Dyskeratosis Congenita: A Rare Case Report

Roy B[1], Mondal G[2], Paul D[3], Kalam A[4], Basu K[5]

[1]Dr. Banasree Roy, MBBS, DCH, MD, R.M.O. cum Clinical Tutor, Dr. B.C.Roy Postgraduate Institute of Paediatric Sciences, Kolkata 70054, West Bengal, India, [2]Dr. Gobinda Mondal, MBBS, MD, Assistant Professor, Department of Paediatric Medicine, Burdwan Medical College, West Bengal, India, [3]Dr. Dilip Kumar Paul, MBBS, MD. Medical Superintendent cum Vice Principal, Dr. B.C. Roy Postgraduate Institute of Paediatric Sciences, Kolkata 70054, West Bengal, India, [4]Dr. Abul Kalam, MBBS, MD, Assistant Professor, Dr. B.C.Roy Postgraduate Institute of Paediatric Sciences, Kolkata 70054, West Bengal, India, [5]Dr. Kausambi Basu, MBBS,DCH. Senior Resident, Dr. B.C.Roy Postgraduate Institute of Paediatric Sciences, Kolkata 70054, West Bengal, India.

Abstract

Dyskeratosis congenita is a rare congenital disorder affecting mainly the integumentary system. It is a progressive disease with involvement of bone marrow. A triad of hyperpigmentation, nail dystrophy and leucoplakia are characteristic of this disease.

Key words: Hyperpigmentation, nail dystrophy, leucoplakia

The Case

A seven year old Hindu boy born out of nonconsanguineous marriage presented with recurrent febrile episodes for last two months and nonspecific symptoms like pallor, lethargy and poor scholastic performance for more than a month.

Examination revealed pallor, few hyperpigmented macules over face (Fig. 1) & limbs, dystrophic nails in all four limbs. Mucosal leucoplakia was present in tongue only (Fig.2). Buccal and oropharyngeal mucosa were not affected.

Finger nails (Fig 3) were involved more than toe nails (Fig.4). All kind of changes like ridging, splitting, progressive atrophy, thinning, pterygium formation, rudimentary nails were present.

Patient gives history of excessive lacrimation without any reddening or irritation of eyes. Patient had no respiratory problem. Examination of abdomen revealed no organomegaly. Testes were palpable bilaterally; genitourinary system examination was within normal limits.

There was no family history of skin and hematological disorders.

Investigation

Blood picture was suggestive of anemia with hemoglobin level of 6.7g/dl; thrombocytopenia, platelet count being 30000 though patient had no spontaneous bleeding from any site. Total leukocyte count was 3400 with 45% polymorphs, 32% lymphocyte, 10% band cell and 12% monocyte and 1% eosinophil. Peripheral blood smear showed anisocytic hypochromic anemia with macro platelets. Reticulocyte count was 1.3%. Direct comb test, Hb electrophoresis, serum iron level, total iron binding capacity were normal. Liver function tests, renal function tests were normal.

Patient had an IQ of 60. Chest X ray was normal. X ray spine and hip were done to find out any scoliosis, avascular necrosis of femur. Only mild osteoporotic changes were noticed. USG abdomen revealed no abnormality.

Bone marrow aspiration study from iliac crest reveled bone marrow hypoplasia, decreased megakaryocytes and RBC precursor in marrow. Skin biopsy report can be mentioned in detail here.

Patient was offered supportive treatment. Patient was also treated with antibiotic. Platelet and packed RBC were transfused when platelet count fell below 20000/cmm and Hb% was 4.2 gm%. Erythropoietin and granulocyte colony stimulating factor injections were also given.

