Congenital dyskeratosis: Zinsser-Cole-Engmann syndrome; a rare cause of aplastic anaemia

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Introduction

Congenital dyskeratosis, also known as Zinsser-Cole-Engmann syndrome is a rare degenerative disease. It is commonly transmitted as an X-linked recessive disorder but autosomal dominant and recessive forms have also been described. In its classical form it is characterised by the triad of abnormal skin pigmentation, nail dystrophy and leukoplakia. It is a rare but important cause of inherited aplastic anaemia.

Case report

A 21 year-old male presented to us with high grade fever associated with chills of one week duration. He was mentally retarded and had a short stature. There was a reticular pigmentation, involving mainly the neck (Figure 1). The skin of the dorsum of the hands and feet was atrophied and palms were hyperkeratotic (Figure 2 & 3). Nail dystrophy was noted with loss of some nails (Figure 2 & 3). There was leukoplakia involving the buccal mucosa. He was pale and there was a firm splenomegaly but liver was not palpable. He had axillary and facial hair and testicles of normal size. There was meatal stenosis. He developed gum bleeding and one episode of profuse haematemesis. There were choreoathetotic movements as well.

Figure 1 - Reticular pigmentation of neck.

Figure 2

Figure 3

Figures 2 & 3 - Atrophied skin on dorsum of hands and nail dystrophy.

His full blood count and blood picture revealed pancytopenia. Bone marrow trephine biopsy showed normal bone marrow architecture with hypocellular marrow spaces which were replaced by fatty tissue. This was compatible with marrow hypoplasia. Ultrasound abdomen showed splenomegaly with normal liver. Upper GI endoscopy demonstrated grade II oesophageal varices. Septic screen was negative with a normal chest X-ray, blood and urine cultures. Liver function tests were normal.

We treated him with IV antibiotics and his fever settled with IV ceftazidime. We transfused him with blood and platelets which temporarily improved his clinical condition. Banding was done for oesophageal varices.

The patient had three brothers: two were phenotypically normal; one had dyskeratosis and nail atrophy.

Discussion

Congenital Dyskeratosis is a rare multisystem, degenerative disorder with an estimated prevalence of 1 in 1,000,000. It shows considerable genetic and clinical heterogeneity. Tissues with high proliferation rates are mainly affected. The hallmark feature is the triad of abnormal skin pigmentation, nail atrophy and leukoplakia which was present in our patient. The skin and nail changes are the first to appear and are progressive. Bone marrow failure and aplastic anaemia appears in 80–90% by the age of 30 and is the leading cause of death. Our patient also had marrow hypoplasia affecting all three cell lines severely. There is variety of other clinical features including mental and physical retardation, absent hair, fragile bones, dental abnormalities, non-cirrhotic portal hypertension, oesophageal stricture, pulmonary fibrosis, primary hypogonadism, meatal stenosis and phimosis. Out of these features our patient had mental retardation, short stature, non-cirrhotic portal hypertension with splenomegaly and oesophageal varices and meatal stenosis. He also had choreoathetosis which was not described earlier.

Diagnosis is arrived at mainly by considering the presence of mucocutaneous triad supported by aplastic anaemia and other variable clinical features. It would sometimes be difficult to diagnose due to highly variable nature of clinical picture, onset and natural course of the disease. Confirmatory test is mutation analysis for genes DKC1(X-linked recessive), TERK, TERT, TINF2 (autosomal dominant), NOLA3 (autosomal recessive). As these tests were not available, it was not done in our patient.

Other than aplastic anaemia, these patients are at a high risk of developing malignancies of mucosal origin such as gastrointestinal and leukemias which further increases mortality. Therefore, screening is warranted. Our patient did not have evidence of any such, at presentation.

An anabolic steroid, oxymetholone can be used with a success rate of 60% for aplastic anaemia in these patients. Also recombinant granulocyte colony stimulating factor together with erythropoietin can be used. The definitive treatment is allogenic haemopoietic stem cell transplantation. Unfortunately, only erythropoietin is available for our patient and we are managing him conservatively at the moment.

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