Hereditary palmoplantar keratoderma with woolly hair: what are the clinical implications?

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Case history

Presenting complaints

- A 15-year-old boy
- presented to OPD with painful thickened fissured skin over palms and soles since infancy
- along with increased itching and oozing lesions of 1 week duration

Past history

- At the age of 10 years, he had similar complaints and evaluated
- history of recurrent skin infections

Case history(Contd.)

Birth history

- The patient was apparently normal at birth with no significant birth history.
- He had woolly hair since birth,
- at the age of 6 days, he developed furrows involving both palms and soles, later progressive thickening of palms and soles.

Family history

- He is a product of second-degree consanguineous marriage and has a healthy younger brother.
- His parents and brother have straight, jet black hair.

Examination

The patient was poorly built and nourished with normal vitals and general examination findings.

Head to toe examination revealed:-

- Light brown woolly hair covering the scalp [Fig.1]
- Angular cheilitis [Fig.2]
- Fissuring of lips [Fig.2]
- No lesions in oral cavity and normal dentition.

Figure 1- Light brown woolly hair

Figure 2- Angular cheilitis along with fissuring of lips

- Multiple keratotic hyperpigmented papules over extensor aspect of forearm [Fig.3]

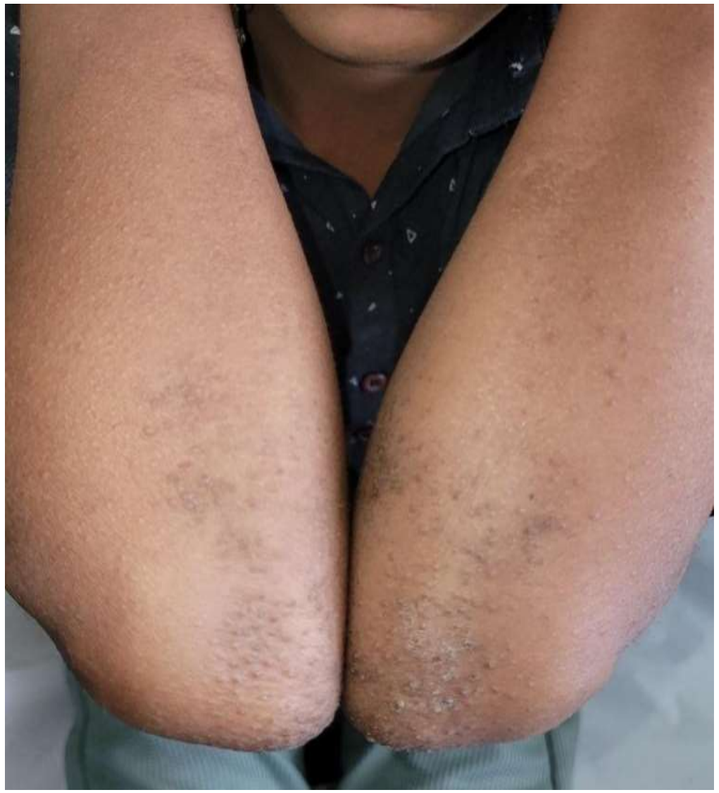

Figure 3-extensor aspect of elbows showing hyperpigmented papules

- Hyperkeratotic lesions involving palms and soles extending to dorsal surface [Fig.4]

