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A case report of Naxos disease from Afghanistan

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ABSTRACT

Naxos disease is a rare genetic disorder in which the gene on chromosome 17 is encoded for plakoglobin which in term plays significant adhesive role in cardiac and dermal junctions on cellular levels resulting in fibro fatty deposits in skin tissues and the heart. Apparently, patients with Naxos disease present with skin related symptoms including woolly hair and keratoderma in palms and soles; however, by the passage of time, these patients develop cardiac manifestations most commonly arrhythmogenic right ventricular cardiomyopathy and left ventricular involvement in the late stages of the disease. Consequently, the aforementioned manifestations cause heart failure, arrhythmia and sudden death. Patients are diagnosed with the aforementioned physical findings and history of the relevant symptoms confirmed by laboratory findings of the genetic abnormality for plakoglobin and/or echocardiographic findings for arrhythmogenic right ventricular cardiomyopathy. Patients are treated symptomatically for keratoderma with certain emollients, keratolytic agents such as 6% salicylic acid and 70% propylene glycol, topical and systemic retinoids, anti-arrhythmic medicines, and implantable cardioverter defibrillator though there is no permanent efficacy in the skin but implantable cardioverter defibrillators reduce premature mortality. Patients with certain phenotypes should be deeply investigated for underlying cardiac manifestations being responsible for poor prognosis in such patients.

Keywords: Naxos disease, Keratoderma, Cardiocutaneous, Woolly hair, Case Report

INTRODUCTION

Naxos disease, first recognized in Greek Island of Naxos (Protonotarios et al., 1986) is a genetic disorder in which gene on chromosome 17 is mutated for plakoglobin which plays significant adhesive role in cardiac and dermal junctions on cellular levels (Hertig et al., 1996) predisposing to fibro-fatty deposition in cardiac and dermal tissues. Individuals with Naxos disease typically display woolly hair and thickened palms and soles, later, these patients develop heart problems such as syncope, heart failure or sudden death at young ages with apparently healthy physique (Protonotarios et al., 1986). Electrocardiogram demonstrates tachycardia, extrasystoles and ventricular tachycardia with concomitant myocardial histologic changes of arrhythmogenic right ventricle dysplasia (Li et al., 2018). A Turkish boy is reported with an unusual presentation of biventricular cardiomyopathy and peculiar dermatologic features of Carvajal-Naxos disease(Kilic et al., 2007). Skin lesions in these patients are reported to be of two types, epidermolytic and non epidermolytic which are neither histologically nor genetically distinguishable

from each other (Norgett et al., 2000; Coonar et al., 1998; Kimyai-Asadi et al., 2002). Phenotype assessment in patients with Naxos disease in a study has shown that patients with homozygous pattern developed serious cardiac disease and had poor prognosis in comparison with a small number of heterozygous patients who did not show any abnormality on electrocardiogram and echocardiography and hence did not show any clinically significant cardiac involvement (Protonotarios et al., 2001).

Case

The patient being 6 years old at presentation in our report belongs to an Afghan family and all her ancestors are known to be from Afghanistan. Upon arrival to surgery department of Nangarhar University Teaching

Hospital Surgery Department, the patient was asymptomatic but complained of hyperkeratotic lesions first on soles and later on palms for a long time since birth. According to her parents, she had woolly hair since her birth and it was different from that of her siblings'. All her siblings were intact and did not reveal any lesions and symptoms. Moreover, she suffered social deprivation for her peculiar lesions. She had used different emollients and keratolytic lesions with in fact no efficacy.

On physical examination, there were hyperkeratotic lesions on her soles and palms and she had peculiar woolly hair (Figure 1). In addition, there was tachycardia during cardiac auscultation but no added cardiac sounds were heard. The patient did not show any signs of heart failure. Her 12-lead electrocardiogram showed normal axis, sinus tachycardia, and asymmetrical T wave inversions in leads 1, AVL, and V1 (Figure 2). Furthermore, her chest radiograph showed cardiomegaly with bilateral open costophrenic angles i.e. no pleural effusion and no signs of pulmonary congestion (Figure 3). Right side chambers were mildly dilated on echocardiography with normal pulmonary arterial pressures and normal left ventricular and atrial dimensions and her ejection fraction was reported normal (Figure 4). She was mildly anemic but the rest of her routine labs were normal. Eventually, the patient was positive for plakoglobin (PK2157del2TG).

Numerous emollients and keratolytic agents such as salicylic acid and propylene glycol, retinoids, and surgical removal procedures were used for the treatment of hyperkeratotic lesions on different occasions but showed almost no efficacy at all and the purpose of different visits were to follow up the patient for the development of cardiac manifestations such as ventricular tachycardia, syncope, or heart failure. No further treatment was offered since the patient was asymptomatic and the patient was only followed up. The patient was followed up for one year and revealed no more changes.