Address for correspondence
Dr. Banasree Roy
E-mail: drbr1978@rediffmail.com

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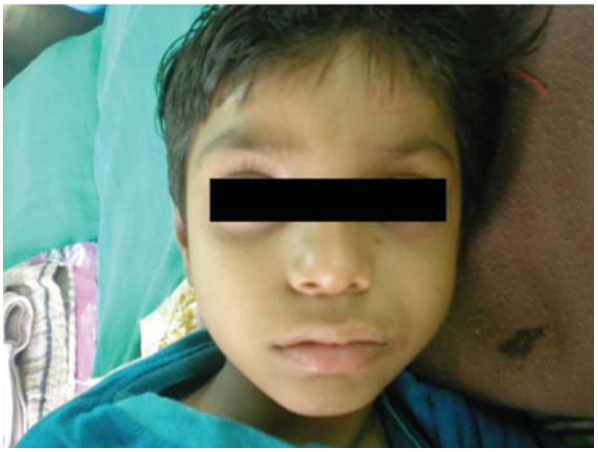

Fig 1: Pallor with hyperpigmented macule

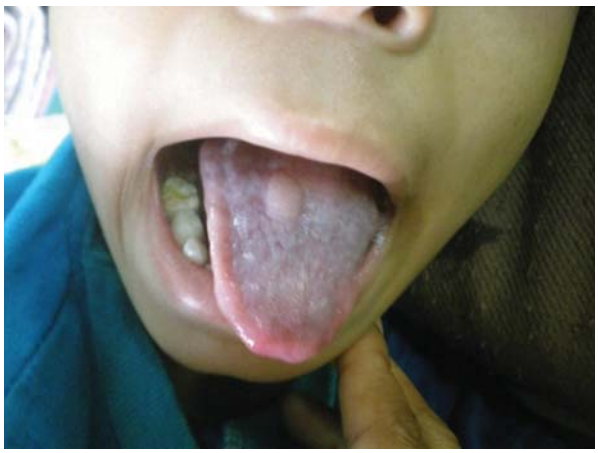

Fig 2: Leucoplakia of tongue

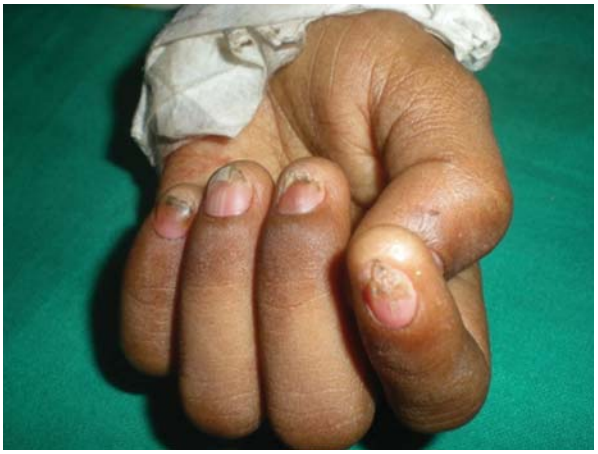

Fig 3: Nail changes of fingers

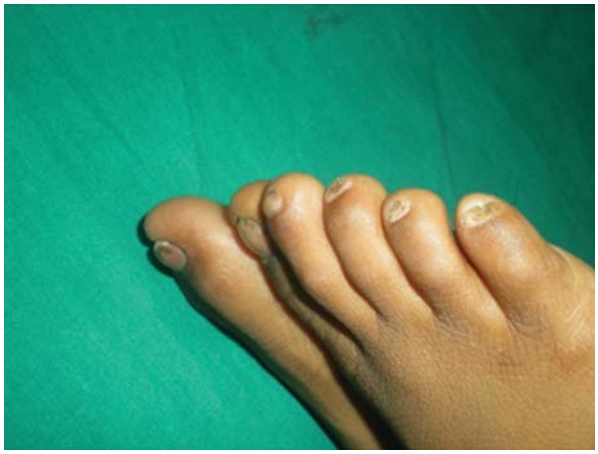

Fig 4: Nail changes of toes

Discussion

Dyskeratosis congenita (DKC) is also called Zinsser-Cole-Engman syndrome[1]. It is an inherited disorder of the mucocutaneous and haematopoietic systems in association with somatic abnormalities[2]. The exact prevalence of dyskeratosis congenita is unknown. It is estimated to occur in approximately 1 in 1 million people[3]. Skin and nail findings become apparent in the first 10 years whereas oral leucoplakia is seen later.The manifestations tend to progress as the patient grows older.

