

## Picture Story

# A female with dyskeratosis congenita

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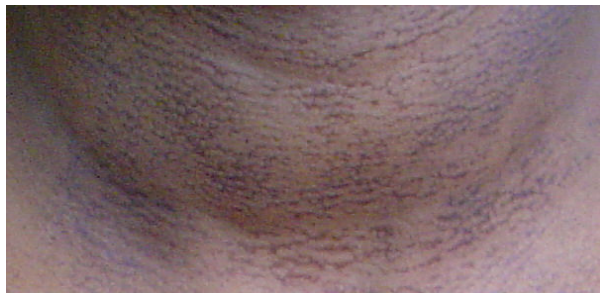
## Introduction

Dyskeratosis congenita is an inherited bone marrow failure syndrome, with multisystem involvement. Incidence is approximately 1 case per million population. 225 individuals have been reported in the literature<sup>1</sup>.

## Case report

An 11 year old girl, born to unrelated parents, was admitted with fever and gum bleeding. She was apparently well up to this presentation. Both parents and siblings (all females) were healthy. She has had learning difficulty in the school.

She was severely pale with no lymphadenopathy or organomegaly. There was reticulated hyperpigmentation prominent over the face, neck, chest and limbs including palms and soles suggestive of poikiloderma (Figure 1).



**Figure 1**

This was later confirmed by a dermatologist. She also had thin sparse hair and an atrophic tongue. Nails were dystrophic with longitudinal ridging (Figure 2).

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**Figure 2**

The haemoglobin was 5.5 g/dl and the platelet count was  $28 \times 10^9/L$ . Blood picture showed normocytic normochromic anaemia with low platelets. There was neutropenia but no atypical or immature cells. Trepine biopsy revealed moderately hypoplastic erythropoietic series and absent megakaryocytes in the bone marrow. A diagnosis of hypoplastic anaemia was made. Ham's test was negative and antinuclear antibodies were absent. A diagnosis of dyskeratosis congenita was made.

Initially she was given blood and platelet transfusions. She was treated with prednisolone 2mg/kg/24hrs. Six weeks later she developed avascular necrosis of the left femoral head and prednisolone had to be tailed off. She needs regular blood transfusions every 2-3 months now.

## Discussion

Dyskeratosis congenita is a rare disease which could be inherited as X linked recessive, autosomal recessive or autosomal dominant forms of inheritance. X linked recessive is the most common form of inheritance. Male: Female ratio is 10: 1<sup>2</sup>. The female carriers may have subtle clinical features. Mutant gene is DKC 1, located at Xq28. It encodes a protein called dyskerin, which has widespread tissue distribution<sup>2</sup>. This is involved in the regulation of the proliferative capacity of the cell.

Diagnosis is based on cutaneous and mucosal findings with bone marrow abnormalities. The cutaneous findings include reticulated or mottled pigmentation of the skin, hyperhidrosis of palms and soles, hyperkeratosis of palms and soles and adematoglyphia. Mucosal findings include leukoplakia mainly on the buccal mucosa, but other mucosal sites can get involved. These mucosal findings may not appear until the second or the third decade and on occasions, not until after the onset of bone marrow symptoms. Incidence of malignant neoplasms, particularly squamous cell carcinomas is increased in these patients. There is an increased incidence of dental caries and early tooth loss. Progressive nail dystrophy with ridging and longitudinal fissures occur with progressive atrophy. Mild to moderate mental retardation is found in 21% of patients.

Median age of diagnosis of initial haematological disease is about 16 years. First haematological manifestation is pancytopenia. Bone marrow shows aplastic anaemia which would develop in approximately 50% of the patients<sup>1</sup>. Hb F is increased<sup>3</sup>. Chromosome breakages have been observed in 10% of patients<sup>1</sup>. Predicted median age of survival is 33 years<sup>1</sup>. Majority of the patients die of bone marrow failure. They are also susceptible to squamous cell carcinomas and gut malignancies.

### **Treatment**

50% of the patients show a transient response to androgens<sup>1</sup> but relapses are common. Oxymetholone was not available for this patient. The only curative therapy to date has been bone marrow transplantation. However, the preparative regimens generally used during the bone marrow transplantation can adversely impact the susceptibility to malignancy. Steroids, granulocyte macrophage colony stimulating factors and erythropoietin may be helpful transiently. Treatment with multiple cytokines (IL-3, IL-6) may offer additional benefits<sup>1</sup>. Anti Thymocytic Globulin (ATG) is not recommended for these patients. Gene therapy may become a feasible consideration.

Once an index case has been identified, genetic counselling is important. The parents must be oriented to the pattern of inheritance and the prospect of prenatal diagnosis. This will allow early harvest and storage of their bone marrow for use after anticipated marrow failure.

### **References**

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