Case Report

Where the mind knows, the eyes see- Dyskeratosis Congenita, A Genetic ILD.

Neethu K Kumar*, Kiran VN Jyothi E***, Suraj KP******

*Junior Resident, **Assistant Professor,
*** Associate Professor, ******Additional Professor. Dept. of Pulmonary Medicine, Govt. Medical College, Kozhikode.

Correspondence: Dr. Suraj KP, Additional Professor,
Dept. of Pulmonary Medicine, Govt. Medical College, Kozhikode. E Mail - drsurajkp@yahoo.com

Abstract

Interstitial lung disease with specific phenotypic clues should be interpreted by the astute clinician to make a proper diagnosis. Dyskeratosis congenita is a progressive, multisystem, inherited disorder of telomere biology with high risk of morbidity and mortality from bone marrow failure, hematologic malignancy, solid tumors, and pulmonary fibrosis. Here we report a case of dyskeratosis congenita with interstitial lung disease.

Key Words - Dyskeratosis congenita, interstitial lung disease (ILD), genetic ILD

Case report.

A thirty four year old male school teacher, non-smoker, non alcoholic, presented to us with fever, cough, and progressive dyspnea on exertion of 3 months duration. His symptoms first developed as low grade fever followed by cough associated with occasional scanty mucoid expectoration. There was insidious onset of dyspnea on exertion which progressed from grade 0 (mMRC scale) to grade II in 2 months and grade IV in last 1 month. There was no history of orthopnea, paroxysmal nocturnal dyspnoea, chest pain, hemoptysis, dysphagia or hoarseness of voice. There was no previous history of hypertension, diabetes mellitus or coronary artery disease. He had no exposure to occupational noxious gas, chemical fumes, organic dusts, pet animals or birds. There was no history of any significant drug intake.

He was tall, lean built and poorly nourished with premature greying of hair and alopecia. The striking features on inspection were generalised hypo pigmented and hyper pigmented macules on the face, trunk and limbs and the proliferative lesion on left eye (Fig 1). He had progressive loss of vision of left eye over the last 20 years and it showed features of severe dry eye with keratinisation and symblepharon. There were multiple hyper pigmented macules and patches in the oral mucosa and dystrophic nails. The respiratory system examination revealed bilateral fine end inspiratory crepitations. The heart sounds were normal without any murmurs. His pulse rate and blood pressure were normal and he was tachypneic.

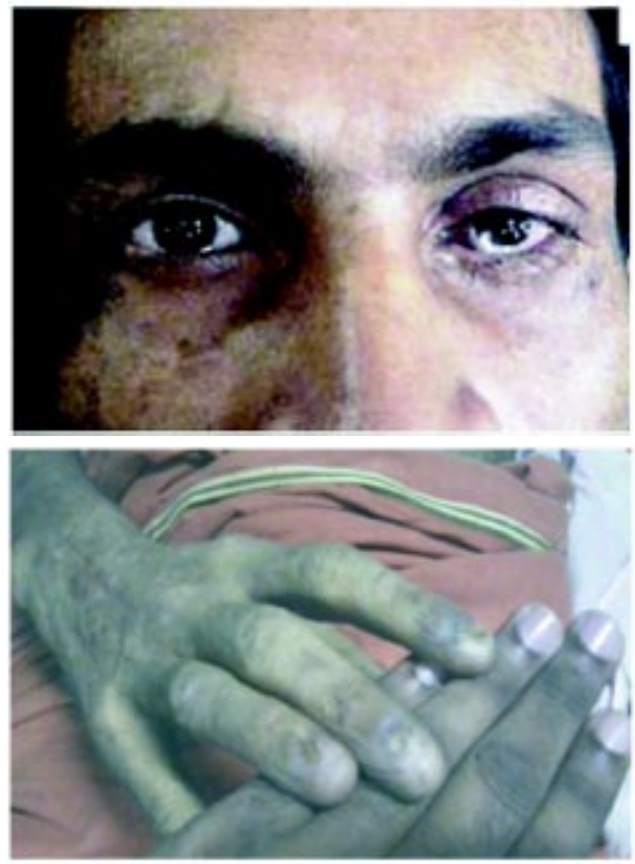

Figure1 : (A) Pigmentation of skin and ocular lesion, (B) Nail changes (compared with normal fingers).

