Case Report

Dyskeratosis Congenita Presenting with Idiopathic Pulmonary Fibrosis: A Rare Case Report

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Abstract

Dyskeratosis congenita is an inherited bone marrow failure syndrome, characterised clinically by the classical triad of abnormal nails, reticular skin pigmentation, and oral leucoplakia and associated with very high risks of developing aplastic anaemia, myelodysplastic syndrome, leukemia and solid tumours. Though rare, it is diagnosed relatively easily when the clinicians suspect it. We present a case of a 70-year-old male presenting with pulmonary fibrosis alongwith dyskeratosis congenita. *To the best of our knowledge after extensive research of the literature so far no such case has been reported from India.*

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Key words: Dyskeratosis congenita , Idiopathic pulmonary fibrosis, Leucoplakia.

Introduction

Dyskeratosis congenita is a rare inherited disorder of ectodermal dysplasia characterised by the classical mucocutaneous triad of abnormal skin pigmentation, nail dystrophy and leucoplakia,[1–3] at least one of which is present in around 80% to 90% of cases of dyskeratosis congenita. The primary causes of death in patients with dyskeratosis congenita are bone marrow failure and immunodeficiency (60%-70%), pulmonary complications (10%–15%), and malignancy (10%).[4] *The present case is being reported because of its extreme rarity in incidence as well as presentation.*

Case Report

A 70-year-old male was referred to our hospital with complaints of breathlessness, cough with scanty mucoid expectoration and intermittent fever for the last six months with a provisional diagnosis of pulmonary tuberculosis. There was a history of tuberculosis five years back when the patient had taken anti-tubercular treatment under Revised National Tuberculosis Control Programme (RNTCP) on sputum positive basis which was completely cured. He remained asymptomatic till almost six months back.

On examination, patient had thickened and coarse nails (Figure 1) in all the fingers of all the four limbs. On further questioning, patient told that these were present since birth. Further evaluation revealed a white film on the tongue of the patient (Figure 2) and inside of the cheeks along with thickening of the skin of the hands and even the trunk. Therefore a diagnosis of dyskeratosis congenita was made, based on the presence of classical mucocutaneous triad. Respiratory system examination showed bilateral basal fine crepitations along with coarse creptitations in the right interscapular area. Examination of the other systems was within normal limits.

Figure 1. Photograph of the patient's hands showing thickened and coarse nails (nail dystrophy).

Figure 2. Photograph showing a white film on the tongue of the patient – oral leucoplakia.

His family includes two brothers who had no skin pigmentation or nail dystrophy. He has two children, one son and one daughter. Presently they also have no symptoms suggestive of dyskeratosis congenita.

Laboratory investigation showed haemoglobin and other biochemical tests within normal limits. Sputum for acid-fast bacilli was negative by Ziehl-Neelsen staining and

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molecular methods. Blood gas analysis showed a ph of 7.36, partial pressure of carbon dioxide (PCO_2) of 44.8, partial pressure of arterial oxygen (PaO_2) of 39.6, arterial oxygen saturation (SpO_2) saturation of 72.2, and a base excess of -1.8. Pulmonary function test revealed a restrictive pattern.

Chest radiograph (postero-anterior view) showed interstitial pattern. Computed tomography (CT) of the chest showed a diffuse parenchymal lung disease pattern with "definite usual interstitial pneumonia (UIP)" pattern (Figure 3). High resolution computed tomography of the chest showed interlobular, intralobular septal and sub-pleural interstitium thickening and reticular markings with traction bronchiectasis alongwith peripheral honey-combing and sub-pleural with basilar predominance suggesting a diagnosis of idiopathic pulmonary fibrosis.

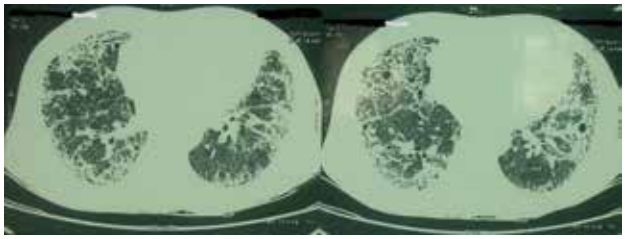

Figure 3. High resolution computed tomography of chest showing a diffuse parenchymal lung disease with "definite usual interstitial pneumonia" pattern.

His symptoms and laboratory findings did not support the possibility of autoimmune disorder. Since the chest computed tomography indicated typical UIP pattern alongwith the classic triad of dyskeratosis congenita, a diagnosis of idiopathic pulmonary fibrosis related to dyskeratosis congenita with leucoplakia was made.

Discussion

Dyskeratosis congenita, also called Zinsser-Cole-Engman syndrome, is a rare progressive congenital disorder with a highly variable phenotype characterised by the triad of abnormal skin pigmentation, nail dystrophy and mucosal leucoplakia. Although the classic triad is not seen in all the cases but its presence usually helps in the diagnosis of this condition, as was the case with our patient. Other common features include bone marrow failure and a variety of other non-cutaneous abnormalities (*e.g.*, dental, gastrointestinal, neurological, ophthalmic, pulmonary and skeletal).[1-3] Mutations in many genes are known to be the cause with X-linked, autosomal recessive and autosomal dominant modes of inheritance recognised alongside sporadic cases.[5] In the studies done so far, genetic success was not confirmed, but it is suggested that X-linked recessive is important because of higher prevalence in males than in females.[6] Although pulmonary manifestations of dyskeratosis congenita were believed to be uncommon, Dokal[1] reported that abnormal pulmonary features may be seen in as many as 10%–15% of the patients, which can be a cause of increased morbidity and mortality. Idiopathic pulmonary fibrosis (IPF) caused increased morbidity in our patient.

Idiopathic pulmonary fibrosis is defined as a specific form of chronic, progressive fibrosing interstitial pneumonia of unknown cause, primarily occurring in older adults, limited to the lungs, and associated with the histopathologic and/or radiologic pattern of usual interstitial pneumonia.[7] In the progressive fibrosis and scarring of the lung parenchyma leads to symptoms, such as dyspnoea on exertion, dry cough and, ultimately, respiratory failure and restrictive pattern on pulmonary function testing.[8] IPF is a complex disease with several aspects that are not fully understood, including its pathogenesis and variable clinical course.

Aberrant repair process by enhanced apoptosis of alveolar epithelial cells plays a critical role in the pathogenesis of pulmonary fibrosis such as idiopathic pulmonary fibrosis, although precise mechanism is still not clear. The mechanism(s) of pulmonary fibrosis in dyskeratosis congenita has also not yet been clarified. However, because mutations in dyskeratosis congenita genes cause short telomere length with functional deficits in telomere maintenance, telomeres in alveolar epithelial cells may be short. In patients with dyskeratosis congenita, we speculate that aberrant lung repair by enhanced cell death causes pulmonary fibrosis, although the short telomere length in alveolar epithelial cells has not been directly demonstrated.[9]

Whenever a case of diffuse parenchymal lung disease is diagnosed for the first time, it is important to rule out the underlying causes provoking it. Dyskeratosis congenita is a rare disease, but it is diagnosed by simple inspection. So pulmonologists should be aware that dyskeratosis congenita is one of the causes of diffuse parenchymal lung disease with maximum association with idiopathic pulmonary fibrosis.

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