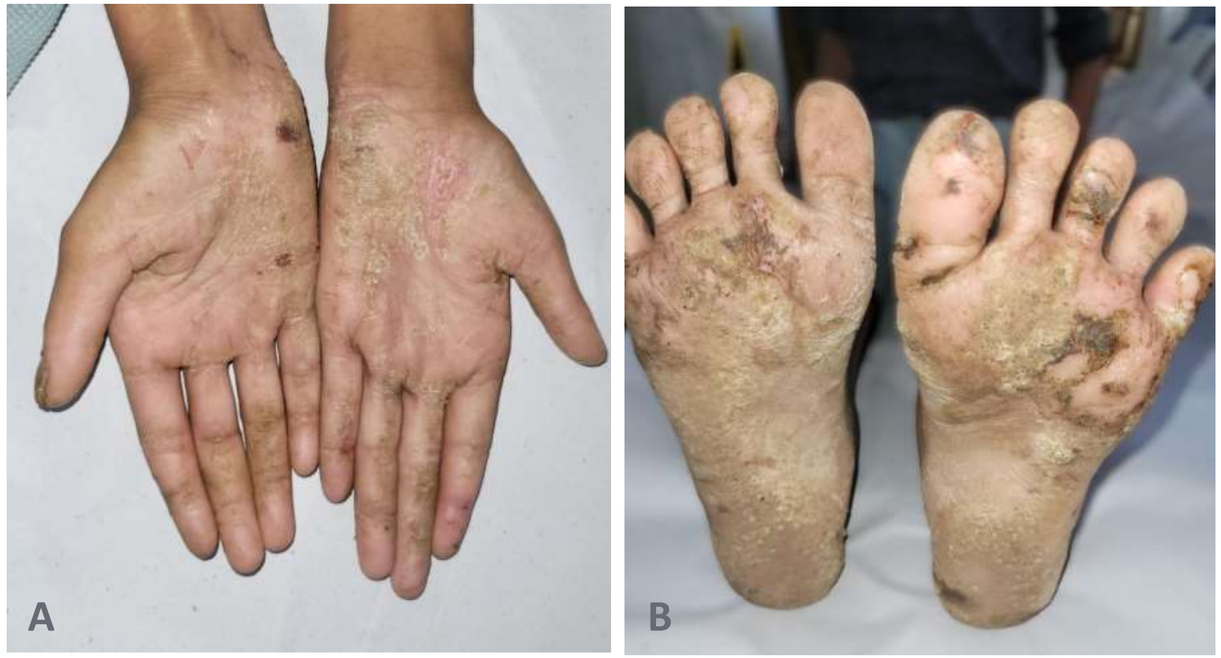

Figure 4(A&B)- Palms and soles showing keratosis and fissures, indicative of striate PPK

- Thickened nails with subungual keratosis and transverse ridges [Fig.5]

