

## Carvajal Syndrome: A Rare Variant of Naxos Disease

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### Abstract

Carvajal syndrome also known as 'Striate palmoplantar keratoderma with woolly hair and cardiomyopathy is a cutaneous condition inherited in an autosomal recessive pattern due to a defect in desmoplakin gene. The skin disease presents as a striate palmoplantar keratoderma particularly at sites of pressure. The patient is at risk of sudden cardiac death due to dilated cardiomyopathy associated with this entity. A variant of Naxos disease, reported as Carvajal syndrome, has been described in families from India and Ecuador. Clinically, it presents with the same cutaneous phenotype and predominantly left ventricular involvement.

**Keywords :** Carvajal syndrome; Naxos disease; Striate palmoplantar; Autosomal recessive keratoderma

### Introduction

Carvajal syndrome also known as 'Striate palmoplantar keratoderma with woolly hair and cardiomyopathy is a cutaneous condition inherited in an autosomal recessive pattern due to a defect in desmoplakin gene. The skin disease presents as a striate palmoplantar keratoderma particularly at sites of pressure. The patient is at risk of sudden cardiac death due to dilated cardiomyopathy associated with this entity. A variant of Naxos disease, reported as Carvajal syndrome, has been described in families from India and Ecuador. Clinically, it presents with the same cutaneous phenotype and predominantly left ventricular involvement.

### Case Report

11 years old boy presented with cough, breathlessness and easy fatigue ability for 3 months duration. On general examination the pt had fine brittle lusterless scalp hair, pallor, stomatitis, keratotic skin over palm, sole and lower half of both lower limbs (Figures 1-3). Pt has tachycardia with HR 140/min, RR 40/min, BP 80/60 mmHg, SPO<sub>2</sub> 72%, raised JVP, with B/L basal crepitations, S3 gallop present. Echocardiographic examination revealed a dilatation of the right and left ventricles with a left ventricular ejection fraction of 35% and biventricular trabecular configuration, predominantly of the left ventricle and also grade I tricuspid and Mitral valve insufficiency (Figures 4 and 5). Patient was treated with diuretics, beta-blockers and ACE inhibitors.

### Discussion

Naxos disease was first described by Protonotarios et al. in families originating from the Greek island of Naxos [1]. It is caused by a recessive mutation in desmoplakin, which maps to 17q21 gene, an intracellular protein that links desmosomal adhesion molecules to intermediate filaments of the cytoskeleton. Patient usually presents with Woolly hair since birth; palmoplantar keratosis develops during first year of life and cardiomyopathy (Rt.ventricular) in adolescence [1-4]. A particular mutation that truncates the intermediate filament-binding site of desmoplakin results in a variant of Naxos disease with predominantly left ventricular involvement, early morbidity and clinical overlapping with dilated cardiomyopathy has been described by Kaplan et al. [5] from Ecuador as Carvajal Syndrome. It is a progressive heart disease and may cause sudden death in a child with early age. Whenever a child presents with such a dermatological manifestation, the paediatric cardiologist's consultation must be done at earliest possible. The differences between

Naxos syndrome and Carvajal syndrome is depicted in Table 1. The primary goal of the management is to prevent sudden cardiac death. Implantation of automatic cardioverter defibrillator, antiarrhythmic drugs and management of heart failure are the recommended treatment modalities [6]. The population at risk should be genetically screened.

### Conclusion

The cardiomyopathy in Naxos syndrome and Carvajal cardiocutaneous syndromes presents with increased arrhythmogenicity and variable left ventricular involvement and is characterized histologically by myocardial loss with fibrofatty or fibrous replacement



Figure 1: Brittle lusterless scalp with woolly hairs.

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Figure 2: Palmoplantar keratoderma of Sole.



Figure 3: Palmoplantar keratoderma of palms.



Figure 4: Echo showing dilated Left Ventricle with global dysfunction.



Figure 5: ECHO PLAX view showing features showing dilated LV.

NAXOS SYNDROME	CARVAJAL SYNDROME
Arrhythmogenic right ventricular dysplasia.1	Left ventricular involvement
Deletion in the plakoglobin gene	Mutations of the desmoplakin gene
Clinically manifests in adolescence. Patients may develop progressive heart disease involving the right or both ventricles. Symptoms of right heart failure are found in the final stages when the right or both ventricles are severely affected.1	Clinically apparent earlier during childhood as DCM. Fifty percent of affected patients develop heart failure, and most of them die during adolescence.
<b>ECG:</b> inverted T waves in V1 - V3 or QRS complex prolongation in leads V1 -V3, Epsilon waves, and complete or incomplete RBBB.	<b>ECG:</b> low voltage and intraventricular conduction defects. T-wave inversion in V1, V2, or V3 or extended to V5 observed.2
Cardiac histology reveals the characteristic loss of the right ventricular myocardium with fibrofatty replacement	Cardiac histology of the Carvajal disease shows areas of extensive myocardial loss and replacement with fibrosis that is very similar to arrhythmogenic right ventricular dysplasia/cardiomyopathy pathology but without the fatty component.4
The affected members of both syndromes have woolly hair at birth, whereas palmoplantar keratoderma appears during the first year of life, when infants start using their extremities.3	

Table 1: Showing the differentiating features between Naxos and Carvajal Syndrome.

at subepicardial and mediomural layers. The clinical heterogeneity and tissue characteristics in this cell-adhesion cardiomyopathy might be mutation specific and leads to consideration that the spectrum of ARVC should be broadened.

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