CASE REPORT

DYSKERATOSIS CONGENITA: A RARE CASE REPORT

Dr. Shreya Das*, Dr. (Prof.) Anjana Mazumdar**, Dr. Sandip Ghose***

ABSTRACT

Dyskeratosis congenita is a rare hereditary disorder, estimated to occur in 1 in 1 million people. Most cases are inherited as X linked recessive trait resulting in a striking male predilection. The disease is characterized by a classic triad: nail dystrophy, skin pigmentation and oral leukoplakia. These patients may also exhibit involvement of various organs like lung, G.I. tract, genitourinary tract, brain and teeth. Early mortality is often due to bone marrow failure, infection, fatal pulmonary complication or malignancy. Here, a case of dyskeratosis congenita in a 14 year old boy is presented who had all the characteristics of classic triad and few additional features.

KEY WORDS

Hyperpigmentation, nail dystrophy, leukoplakia

ABOUT THE AUTHORS

*3rd year PGT, **Professor & Head Of The Department ***Assistant Professor

Department Of Oral Pathology, Dr. R. Ahmed Dental College & Hospital, Kolkata-700014

INTRODUCTION

Dyskeratosis congenita, (DKC) also known as Zinsser-Engman-Cole syndrome, is a multisystem disorder[1]. It is characterized by hyperpigmentation, abnormal nail growth, lesion in the mouth, progressive bone marrow failure, pulmonary disease and an increased risk of malignancy. Although it is estimated to occur in 1 in 1 million people but it is important for clinician to diagnose and thereby prevent early death[2]. 85% of all cases are inherited as X linked recessive form and rest 15% is either autosomal dominant or recessive. Since the X linked variant of Dyskeratosis congenital is most commonly observed, the ratio of affected men to women is approximately 13:1[3]. Mutation in the DKC1 gene, located at the Xq28 site is responsible for the X-linked form of Dyskeratosis congenita whereas the disease with autosomal dominant inheritance is due to mutation in other genes such as telomerase RNA component /TERC and TERT, TINF2. Mutation in NOP10 (also known as NOLA3) causes autosomal recessive type of DKC.

CASE REPORT

A 14-year-old boy was referred to the Department of Oral Pathology at the Dr. R. Ahmed Dental College and Hospital (Kolkata-14) from an outside clinic regarding the management of severe burning sensation all over the mouth during taking hot and spicy food. The patient presented with a 1-year history of nail dystrophy which was unresponsive to antifungal therapy and 3-month history of extensive oral ulceration that failed to respond to topical corticosteroid therapy.

His medical history revealed mild dysphagia for past 2 years along with learning difficulties. He had no other complain like cough, bowel or urinary problems.

A. CLINICAL EXAMINATION

Upon first visit to the Oral Pathology OPD, a thorough clinical examination revealed bilateral hyperkeratotic white patch on buccal mucosa (fig- 1) which was present for last three months. The patches were symmetrical and measured about 1 cm in


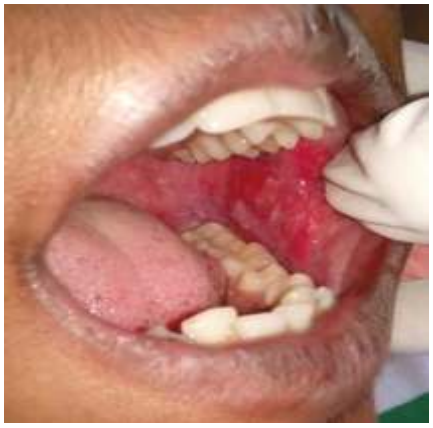

Fig 1 : Showing hyperkeratotic white patch on buccal mucosa (A &B)

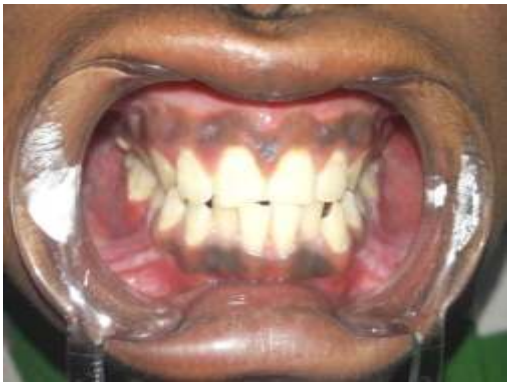
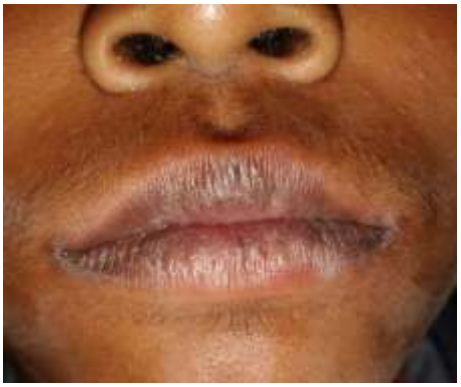

Fig 2 : showing hyperpigmented areas over attached gingiva and lips (A & B)