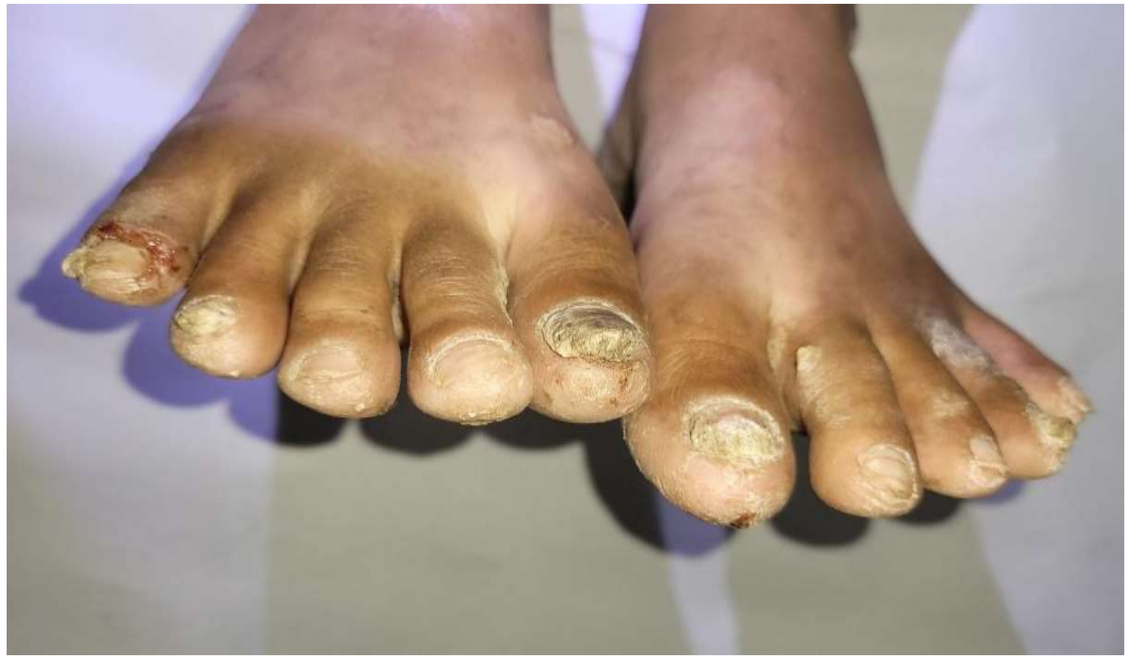

Figure 5- Nails showing subungual keratosis and transverse ridges

Differential diagnosis

In view of Palmoplantar keratoderma (PPK) with woolly hair, we considered the following syndromes:

- ✓ Type 1 Naxos syndrome, associated with arrhythmogenic **right ventricular** cardiomyopathic ventriculopathy with defect in gene encoding plakoglobin, **symptoms typically appear in adolescence**.
- ✓ Type 2 Carvajal syndrome starts in **early childhood**, has **dilated left ventricular** cardiomyopathy, and is associated with defects in desmoplakin.
- ✓ Type 3 Naxos like phenotype with milder PPK, and gene encodes desmocolin 2.
- ✓ Type 4 Woolly hair with PPK without cardiac abnormality.

	Type 1 Naxos syndrome	Type 2 Carvajal syndrome	Type 3 Naxos-like phenotype	Type 4
Age	Presents in adolescents	Presents during early childhood	-	-
Clinical features	Diffuse PPK Woolly hair Arrhythmogenic ventricular cardiomyopathy	Striate PPK Woolly hair Dilated ventricular cardiomyopathy	Mild PPK Woolly hair Arrhythmogenic ventricular myopathy	PPK Woolly hair
Gene involved	JUP gene (plakoglobin protein)	DSP gene (Desmoplakin protein)	DSC gene (Desmocolin-2)	KANK2 gene
Prognosis	High risk of sudden cardiac death	Heart failure and Sudden cardiac death can occur in adolescence	-	Good prognosis due to absence of cardiac involvement

Source- Hassanandani T, Agarwal A, Kar BR. Type 4 Woolly Hair-Palmoplantar Keratoderma Syndrome: A Rare Entity. Indian J Dermatol. 2021 Nov-Dec;66(6):693-695. doi: 10.4103/ijd.IJD_107_21. PMID: 35283492; PMCID: PMC8906310.

Table no. 1- Description of PPK-Woolly hair syndromes

Investigations

At the age of 10 years, evaluated for cardiac involvement which was not indicative of any pathology.

Repeat evaluations were done including the following:-

1. Echocardiography (Echo) showing
   - reduced ejection fraction
   - Biventricular dilatation
   - Hypokinetic right and left ventricles
   - Trivial mitral regurgitation

Investigations

2. Electrocardiography (ECG) showing irregular rhythm in lead II, with T-wave inversion in leads V1-V4, along with ectopic wave.

Both results indicative of Dilated cardiomyopathy involving Right and left ventricles.

The patient was advised cardiac MRI for further diagnosis.

