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Case Report

Beyond bones and teeth: Langer–Giedion syndrome revealed through oral and psychiatric clues — a multisystem case report

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ABSTRACT

Langer–Giedion syndrome (LGS), also known as trichorhinophalangeal syndrome type II (TRPS II), is a rare contiguous gene deletion disorder involving chromosome 8q24.11–q24.13, resulting in loss of the TRPS1 and EXT1 genes. The syndrome is characterized by distinctive craniofacial dysmorphism, multiple osteochondromas, skeletal abnormalities, intellectual disability, and dental anomalies. Psychiatric and neurodevelopmental manifestations remain underreported despite their significant impact on functioning and quality of life. We report a 19-year-old female who presented with dental pain and was subsequently found to have classical craniofacial, skeletal, oral, neurodevelopmental, and psychiatric features consistent with Langer–Giedion syndrome. Clinical examination revealed microcephaly, a bulbous nasal tip, prominent ears, multiple bony exostoses, short stature, hypodontia, malocclusion, and retained deciduous teeth. Developmental history demonstrated delayed motor milestones, while psychiatric evaluation revealed borderline intellectual functioning, social immaturity, and emotional dysregulation. Radiographic imaging demonstrated multiple enchondromas and impacted teeth. This case emphasizes the importance of recognizing oral and behavioural manifestations as diagnostic clues in rare genetic syndromes and underscores the necessity of multidisciplinary management incorporating psychiatric care.

Keywords: Langer–Giedion syndrome, Chromosome, Psychiatric

INTRODUCTION

Langer–Giedion syndrome (LGS), also termed trichorhinophalangeal syndrome type II, is a rare autosomal dominant contiguous gene deletion syndrome caused by microdeletions involving chromosome 8q24.11–q24.13.[1,2] The condition was initially described by Giedion in 1966 and later further delineated by Langer and colleagues, establishing its recognition as a distinct clinical entity.[3-5] The deleted chromosomal region includes the *TRPS1* gene, which encodes a zinc-finger transcription factor essential for chondrocyte differentiation, craniofacial development, and hair follicle regulation, as well as the *EXT1* gene, which plays a critical role in heparan sulfate biosynthesis and normal endochondral ossification.[6-10]

Loss of *TRPS1* results in the characteristic craniofacial phenotype, brachydactyly, and cone-shaped epiphyses, whereas deletion of *EXT1* leads to the development of multiple osteochondromas.[9-11] In a subset of patients, the chromosomal deletion extends to include the *RAD21* gene, a component of the cohesin complex, which has been implicated in neurodevelopmental impairment and intellectual disability.[12,13] The size of the deletion correlates with phenotypic severity, particularly with respect to cognitive and behavioral manifestations.[14]

Despite the presence of recognizable clinical features, LGS is frequently underdiagnosed, particularly in low-resource settings where access to genetic testing is limited.[15] Patients may present late to non-genetic specialties, such as dentistry or orthopedics, with complaints that obscure the underlying syndromic diagnosis. Psychiatric and adaptive functioning impairments are insufficiently emphasized in the literature, despite their profound influence on long-term outcomes and quality of life.[16-22] This case report highlights the role of oral and psychiatric findings in identifying LGS and underscores the importance of a holistic, multidisciplinary diagnostic approach.

CASE REPORT

A 19-year-old female presented to the Department of Oral Medicine and Radiology with a chief complaint of pain in the upper right posterior region of the jaw for three months. The pain was intermittent, dull in character, and exacerbated by mastication. The patient was accompanied by her mother, who reported long-standing developmental delays and learning difficulties.

The patient was born to non-consanguineous parents and was the second of three siblings. Both siblings were reportedly healthy, with normal physical growth and cognitive development. There was no family history of skeletal dysplasia, intellectual disability, or congenital anomalies, suggesting a sporadic de novo chromosomal deletion, which is consistent with the majority of reported LGS cases.

Perinatal and developmental history

The antenatal period was reportedly uneventful, and the patient was delivered at term via normal vaginal delivery. However, she did not cry immediately after birth and was noted to have birth asphyxia. Her birth weight was 2.25 kg, fulfilling World Health Organization criteria for low birth weight. Early developmental history revealed significant delays in gross motor milestones, with independent walking achieved only after three years of age. Speech development was delayed, and academic performance remained consistently below age-appropriate expectations. Formal schooling was discontinued during early adolescence due to persistent learning difficulties and social maladjustment. These developmental concerns were never formally evaluated or managed through structured neurodevelopmental interventions.