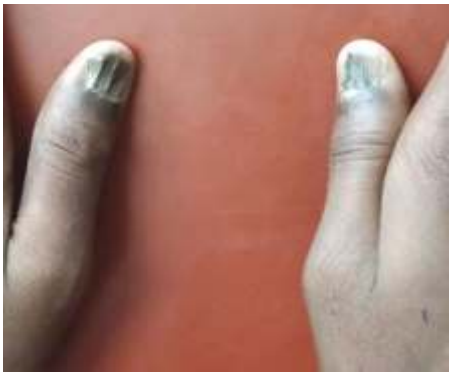


Fig 3 A: Showing dystrophic finger nails with ridging and longitudinal fissuring B. Progressive atrophy, thinning and distortion of nails after few months

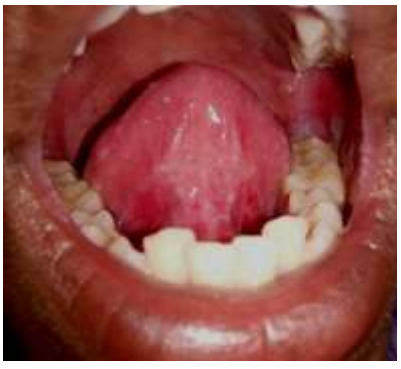
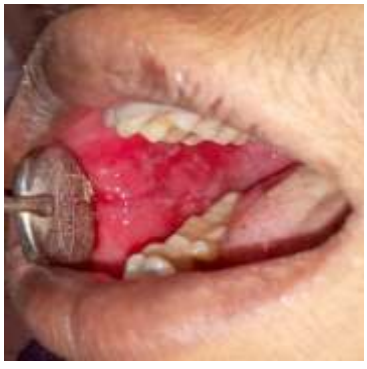

Fig 4 A : showing erythematosus patch over ventral surface of tongue B. over buccal mucosa

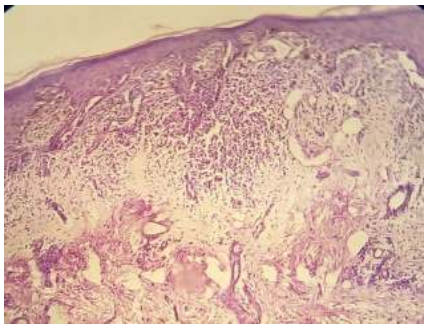

Fig 5: showing cross-sectional slide of biopsy of the buccal mucosa displaying inflammatory infiltrate in the subepithelial and perivascular region (hematoxylin-eosin stained)

diameter. Hyperpigmented areas were also observed over lips and attached gingiva (fig-2). Some of his finger nails were markedly dystrophic. Patient reported disfigurement of the nails which started 2 months back. Mainly the finger nails were affected but not toe nail (fig-3a). These nails were almost lost after few months (fig-3b). His medical examination revealed that his blood pressure, pulse rate, respiratory rate, and body temperature were within normal limit. Auscultation of the lung revealed clear breath sound without wheezes or rhonchi. The heart beat sounded regular without murmur.

B. FAMILY HISTORY

No family member ever complained of similar symptoms. He has siblings but they do not have any oral lesion, skin pigmentation or nail dystrophy. He had an uncle (maternal side) who died of blood cancer few years back.

C. PROVISIONAL DIAGNOSIS

The white patches were provisionally diagnosed as Leukoplakia.

D. INVESTIGATION

After thorough clinical examination, patient was advised for complete blood count, blood sugar estimation both Fasting and PP, bleeding and clotting time, serum vitB12 level, and antibodies for HIV, Hepatitis B and C, thyroid and liver function test, Chest X-ray, USG of whole abdomen. Hematologic investigation was performed to explore common causes of oral ulceration e.g. hemoglobin deficiencies or neutropenia. Radiologic investigation (orthopantomogram) was done to assess the dental status of the patient.

E. INVESTIGATION REPORTS

The investigation reports showed Hb level 10 gm/dl. Viral markers for hepatitis B, C and HIV were negative. Others (CBC, blood sugar both F and PP, BT, CT, serum vitB12 level) were within normal limit. Liver and thyroid function tests were normal. USG of whole abdomen and CT scan of the chest showed no abnormality. Nothing abnormality was detected in OPG. The day when patient turned up with his investigation reports, an additional finding of erythematous patch with peripheral radiating striae on ventral surface of the tongue was observed which was not present previously (fig-4a). These appeared to be like OLP. The oral lesions on the buccal mucosa had increased in size (fig-4b). Then the patient was advised for incisional biopsy for confirmation of provisional diagnosis of leukoplakia.

F. HISTOPATHOLOGY

Section stained with Hematoxylin and Eosin revealed the presence of hyperparakeratinized atrophic stratified squamous epithelium backed by fibro cellular connective tissue stroma with thick collagen bundles. Sub-basilar split was also noted. Few chronic inflammatory cells infiltrated in the connective tissue mainly in perivascular and juxta-epithelial areas (fig-5).