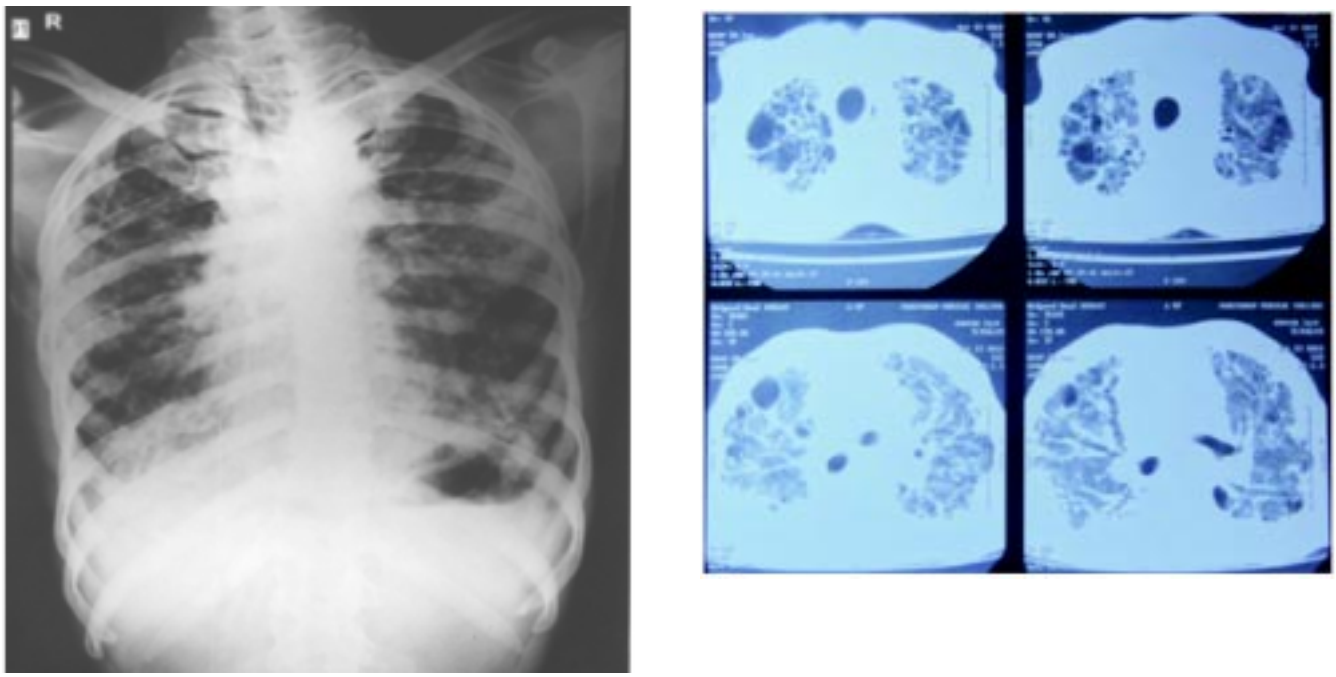

Figure 2: (A) Chest X ray , (B) HRCT

The routine blood investigations were within normal limits except for an elevated ESR value of 112 mm/1st hour. Sputum AFB was negative, Mantoux with 5TU nonreactive, and sputum culture yielded normal flora. Screening for viral markers were also negative.

Chest X- ray revealed bilateral reticulonodular infiltrates in both lung fields with evidence of volume loss involving the right lung. The spirometry showed a restrictive pattern with forced vital capacity (FVC) 1.19L (34.5% of predicted value), forced expiratory volume 1 second (FEV1) 1.17L (39.7% of predicted value) and FEV1/ FVC of 97.9.He was not able to perform a DLCO (Diffusion capacity of lung for carbon monoxide). HRCT Thorax showed diffuse interstitial thickening, peribronchovascular thickening, traction bronchiectasis, areas of subpleural honey combing, few cystic lesions, fibrotic strands and pleural thickening (Fig 2).

