximately 70% of deaths related to bleeding and opportunistic infections. Increased risk of malignancies (8.8%) especially malignant mucosal neoplasms like squamous cell carcinoma (SCC) of mouth, nasopharynx, oesophagus, rectum, vagina or cervix (often occur at sites of leukoplakia), SCC of skin, Hodgkin lymphoma, adenocarcinoma of GIT, myelodysplasia and bronchial and laryngeal carcinoma (8). Malignancies tend to develop in third decade of life.

Accurate diagnosis of DKC is critical, especially because therapy for complications, such as BMF or cancer, often is urgent (3). Appropriate tests should be performed to screen for bone marrow failure, pulmonary disease, neurological disease and mucosal malignancies. Mutation analysis is useful in confirming diagnosis. Genetic testing for occult DKC should be considered in patients with aplastic anaemia. Patients and family members without a known mutation can be screened with fluorescence in situ hybridization (FISH), which can identify very short telomeres in both clinically apparent and silent disease (13).

The medical management of DKC is complex and must be based on patient-specific needs. Short term treatment options for bone marrow failure (BMF) in patients with DKC include anabolic steroids (oxymethalone), granulocyte macrophage colony-stimulating factor, granulocyte colony-stimulating factor, and erythropoietin (14). However, the long-term curative option is hematopoietic stem cell transplantation (HSCT). Patients with DKC are at high risk for malignancies and bone marrow failure, frequent monitoring for early detection of these complications is recommended.

The diagnosis of DKC in index patient was supported

by the presence of classical triad of pigmentary changes of the skin, nail dystrophy, leukoplakia and black pigmentation of dorsum of the tongue. In addition, he had hyperhydrosis, hepatomegaly, malrotation of gut and hiatus hernia. There was no hematological abnormality in our patient. He is in regular follow up and doesn't manifest any features of bone marrow failure, malignancy or any other complication over last 2 years.

### Conclusion

A 12 years boy is reported with X-linked recessive DKC with malrotation of gut and hiatus hernia but without bone marrow involvement. Malrotation of gut and hiatus hernia are reported first time in association with DKC.

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