sciendo
10.2478/AMB-2025-0021

CASE REPORT

LELIS SYNDROME: UNVEILING A RARE PHENOMENON

S. Sivadas, K. Rao, V. Ajila, Y. Jain

Department of Oral Medicine and Radiology, Nitte (Deemed to be University) A B Shetty Memorial Institute of Dental Sciences, Mangalore, India

Abstract. Background: *Lelis Syndrome is a rare hereditary disorder, distinguished by the coexistence of acanthosis nigricans and ectodermal dysplasia with a recessive mode of inheritance. Clinical characteristics seen are hypodontia, perioral and periorbital hyperpigmentation, leukoderma, palmoplantar hyperkeratosis, nail dystrophy, and intellectual disability.* ***Clinical case description:*** *A male patient in his 30s who was initially diagnosed with acanthosis nigricans was referred to the authors' department for dental evaluation and opinion. The patient manifested features of Ectodermal Dysplasia which consisted mainly of the inability to sweat, lower heat tolerance, and brittle/thin hair with the absence of facial hair along with manifestation of thickening/hyperpigmentation of the neck and axilla indicative of Acanthosis Nigricans.* ***Conclusion:*** *The dermatological findings in the current patient were typical of acanthosis nigricans and the symptoms were typical of ectodermal dysplasia which collectively led to the diagnosis of Lelis syndrome.*

Key words: *acanthosis nigricans, Lelis syndrome, ectodermal dysplasia, rare genetic disease*

Corresponding author: *Dr. Kumuda Rao, Nitte (Deemed to be University), A B Shetty Memorial Institute of Dental Sciences, Department of Oral Medicine and Radiology, Mangalore-575018, India, tel: +9448696705, email: drkumudarao@yahoo.in*

ORCID: *0009-0001-2676-5349 – Smrithy Sivadas K*

ORCID: *0000-0002-6214-1381 – Kumuda Rao*

ORCID: *0000-0002-5744-9322 – Vidya Ajila*

ORCID: *0009-0008-9294-7758 – Yashika Jain*

Received: *08 July 2024;* ***Revised/Accepted:*** *05 August 2024*

INTRODUCTION

Lelis syndrome (LS), alternatively recognized as ectodermal dysplasia (ED) accompanied by acanthosis nigricans (AN), stands as a rare autosomal recessive disorder with limited documented occurrences worldwide, initially documented by the Lithuanian Dermatology Professor Jonas Lelis [1]. In 1978 and 1979, Lelis detailed four unrelated individuals of Eastern European descent exhibiting both ED and AN [1]. In 2009, Van Steensel and Van Der Hout suggested that Lelis syndrome may be a manifestation of X-linked hypohidrotic ectodermal dysplasia (HED) [2]. The etiopathogenesis of LS remains elusive, with some researchers proposing it as a variant of hypohidrotic ectodermal dysplasia, while others designate it as a rare presenter of AN [3]. Noteworthy features in affected individuals may encompass palmoplantar hyperkeratosis, nail dystrophy, intellectual impairment, disruptions in skin pigmentation, and hypodontia [4]. It has been suggested to use electron microscopy for investigating ultrastructural studies of the epidermis using skin samples of HED patients to delineate the relation between ectodysplasin sig-

nalling and epidermal differentiation [2]. Herein, we present a male patient who presented with the symptoms of both ED and AN, and hence was diagnosed with LS. This case report aims to serve as a contribution to an extremely rare genetic disease and as a novel clinical entity.

CLINICAL CASE DESCRIPTION

A male patient in his 30s presented to our department with a diagnosis of AN from dermatology and a differential diagnosis of ED. The case history revealed that the patient complained of an inability to sweat, lower heat tolerance, and brittle and thin hair since childhood with no facial hair since puberty. The patient reported history of noticing asymptomatic lesions over the face, flexures, and intertriginous areas for about five years. There was no history of early-onset primary tooth loss or delayed eruption of permanent teeth. There was no history of consanguineous marriage of parents nor any contributing family history. The patient mentioned nail changes during adolescence and difficulty in taking hot water baths.

The patient appeared well-nourished and well-built. Axillary hair was thin and sparse and the skin was thick, uneven, and dry. The right little finger and toenails on both palms and feet exhibited brachydactyly, dystrophy, and irregularity (Figures 1A and B). Palmoplantar and foot hyperkeratosis were also observed bilaterally (Figures 1C and D).

On extraoral examination, the patient's face, neck, malar area, beard, moustache, and eyelashes were devoid of hair with sparse eyebrows (Figure 1E). An everted and bulged lower lip, and a protruding chin were also noted along with beaking of tip of nose. The patient also exhibited perioral radial furrows and perioral hyperpigmentation (Figures 1E and F). The patient presented with a hoarse voice. Lacrimal gland and ophthalmologic examinations revealed no abnormalities.