This constellation of findings led us to the clinical suspicion of Dyskeratosis congenita associated interstitial lung disease. So to confirm the diagnosis, dermatology, ophthalmology and oral medicine consultations were done.On fibreoptic bronchoscopy there were white patches in posterior pharyngeal wall suggestive of leukoplakia and the trachea was congested. A transbronchial lung biopsy was taken from the right middle lobe which revealed interstitial fibrosis with probable usual interstitial pneumonia pattern on histopathology. An open lung biopsy via mini thoracotomy confirmed UIP pattern on histopathology. A Biopsy of the oral mucosa showed leukoplakia. So with the classical triad of mucosal leukoplakia, dystrophic nails, abnormal skin pigmentation along with biopsy proven interstitial lung disease, we confirmed the diagnosis of dyskeratosis congenita associated interstitial lung disease. Subsequently he was started on corticosteroids, N acetyl cysteine and other supportive measures. Although he showed an initial improvement, his course in the hospital over the next month was stormy and he deteriorated rapidly and succumbed to the illness.

Discussion

Dyskeratosis congenita (DC), is a rare inherited multi system disorder of telomere biology characterized by a triad of nail dystrophy, lacy reticular pigmentation, and oral leukoplakia. The prevalence of Classic dyskeratosis congenita is approximately 1/1,000,000 individuals. Patients with DC are at very high risk of bone marrow failure (BMF), malignancies including head and neck or other cancers, leukemia, and myelodysplastic syndromes (MDS).They are also prone to pulmonary fibrosis, liver disease, neurological, ophthalmic, genitourinary, and gastrointestinal abnormalities. The primary causes of death in patients

with dyskeratosis congenita are bone marrow failure(BMF) and immunodeficiency (60-70%), pulmonary complications (10-15%), and malignancy (10%)[1].

Telomeres, which consist of TTAGGG nucleotide repeats and a protein complex at chromosome ends, are essential for chromosome stability[2]. They are generally very short in individuals with DC. Approximately 60% of persons with DC have an identifiable mutation in one of seven genes important in telomere biology. Inheritance of DC may follow X-linked recessive (DKC1 gene), autosomal dominant (TERC, TERT, or TINF2), or autosomal recessive patterns (NOP10, NHP2, TERT, or TCAB1). Hematopoietic stem cell transplantation (HSCT) can correct BMF and other hematologic complications (i.e., MDS or leukemia), but it does not improve other DC-related manifestations.

Classical DC is an inherited BM failure syndrome characterised by the mucocutaneous triad, also called Zinsser- Engman-Cole syndrome. Clinical manifestations in DC often appear during childhood although there is a wide age range. The skin pigmentation and nail changes typically appear first, usually by the age of 10 years. BMF usually develops below the age of 20 years. In some patients BM abnormalities may appear before the mucocutaneous manifestations and can lead to the initial diagnosis of idiopathic aplastic anemia.

Hoyeraal-Hreidarsson syndrome is an atypical form of DC that can present in the neonatal period and infancy. These are severe variant of DC where death from BM failure/ immunodeficiency occurs before the appearance of the diagnostic features of DC.

Management of DC patients requires a multi-disciplinary approach. General measures like avoidance of direct sunlight, abstinence from smoking and alcoholism is imperative. Oxymetholone can produce an improvement in haemopoietic function in many patients. Successful response to hematopoietic growth factors like GM-CSF, G-CSF and erythropoietic growth factors have also been reported. The main treatment for severe BM failure is allogenic haemopoietic stem cell transplantation. For pulmonary fibrosis associated with DC there are case reports of successful bilateral lung transplantation.

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Answer

Re expansion pulmonary edema.

The first Chest X-ray PA view clearly shows the presence of a left sided pneumothorax with the collapsed lung assuming a rounded opacity in the left hilar region. The second X-ray shows an ICD in situ on the left side with minimal surgical emphysema and a non homogenous opacity more confluent in the midzone extending from the hilum to the periphery and partly involving the upper and lower lung zones with clear costophrenic and cardiophrenic angles in the almost fully expanded lung. The last X-ray shows total clearance of the shadows in the left lung zones with conservative management which is most likely due to re expansion pulmonary edema.

Re-expansion pulmonary edema is an uncommon complication following drainage of a pneumothorax or pleural effusion. Re-expansion pulmonary edema in many instances is clinically mild as in this case as it was unilateral and hence the reported incidence is 1% in many studies. Increased pulmonary hydrostatic pressure caused by enhanced venous return, pressure-induced mechanical disruption of the alveolar capillaries, decreased levels of functional surfactant are some of the proposed mechanisms.Treatment is generally supportive, ranging from oxygen supplementation to noninvasive and invasive ventilation. Preventive strategies include the use of low negative pressure (< -20 cm H2O) for suctioning and limiting drainage of pleural fluid if patient develops more than minimal cough,dyspnoea,chest tightness or pain.

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