Dilated Cardiomyopathy in Two Patients with Xeroderma Pigmentosum Disease: A Case Report

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Abstract- Xeroderma pigmentosum (XP), is an autosomal recessive genetic disorder of DNA repair in which the ability to repair damage caused by ultraviolet (UV) light is deficient. The oxidative stress caused by decline catalase activity as an antioxidant enzyme, has been illustrated in these patients. This is the first case report of dilated cardiomyopathy in two patients with XP, A 26 year old girl and her younger brother. Laboratory studies demonstrated severe vitamin D deficiency in both of them. Cardiac dysfunction in the presented cases with XP might be caused by vitamin D deficiency. But this question still remains: whether chronic oxidative stress can involve the heart and can be a predisposing factor or even an underlying factor for dilated cardiomyopathy in XP, or not. More studies are needed for demonstrating this hypothesis.

Keywords: Xeroderma pigmentosum (XP); Ultraviolet (UV); Vitamin D deficiency; Oxidative stress; Dilated cardiomyopathy

Introduction

Xeroderma Pigmentosum (XP) is a rare autosomal recessive disease characterized by photosensitivity, pigmented changes, premature skin ageing, neoplasia and abnormal DNA repair. Some patients with XP also have neurological complications. Approximately 80% of patients with XP show a defect in the initiation of DNA excision repair of UV photoproducts. In these patients it has since been shown that repair replication is reduced in all cell types examined. Freckling and increasing dryness on light exposed surfaces are usually the earliest manifestations; they may follow an acute sunburn or more persistent erythema. Superficial ulcers, scars and contractures may produce ectropion and obliterate the outline of the eyelids. Malignancies, metastases and infections are the causes of death in these patients. Neurological abnormalities occur in approximately 20% of XP patients (mental retardation, areflexia or hyporeflexia, spasticity, ataxia, sensorineural deafness, dysphagia and abnormal electroencephalogram) (1).

On the other hand some studies illustrated that antioxidant activity is decreased in patients with XP (9) and oxidative stress is responsible for some involvements in these patients, independent of ultraviolet induced DNA damage (10,11).

Case Presentation

A 26 year old girl, known case of XP presented to the hospital with chief complaints of dyspnea and cough since two weeks ago. At presentation, she had stable vital signs and no sign of respiratory distress. General inspection of the patient revealed eyebrow and eyelash hair loss, hyperpigmented macules over face, neck, trunk, extremities and freckles on her face (Figure 1).

Figure 1. Hyperpigmented macules and freckles face.

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Figure 2. ECG shows low voltage in limb leads, Sinus tachycardia with left bundle branch block pattern and prolonged corrected QT interval.

Ascites shed led to abdominal distension. Right eye blindness due to corneal opacification and photophobia were detected. In palpation there were right ventricular heave, right upper quadrant tenderness and 2+ pitting edema at lower extremities. In auscultation summation gallop and bilateral basal fine crackles of the lungs were audible. In her family history, her younger brother and sister and her father's relatives had been diagnosed with XP. There was not any history of cardiac diseases in her family.

She did not have any underlying common causes for dilated cardiomyopathy such as coronary artery disease, myocarditis, or certain chronic hormonal disorders.

Laboratory studies showed, normochromic normocytic anemia, biochemistry within normal limits except hypokalemia, increased LDH (lactate dehydrogenase) up to about 600. The last laboratory study showed lower limit of normal calcium (8.7 mg/dl), normal phosphorus level (4.3 mg/dl), normal serum albumin, high parathyroid hormone level (174 pg/ml) and very low vitamin D level (4.8 ng/ml). She did not have clinical evidence of osteomalacia. Vitamin D replacement therapy began for patient under the diagnosis of vitamin D deficiency.

Sinus tachycardia with left bundle branch block pattern and prolonged corrected QT interval (500 ms) were detected in electrocardiogram (ECG)(Figure 2).

On echocardiography severe left ventricular enlargement with severe systolic dysfunction, (ejection fraction: 10 %), mild to moderate mitral regurgitation, moderate pericardial effusion, bilateral pleural effusion and high normal pulmonary artery pressure (PAP=35mmHg) were detected.

Figure 3. CXR shows cardiomegaly, pleural effusion and hilar prominence.

Her chest X-ray (CXR) revealed cardiomegaly, pleural effusion and hilar prominence (Figure 3).

The patient underwent heart failure treatment with furosemide, losartan, spironolactone and carvedilol. She was relieved after four days of admission and continued on mentioned treatment after discharge.

We evaluated the brother of the previous case by echocardiography and quantifying the level of calcium and vitamin D in his blood. He was 25 year old man with XP. Although he did not suffer from any cardiac symptoms, but the echocardiography (Figure 4) demonstrated severe left ventricular enlargement based on his body surface area with moderate systolic dysfunction (ejection fraction: 40%), and he had vitamin D deficiency like her sister.

The sun is an important source of vitamin D. So in our patients who have been advised to decrease sun

Figure 4. Echocardiography of the second patient: Left ventricular end diastolic dimension=55mm, Left ventricular end systolic dimension=37mm, right ventricular end diastolic dimension=30mm, left ventricular mass index=106.4 g/m^2.
exposure because of their underlying disorder, vitamin D deficiency is possible.

**Discussion**

The low vitamin D status can be a contributing factor in the pathogenesis of congestive heart failure(2). Association between low levels of 25-hydroxy vitamin D and 1,25-dihydroxyvitamin D with myocardial dysfunction has been illustrated by Pilz et al.(3). Based on a study, indicators of ultraviolet exposure are reduced in patients with congestive heart failure compared to healthy controls(4). There are several case reports about dilated cardiomyopathy in infants with vitamin D deficient Rickets (5,6). Despite all these information, still a question remains in mind: whether XP can induce cardiomyopathy itself or not.

While reviewing the literature on XP, we found that there is an oxidative stress status in these patients and the pathogenesis and carcinogenesis of the XP can be the results of oxidative stress (7). Based on a study increased level of oxidative stress in these patients may not be associated directly with XP genes (7). According to a study catalase activity decreases progressively from the onset of the XP disease to tumorogenesis (8). Vuillaume *et al.* found that the catalatic activity is 3 or 4 times lower in patients with XP (9). Hyashi *et al.* suggest that neurodegeneration in patients with XP is caused by oxidative nucleotides damage and disturbed superoxide dismutase as an antioxidant enzyme (10). It seems that genotoxicity caused by oxidative stress in patients with XP is a risk factor for malignancy (11). Cardiomyopathy has not been reported in patients with XP so far. But the effects of oxidative stress on heart are well documented. Exposures to reactive oxygen species result in reduction of high energy phosphates and heart contraction and induce structural abnormalities of the heart (12). The effect of increased oxidative stress and depressed antioxidant on cardiac structure and function has been documented by the other studies (13). In conclusion, this is the first case report of dilated cardiomyopathy in two patients with XP. As mentioned before, vitamin D deficiency can induce cardiac remodeling. It seems that cardiac dysfunction in the presented cases with XP might be caused by vitamin D deficiency. But this question still remains: whether chronic oxidative stress which is demonstrated in patients with XP, can involve the heart and can be a predisposing factor or even an underlying factor for dilated cardiomyopathy in XP or not.

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**References**


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Dilated cardiomyopathy and xerodermapigmentosum