Patients develop aplastic anemia about 50% cases. It is also considered to be a premalignant condition[4]. Male to female ratio is 13:1[5]. Up to 85% of cases are inherited as X linked recessive form and rest 15% is either autosomal dominant or recessive forms. Major protein affected is dyskerin.These mutations affect telomerase activity[6].

Abnormal skin pigmentation is one of the prominent findings. Hypo or hyperpigmented macules or patches in a motteled or reticulate fashion are found. It is mainly found in sun exposed areas of skin. Alopecia of scalp may be associated[7]. In our patient only few hyperpigmented macules were present over face and upper limb. Typical skin changes were absent, so skin biopsy revealed only mild increase in melanin in dermis.

Mucosal leucoplakia occurs in approximately 80% of patients and typically involves the buccal mucosa, tongue, and oropharynx[7]. In our case leucoplakia was present over the tongue.

Approximately 90% of affected individual have peripheral cytopenia of one or more lineages. In some cases, this is the initial presentation as in our case, with a median age of onset of 10 years. Bone marrow failure is a major cause of death. Approximately 20% of individuals with DKC develop pulmonary complications, including pulmonary fibrosis and abnormalities of pulmonary vasculature[8].

Patients have an increased prevalence of malignant mucosal neoplasms, particularly squamous cell carcinoma of the mouth, nasopharynx, esophagus, rectum, vagina, or cervix. These often occur within sites of leucoplakia. The prevalence of squamous

cell carcinoma of the skin is also increased. Other malignancies reported include Hodgkin lymphoma, adenocarcinoma of the gastrointestinal tract, and bronchial and laryngeal carcinoma[9]. Malignancy tends to develop in the third decade of life. Patients may have learning difficulties and mental retardation. In our case no malignancy was detected.

DKC reportedly is associated with conjunctivitis, blepharitides, and pterygium. Lacrimal duct stenosis resulting in epiphora[9] occurs in approximately 80% of patients and it was one of the problems in presented case. Patients may have mandibular hypoplasia, osteoporosis, avascular necrosis, [10] and scoliosis. But only generalized osteoporotic changes were detected in present case.

Gastrointestinal system involvement may include esophageal webs, hepatosplenomegaly, enteropathy; cirrhosis and genitourinary system involvement like hypo spastic testes, hypospadias, and ureteral stenosis are occasionally found[11]. These findings were absent in our case.

Sufferers of DKC have been shown to have a reduction in telomerase RNA component (TERC) levels invariably affecting the normal function of telomerase which maintains these telomeres.[12,13,14] TERC levels down, telomere maintenance during development suffers accordingly

Genetic tests help identify the DKC1 gene mutation. Flow-FISH analysis can distinguish affected cases due to the very short telomeres compared to age-matched controls[15]. But this test was out of our scope.

There is no definite cure at this time for dyskeratosis congenita. Treatment is aimed at maintaining bone marrow function as this is the major cause of death. Few options are 1. Oxymetholone – an anabolic steroid that helps bone marrow function in two-thirds of patients for several years. 2. Haematopoietic growth factors – erythropoietin, granulocyte macrophage colony-stimulating factor and granulocyte colony-stimulating factor. 3. Bone marrow transplant from an unaffected family member or from unrelated donor with less aggressive pre-transplant therapy[16,17,18].

Although dyskeratosis congenita would seem to be an ideal condition for gene therapy, no progress has been made in this direction yet. Genetic counseling is important for the planning of future pregnancies. Ante-natal diagnosis has been achieved successfully. Since the DKC1 gene mutation has been associated with dyskeratosis congenita, individuals in the family of a person affected by the disorder can have genetic testing, and females who are carriers of the defective gene can be identified. An infant at risk for inheriting the disorder can be tested prenatally or after birth, allowing for early diagnosis and treatment respectively.

Our patient was discharged in afebrile condition. Parents were counseled for bone marrow transplantation. All the family members were screened by physical examination and peripheral blood picture.

Conclusion

Dyskeratosis congenita may present with pancytopenia initially before marked skin changes. It is important to consider the diagnosis in cases of bone marrow failure where no other cause has been identified and oral leucoplakia in a young person with no history of tobacco use and in early onset cancers.

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