e-ISSN: 0976-822X, p-ISSN:2961-6042

Available online on http://www.ijcpr.com/

International Journal of Current Pharmaceutical Review and Research 2025; 17(8); 1691-1694

Original Research Article

Scalp-Ear-Nipple Syndrome: A Case Report of KCTD1 Mutation in an Adolescent Female with Comprehensive Clinical Manifestations

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Received: 27-06-2025 / Revised: 25-07-2025 / Accepted: 27-08-2025

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Conflict of interest: Nil

Abstract:

Background: Scalp-Ear-Nipple (SEN) syndrome represents a rare autosomal dominant ectodermal dysplasia characterized by aplasia cutis congenita of the scalp, breast malformations, and ear anomalies.

Case Presentation: We present a 15-year-old female with classical features of SEN syndrome including athelia, aplasia cutis of the scalp, ear dysplasia, and neurological complications. The patient demonstrated delayed pubertal development, epilepsy, and multiple dysmorphic features. Genetic analysis confirmed a pathogenic mutation in the KCTD1 gene.

Conclusion: Early recognition of SEN syndrome facilitates appropriate multidisciplinary management and genetic counseling. This case highlights the variable expressivity of the condition and emphasizes the importance of comprehensive clinical evaluation.

Keywords: Scalp-Ear-Nipple Syndrome; KCTD1 Gene; Athelia; Ectodermal Dysplasia; Aplasia Cutis Congenita

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Introduction

Scalp-Ear-Nipple (SEN) syndrome, first described by Finlay and Marks in 1977, is an extremely rare autosomal dominant disorder with an estimated prevalence of less than 1 in 1,000,000 births [1]. The condition is characterized by a triad of clinical features including aplasia cutis congenita of the scalp, breast anomalies ranging from athelia to amastia, and minor external ear malformations [2]. The syndrome results from heterozygous mutations in the KCTD1 gene located on chromosome 18q11.2, which encodes a potassium channel tetramerization domain-containing protein involved in neurodevelopmental processes [3].

The clinical spectrum of SEN syndrome extends beyond the classic triad to include dental anomalies, nail dystrophy, digital malformations, and variable degrees of intellectual disability [4]. Recognition of this rare condition is crucial for appropriate management and genetic counseling. We report a case of SEN syndrome in an adolescent female presenting with comprehensive clinical manifestations and confirmed KCTD1 mutation.

Case Presentation

Clinical History: A 15-year-old female presented to the gynecology outpatient department with primary concerns of absent breast and nipple development accompanied by progressive hair thinning and decreased scalp hair density. The patient had achieved menarche at 12 years of age with subsequent irregular menstrual cycles of normal flow volume.

Birth and Developmental History: The patient was born via spontaneous vaginal delivery as a late preterm infant with a history of neonatal respiratory distress requiring supportive care. Seizure disorder manifested at 5 months of age, subsequently diagnosed as epilepsy. Current antiepileptic management includes oxcarbazepine 450 mg twice daily, with seizure episodes occurring approximately every 5-6 years. Developmental milestones revealed delayed learning capabilities, reduced social interaction, and limited verbal communication skills.

Physical Examination

General Appearance: The patient exhibited mild facial dysmorphism with characteristic features consistent with ectodermal dysplasia.

Scalp and Hair: Examination revealed sparse, coarse, and woolly-textured hair with a lumpy and boggy scalp surface consistent with aplasia cutis congenita.

Craniofacial Features:

- Eyes: Puffy eyelids with narrow palpebral fissures and reduced eye opening
- Dental: Widely spaced teeth with high-arched palate
- Ears: Low-set, small, and cup-shaped pinnae

Breast Examination: Complete absence of nipples (athelia) with poorly developed breast tissue despite appropriate chronological age for pubertal development.

Dermatological Findings:

- Axillary hair: Markedly sparse
- Pubic hair: Normal distribution and density
- Nails: Brittle and dysplastic changes affecting multiple digits

Laboratory Investigations

Hematological and biochemical parameters revealed:

- Hemoglobin: 9.6 g/dL (mild anemia)
- Fasting blood glucose: 87 mg/dL (normal)
- Erythrocyte sedimentation rate: 22 mm/hr (mildly elevated)

Endocrine Profile:

- Thyroid-stimulating hormone: 1.4 mIU/L (normal)
- Prolactin: 7.12 ng/mL (normal)
- Follicle-stimulating hormone: 3.69 mIU/mL (normal)

Imaging Studies

Abdominal Ultrasonography: Bilateral nephrolithiasis was identified with normal kidney size bilaterally. Uterine and adnexal structures demonstrated normal size and morphology.

Neurological Investigations:

- Magnetic resonance imaging of the brain: No abnormal findings detected
- Electroencephalography: Normal wave patterns
- Electrocardiography: Normal sinus rhythm

Genetic Analysis: Molecular genetic testing confirmed the presence of a pathogenic mutation in the KCTD1 gene, establishing the definitive diagnosis of SEN syndrome.