Discussion

This was an interesting report exploring cardiac mystery behind easily understandable skin lesions which is often not investigated. In fact, such patients visit dermatologists who treat them symptomatically with emollients, keratolytic agents, and both topical and systemic retinoids, but mystery behind the superficial easily understandable lesions often remain unexplored and patients face worst consequences in their early lives. Unfortunately, we could not contact patient's attendant for more than a year and lost follow up.

Naxos disease is an autosomal recessive pattern of the combined ectodermal (skin and hair) and mesodermal (heart) disorders (Protonotarios et al., 1986). Patients with Naxos disease present with woolly hair in early age, palmoplantar keratoderma in childhood, and arrhythmogenic right ventricular cardiomyopathy in adolescence (Protonotarios et al., 2001; Protonotarios, et al., 2002). In other words, not all patients with Naxos disease develop cardiomyopathy simultaneously with skin lesions (Baykan et

al., 2015). Genotype assessment in patients with Naxos disease in a study has shown that patients with homozygous pattern developed serious cardiac disease and had poor prognosis in comparison with a small number of heterozygous patients who did not show any abnormality on electrocardiogram and echocardiography and hence did not show any clinically significant cardiac involvement (Protonotarios et al., 2001). Moreover, patients with Naxos disease are shown to die from malignant arrhythmias, heart failure and sudden death (Protonotarios et al., 1986). In fact, most patients with arrhythmogenic right ventricular cardiomyopathy undergo implantable cardioverter defibrillator for the prevention of fatal arrhythmic episodes (Gatzoulis et al., 2000). Clinicians should be curious while visiting patients with certain dermatologic lesions and woolly hair and should refer them to cardiologists for specific investigations to early diagnose their cardiac involvement in case of Naxos disease in order to prevent adverse outcomes and premature mortality by providing special care.

We received written consent from the patient's parent for publication of the photos and case report and would be available in a separate when requested.

Author Contribution

Abdul Nasir Shams: Conceptualization, Methodology, Investigation, Writing, Original draft preparation. Ikramullah Ibrahimi Reviewing and editing, Investigation, Zahid Mir Sahibzada: Conceptualization, Visualization, Investigation, and Writing.

Conflict of Interest

The authors report no conflicts of interest.

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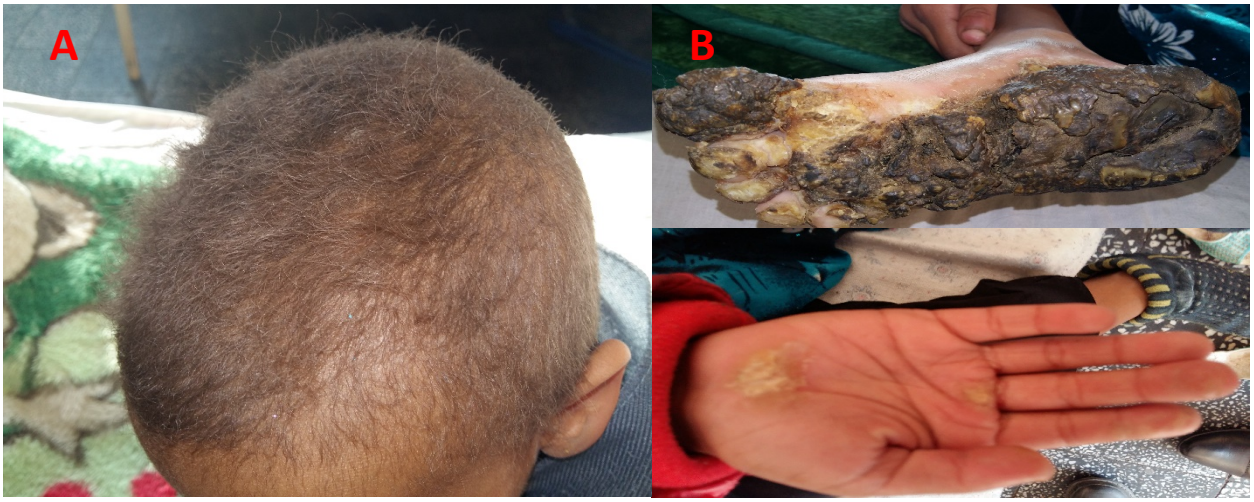