G. MANAGEMENT

He had taken several medications for his illness like antibiotic, corticosteroid, both systematically as well as topically with no improvement. Topical antifungal cream was prescribed to reduce the chances of superadded fungal infection. Topical anesthetic ointment was also advised to give comfort during eating. The patient was advised grinding of all sharp cuspal edges to prevent any trauma during mastication or any other jaw movements. Oral prophylaxis was performed and after that the patient was requested to maintain oral prophylaxis properly. He was given an alcohol free mouthwash to maintain the level of oral micro flora. On follow up it was found that the clinical symptoms like burning sensation, discomfort while taking food were reduced but the lesions persisted. Gradually complete resolution of the oral ulceration was achieved. Though bone marrow transplantation was not advised because there was no sign of bone marrow failure but a disturbing finding was the consistently deteriorating hemoglobin level, noted at 3 months interval after initial consultation. This prompted a referral to the Hematology Department of N.R.S. Medical Hospital (Kolkata). The patient remains well.

DISCUSSION

Dyskeratosis congenita (DKC) was first described by Zinsser in 1910. All genes associated with Dyskeratosis Congenita (DKC1, TERC, TERT, TINF2 and NOP10) encode proteins in the telomerase enzyme that is responsible for maintaining telomere length by addition of guanine-rich repetitive sequences[4]. However, the gene DKC1 mostly found to be mutated in X-linked 5 type of Dyskeratosis Congenita is located at Xq28. This gene encodes a protein, dyskerin which is involved in the production of ribosomal RNA, a chemical cousin of DNA, required for assembling protein building blocks (amino acid) into functioning proteins. Telomeres are found at the ends of chromosomes that function to stabilize chromosome. They have a critical role in preventing cellular senescence and cancer progression. Patients with DKC have reduced telomerase activity and abnormally short length of telomeric DNA compared to normal controls. It results in chromosomal shortening and gene loss during cell replication which ultimately leads to cell

apoptosis, particularly in highly proliferative tissues such as the hematologic and dermatologic systems[5]. Flow-FISH can distinguish the affected cases by the analysis of telomere length in comparison to age-matched controls[6]. DKC is characterized by the triad of skin hyperpigmentation, nail dystrophy and white plaque typically occurring in the oral cavity[7]. Nail dystrophy (mainly fingernail >toe nail) is the first sign of the syndrome to appear. Progressive atrophy, thinning and distortion result in small, rudimentary or absent nails[8]. In mild cases ridging and longitudinal fissuring occur. In this case, few finger nails were dystrophic. The mucocutaneous features of DKC typically develop between ages 5 and 15 years. The manifestations tend to progress as the patient grows older. Hypo or hyperpigmented macules or patches in a mottled or reticulate fashion are found mainly in the sun exposed areas of skin. In our patient few hyper pigmented areas were seen over lips and gingiva. Oral leukoplakia typically involves the buccal mucosa, tongue and oropharynx[9]. In this case, leukoplakia was present on the buccal mucosa and tongue. Other features occur with lower frequencies and involve virtually every organ[10]. The main causes of death are bone marrow failure/immunodeficiency, pulmonary complications including pulmonary fibrosis, abnormalities of pulmonary vasculature and malignancy[10,11]. In this case both lungs were completely normal.

Patients have an increased prevalence of malignancy mainly in the third decade of life, particularly squamous cell carcinoma of the mouth, nasopharynx, esophagus, rectum, vagina, or cervix. These often occur within the sites of leukoplakia. Other reported malignancies include Hodgkin lymphoma, leukemia, adenocarcinoma of the gastrointestinal tract, bronchial and laryngeal carcinoma[12]. In this case no malignancy was detected. Patients may have learning difficulties. Some patients are associated with conjunctivitis, lacrimal duct stenosis resulting in epiphora[12]. Patients may have mandibular hypoplasia, osteoporosis, avascular necrosis and scoliosis[13]. Some problems in gastrointestinal system such as esophageal webs, hepatosplenomegaly, enteropathy; cirrhosis and in genitourinary system like hypospastic testes and ureteral stenosis are occasionally found [14]. These findings were absent in this case except for learning difficulties. DKC is usually diagnosed by physical findings and with the help of telomere length testing and mutation analysis. The diagnosis of dyskeratosis congenita in this patient was supported by the presence of characteristic triad-hyperpigmentation, nail dystrophy, leukoplakia and few additional features like short stature, learning difficulties, dysphagia, anemia and epiphora. All the family members were screened by physical examination.

CONCLUSION

Dyskeratosis congenita though rare, is an devastating disorder with high morbidity and mortality and important for clinicians and dental surgeons to diagnose early and prevent death. There is no definite cure at this time for dyskeratosis congenita. Maintaining bone marrow function is the main goal as treatment protocol as this is the major cause of death. However, the long-term survival is impossible at present but the initial diagnosis is an effective treatment for DKC. Genetic counseling is also important for the planning of future pregnancy. Females who are carriers of the defective gene should be identified. An infant at risk for inheriting the disorder can be tested prenatally or after birth to allow for early diagnosis and treatment respectively.

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