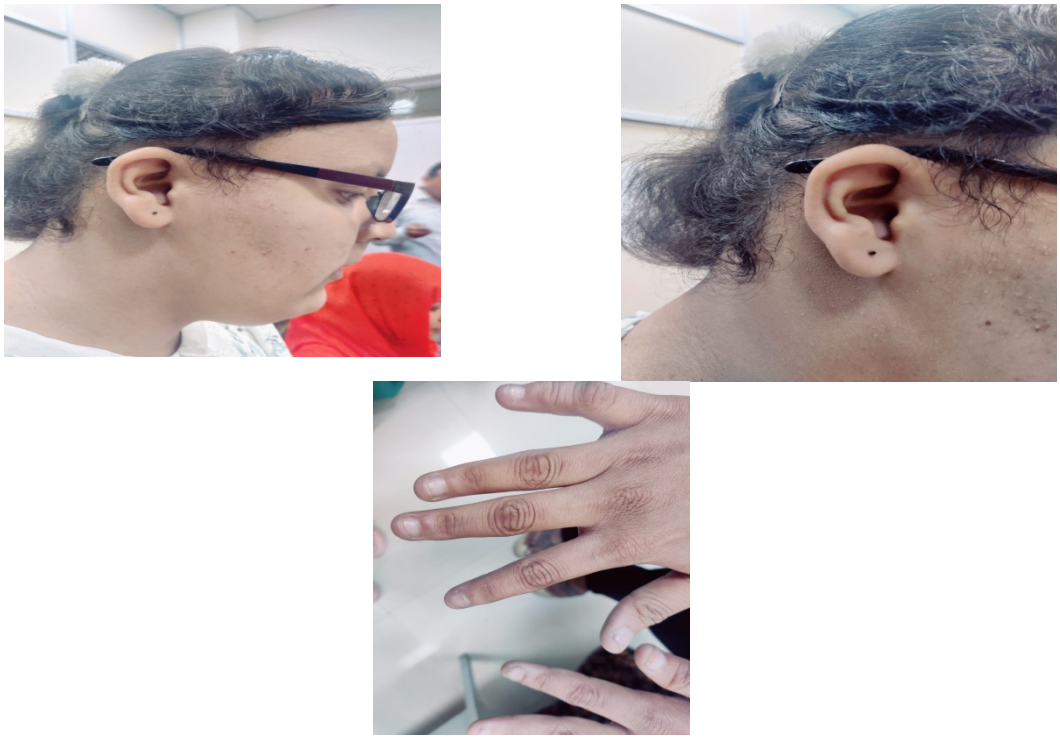

Figure 1

Discussion

The present case demonstrates classical manifestations of SEN syndrome with comprehensive involvement of multiple organ systems. Our patient exhibited 9 out of 13 recognized clinical features associated with this rare condition [5]. The constellation of findings included:

1. **Scalp abnormalities:** Aplasia cutis with characteristic nodular appearance
2. **Facial dysmorphism:** Short columella and mild prognathism
3. **Ear malformations:** Rudimentary tragus and antitragus, low-set positioning, cup-shaped appearance
4. **Ocular features:** Puffy eyelids with narrow palpebral fissures
5. **Dental anomalies:** Widely spaced teeth with missing secondary dentition
6. **Breast malformations:** Athelia with hypoplastic breast tissue
7. **Genitourinary abnormalities:** Nephrolithiasis
8. **Dermatological manifestations:** Sparse hair and nail dystrophy
9. **Neurological complications:** Epilepsy with developmental delay

SEN syndrome demonstrates autosomal dominant inheritance with high penetrance but variable expressivity [6]. While most cases follow dominant transmission patterns, rare autosomal recessive cases have been documented in the literature [7]. The KCTD1 gene encodes a protein essential for proper neurodevelopmental processes, explaining the neurological complications observed in some patients.

The neurological manifestations in our patient, including epilepsy and developmental delay, represent less common but significant features of SEN syndrome. These complications occur in approximately 20-30% of reported cases and may significantly impact quality of life [8]. The presence of nephrolithiasis further expands the clinical spectrum, suggesting potential involvement of renal developmental pathways.

Management of SEN syndrome requires a multidisciplinary approach involving dermatology, gynecology, neurology, nephrology, and genetics specialists. Treatment remains primarily supportive, focusing on symptomatic relief and cosmetic reconstruction when indicated. Breast reconstruction surgery may be considered during late adolescence or early adulthood to address psychological and social concerns related to athelia and breast hypoplasia.

Genetic counseling plays a crucial role in patient management, particularly given the autosomal dominant inheritance pattern and 50% recurrence risk for future pregnancies. Prenatal diagnosis may be available through molecular genetic testing for families with known mutations.

Conclusion

SEN syndrome represents a rare but clinically recognizable congenital disorder requiring prompt diagnosis and comprehensive management. The variable clinical expressivity necessitates thorough evaluation of multiple organ systems. Early identification enables appropriate symptomatic treatment, genetic counseling, and psychological support to optimize patient outcomes and quality of life. This case underscores the importance of maintaining clinical suspicion for rare genetic disorders in patients presenting with multiple congenital anomalies.

Declarations

Patient Consent: Written informed consent was obtained from the patient and legal guardian for publication of this case report.

Ethical Approval: This case report was conducted in accordance with the Declaration of Helsinki and institutional ethical guidelines.

Funding: No funding was received for this case report.

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