Figure 1: A. Woolly hair B. Palmoplantar keratoderma

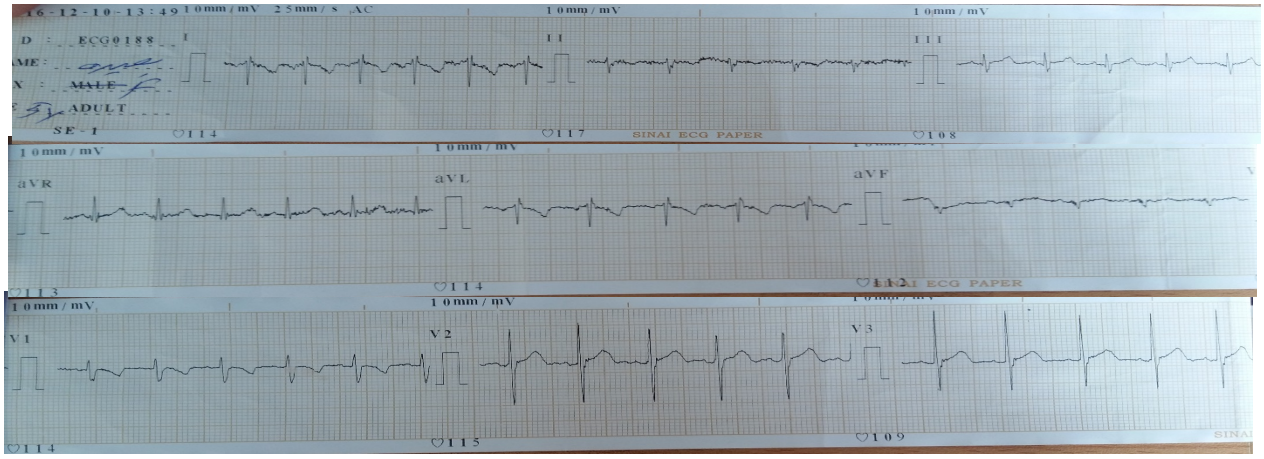

Figure 2: Electrocardiogram showing normal axis, sinus tachycardia, and asymmetrical T wave inversion

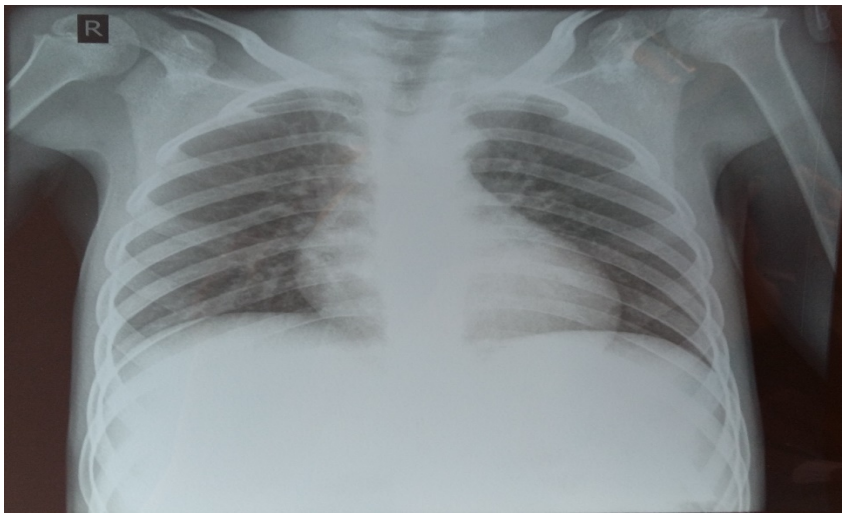

Figure 3: Chest X ray showing cardiomegaly

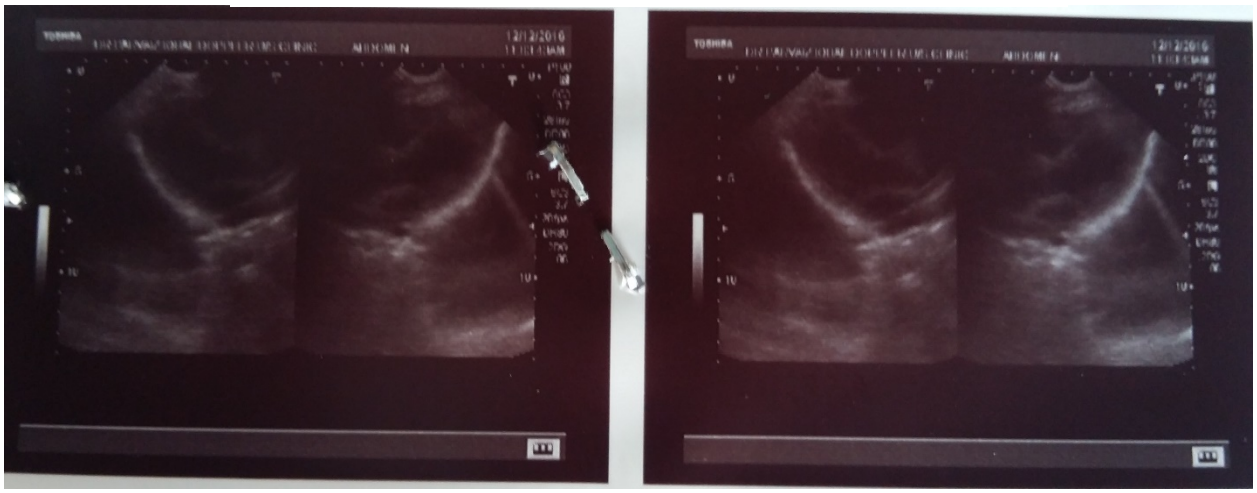

Figure 4: Two-dimensional Echocardiography showing mildly enlarged right side chambers

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