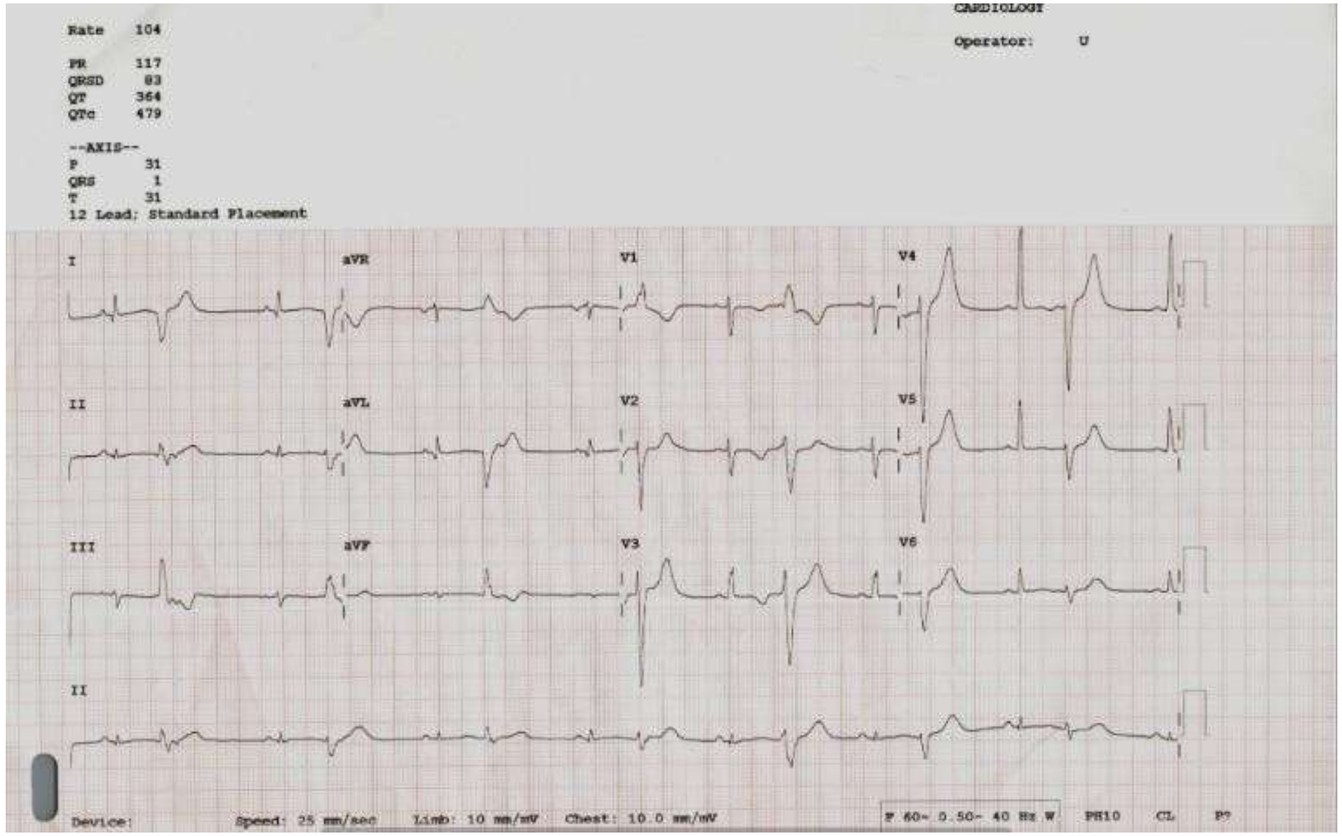

Figure 6- ECG taken at the age of 15 years; depicting t-wave inversion in leads V1-4 indicative of cardiomyopathy

DIAGNOSIS: CARVAJAL SYNDROME

Treatment

- It requires lifelong treatment and monitoring
- Management of PPK : use of topical keratinolytic, emollient and moisturising soaps and creams.
- Cardiomyopathy: pharmacological management involving beta-blockers, angiotensin receptor blockers and aldosterone antagonist which prevent occurrence of arrhythmias and cardiac remodelling.
- Lifestyle changes avoiding exertional activities are advised.
- Regular follow up with cardiac monitoring advised.

Discussion

- **Carvajal Syndrome** is a rare (incidence <1 in 1,000,000) autosomal disease, which can be recessive [1] or more rarely dominant [2], due to mutation in DSP gene.
- DSP I and DSP II genes [3], code for desmoplakin protein. The mutation disrupt tissue integrity causing epidermolysis and discontinuity followed by fibro-fatty deposition in tissues like heart and skin [5].
- The symptoms include palmoplantar keratoderma (prevalence of PPK in South India approximately 1:2000 [6]), woolly hair and cardiomyopathy [3,4].
- Other features include angular cheilitis, muco-cutaneous blisters, dental abnormalities (oligodontia), nail abnormalities (leukonychia, subungual hyperkeratosis) are also seen. [4,5]
- Cardiac complications may lead to arrhythmia, sudden cardiac death, etc responsible for morbidity and mortality(50%) [7]. Hence prompt treatment is required.