Intra-oral examination revealed an anterior open bite, macroglossia, high-arched palate, and labially positioned lower right canine (Figures 2A, B, and C). The tongue-blade test was positive, indicating decreased salivation. An orthopantomogram revealed a hyperplastic mandible, and altered morphology of the condylar head with flattening. The teeth 16 and 17 showed coronal radiolucency involving enamel and dentin, approaching the pulp suggestive of deep dentinal caries. Below the left inferior alveolar nerve canal, a well-defined radio-opacity of about 0.5 x 0.5 cm was observed, resembling a phlebolith (Figure 2D).

Further investigations of blood, urine, and stool were reported to be under normal range. Considering the clinical features of full penetrance (100%) of hypohidrosis and sparse hair of ED together with AN, the diagnosis of LS was designated. Additionally, the complex entity (syndrome) is exceptionally rare, and there is no evidence of a certain type of recessive inheritance yet to be ascertained like autosomal or X-linked with locus genetic heterogeneity of different genes and/or alleles involved. But the fact that the physical expression of LS is due to DNA mutation appreciates whole-exome sequencing (WES) greatly. The patient was referred for restoration with respect to teeth 16 and 17 and then back to the Dermatology Department and kept on follow-up.

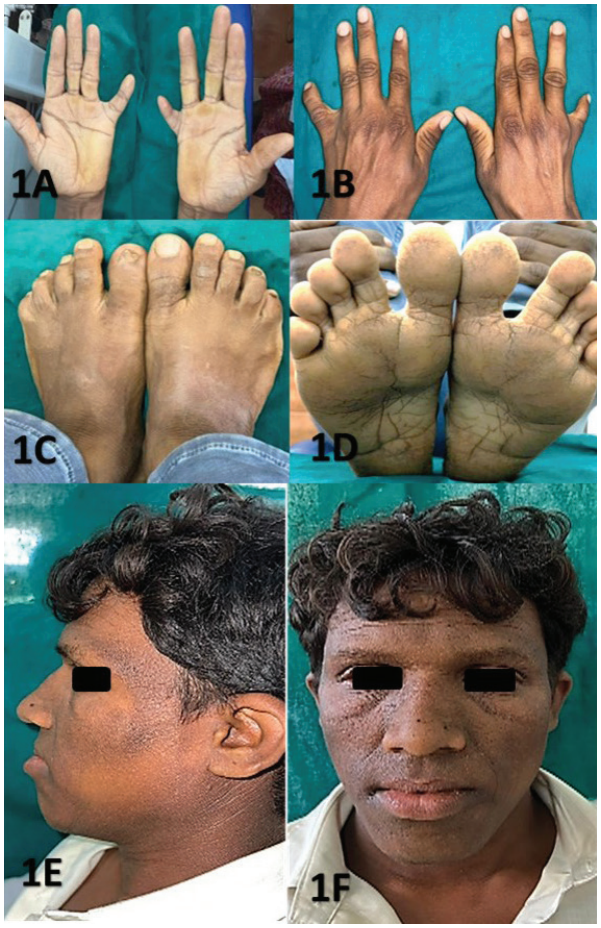

Fig. 1. A) Hyperkeratosis on the palmar aspect of hands with prominent crease lines; **B)** Hyperkeratosis of the plantar aspect of hands with brachydactylic right little finger; **C)** Hyperkeratosis of the plantar aspect of feet with nail dystrophy; **D)** Hyperkeratosis of the palmar feet with prominent crease lines; **E)** Lateral profile of the patient with prognathic mandible, thickening of the skin over zygoma, neck, absence of beard and moustache; **F)** Front profile with absence of facial hair, thickened skin over the forehead, malar area, neck, and missing eyelashes, sparse eyebrows