Discussion

- The diagnosis is based on clinical features and cardiac investigations like electrocardiogram (ECG), echocardiography, cardiac MRI and genetic testing.
- Due to development and increased availability of advanced genetic tests, various mutations and clinical features have been identified. [7]
- Treatment of PPK is prolonged and lifelong and includes emollient, moisturizing agents and keratolytics. [1]
- Infections, if any are to be treated with appropriate antibiotics,
- Prompt and adequate management of cardiomyopathy with beta-blocker, neprilysin inhibitor, ARB, diuretic and avoidance of exertional activities is most important. [1]

This case is important for the fact that skin manifestations could help in diagnosis of hidden cardiac abnormality, which otherwise could have led to sudden death at an early age.

References

Source of TABLE NO. 1- Hassanandani T, Agarwal A, Kar BR. Type 4 Woolly Hair-Palmoplantar Keratoderma Syndrome: A Rare Entity. Indian J Dermatol. 2021 Nov-Dec;66(6):693-695. doi: 10.4103/ijd.IJD_107_21. PMID: 35283492; PMCID: PMC8906310

1Zhao XJ, Bai CY, Li XY, Wang L, Wang RP, Xia Y, Liu G, Zhao HL, Xu HZ.A Novel Variant in the Desmoplakin Gene in One Case of the Rare Carvajal Syndrome with Dilated Cardiomyopathy : A Case Report and Literature Review. Clin Cosmet Investig Dermatol. 2023 Sep 29;16:2737-2748. doi:10.2147/CCID.S429030. PMID:37799505; PMCID:PMC10547600.

2Kincaid C, Horton L, Cheung B, Esse I, Gradus-Pizlo I, Mesinkovska NA. Desmoplakin mutation underlying autosomal dominant arrhythmogenic cardiomyopathy, palmoplantar keratoderma, and curly hair. JAAD Case Rep. 2023 Apr 15;36:56-59. doi: 10.1016/j.jdcr.2023.03.018. PMID:37250009; PMCID:PMC10213094.

3Yuan ZY, Cheng LT, Wang ZF, Wu YQ. Desmoplakin and clinical manifestations of desmoplakin cardiomyopathy. Chin Med J(Engl).2021 Aug 2;134(15):1771-1779.doi: 10.1097/CM9.0000000000001581.PMID:34343150; PMCID:PMC8367056.

4De Gregorio MG, Girolami F, Tomberli B, Rossi G, Tomberli A, Baldini K, Olivotto I. Comprehensive Risk Management in Arrhythmogenic Cardiomyopathy Associated with Autosomal Dominant Carvajal Syndrome: Protecting Families. JACC Case Rep.2020 Jun 17;2(6):925-929.doi:10.1016/j.jaccas.2020.03.033. PMID:34317383; PMCID:PMC8302052.

5Mahoney MG, Sadowski S, Brennan DC, Pekka Pikander, Pekka Saukko, Wahl JK, et al. Compound Heterozygous Desmoplakin Mutations Result in a Phenotype with a Combination of Myocardial, Skin, Hair and Enamel Abnormalities. Journal of Investigative Dermatology.2010 Apr 1;130(4):968–78.

6 Gulati S, Thappa DM, Garg BR. Hereditary Palmoplantar Keratodermas in South India. The Journal of Dermatology. 1997 Dec;24(12):765–8.

7Protonotarios N, Tsatsopoulou A. Naxos disease and Carvajal syndrome: cardiocutaneous disorders that highlight the pathogenesis and broaden the spectrum of arrhythmogenic right ventricular cardiomyopathy. Cardiovasc Pathol.2004 Jul-Aug;13(4):185-94.doi:10.1016/j.carpath.2004.03.609. PMID:15210133.

Thank you