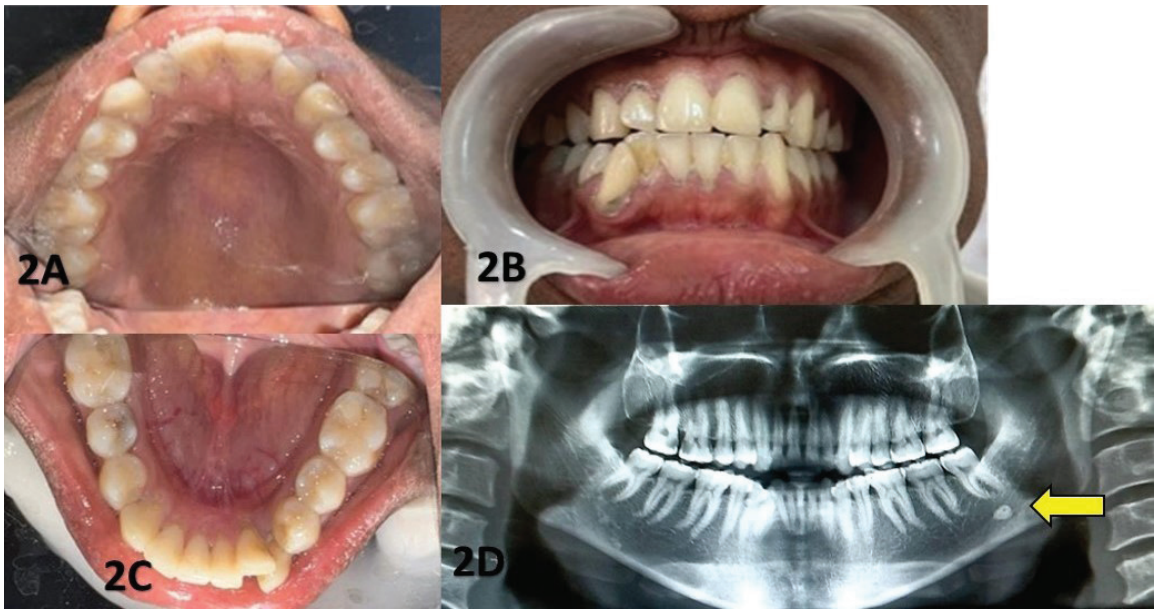

Fig. 2. A, B, C) Intraoral images showing high arched palate, labially placed 43 with no other morphological abnormalities; **D)** Orthopantomogram showing altered condylar morphology and hyperplastic mandible. The arrow points toward the phlebolith

DISCUSSION

LS also known as ED-AN syndrome is reported to have a prevalence rate of approximately 1 in 1,000,000 and exhibits autosomal inheritance. The onset is seen in childhood and adolescence with ectodysplasin A (EDA gene) being the implicated gene [5]. Only 8 cases have been reported in the literature, with all being inherited in an autosomal recessive manner [6, 7, 8]. The characteristics defining the condition are hypohidrosis and hypotrichosis, with frequent dental abnormalities. Our patient exhibited anterior open bite, macroglossia, high-arched palate, scant lateral eyebrows, mandibular prognathism, absence of lower eyelashes, midface retrusion, and aberrant toenail morphology [3].

This syndrome was initially described in Lithuania by a few researchers and was considered as a form of ED, but later Lelis described it in Brazil in 1978. It is thought to impact roughly 7/10 000 newborns despite the absence of accurate incidence data [8, 9]. Hypotrichosis, hypohidrosis, and AN are invariably present in LS; they were also noted in the presented patient.

Many cases of LS show intellectual incapacity and palmoplantar hyperkeratosis. The current patient was cooperative and oriented and had no signs of intellectual deficiency but did show features of palmoplantar hyperkeratosis. Hyperconvex dystrophic nails have been observed in 62% of reported instances. Most patients lack pubic or axillary hair and lower eyelashes [1, 3, 5]. Our patient, presented all these traits as described above. Hystrix-like ichthyosis has been observed in a few cases, especially in the axillary regions, and in around 12.5% of recorded instances, patients also presented with vitiligo [4, 5], which was absent in our patient. Long, narrow faces with up-sloping palpebral fissures, perioral radial furrows, midface hypoplasia, strabismus, proptosis, and perioral hyperpigmentation are also among the distinctive characteristics of LS [10].

The management of LS should be inclusive of meeting the treatment expectations of all the symptomatic clinical manifestations including treating teeth disorders, relief of low heat tolerance, and reducing hyperkeratosis. Cases of anodontia or altered teeth morphologies can be managed by functional rehabilitation and esthetic interventions [9]. Reported cases of Lelis syndrome have been treated with acitretin starting at the dosage of 0.5 mg/kg/day and gradually tapered to 0.3 mg/kg/day which provided favourable results by decreasing the associated hyperkeratosis and scaling of the skin [10]. Regular follow-ups should be planned for these patients.

CONCLUSION

The symptoms of LS usually begin in childhood and Adulthood. The diagnosis of LS in the current patient was incidental, as the skin findings in the current patient were typical of AN, and the symptoms were typical of ED. Dental surgeons and dermatologists should be aware and knowledgeable of these signs and symptoms typically involving the combination of teeth and skin manifestations which is extremely nec-

essary for the prompt diagnosis followed by efficient management of the condition.

Conflict of interest: *The authors declare no conflicts of interest related to this work.*

Funding: *The authors did not receive any financial support from any organization for this research work.*

Informed Consent for a Clinical Case: *Written informed consent was obtained from the patient for the publication of this case report, including any accompanying images. A copy of the written consent is available for review by the journal's editorial office upon request.*

Ethical statement: *This study has been performed in accordance with the ethical standards as laid down in the Declaration of Helsinki.*

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