General physical and craniofacial examination

General physical examination revealed short stature and a distinctly dysmorphic craniofacial appearance. Head circumference was below the third percentile for age and sex, consistent with microcephaly. The patient exhibited a short forehead with excessive frontal hair growth, a bulbous nasal tip with thickened alae, a long philtrum, and a thin upper lip. The ears were large and prominently protruding. These craniofacial features are characteristic of trichorhinophalangeal spectrum disorders and are considered highly suggestive of LGS when seen in combination with skeletal abnormalities. The patient's voice was low-pitched and poorly modulated, likely reflecting both anatomical differences and neurodevelopmental involvement.

Figure 1 (A and B): Craniofacial features characteristic of LGS.

Skeletal examination

Musculoskeletal examination revealed palpable bony prominences over the elbows, wrists, and knees, consistent with multiple osteochondromas. Brachydactyly with disproportionate fingers and a sandal gap deformity of the feet were also noted. Joint movements were mildly restricted, though not painful at rest. These findings are consistent with skeletal dysplasia resulting from deletion of the *EXT1* gene and abnormal endochondral ossification.

Psychiatric and neurodevelopmental assessment

Mental status examination demonstrated borderline intellectual functioning, with concrete thinking, limited abstract reasoning, and reduced problem-solving abilities. The patient exhibited social immaturity, dependency traits, and difficulty interpreting social cues. Emotional regulation was impaired, with low frustration tolerance and episodic irritability, particularly in unfamiliar environments. There was no evidence of psychosis, mood disorder, or substance use. Insight into her condition and

healthcare needs was limited. These psychiatric and adaptive functioning deficits significantly interfered with daily living skills and healthcare engagement. Such neuropsychiatric manifestations are increasingly recognized in LGS, particularly in patients with larger deletions involving the *RAD21* gene.

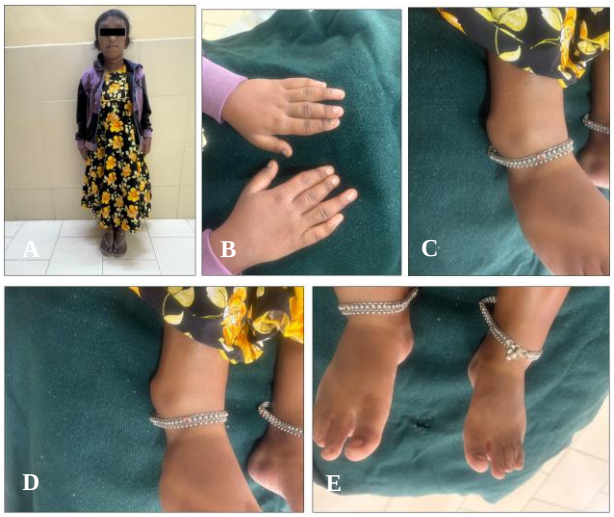

Figure 2 (A-E): Skeletal abnormalities including osteochondromas, short stature and disproportionate digits.

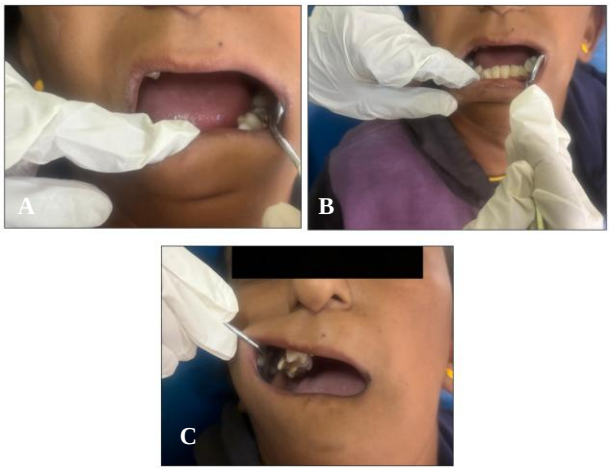

Figure 3 (A-C): Intraoral findings showing malocclusion, retained deciduous teeth, and carious lesions.

Oral and dental findings

Intraoral examination revealed extensive dental pathology. Deep dentinal caries were present in the maxillary right first molar and mandibular left first molar, while root stumps were observed in the maxillary right second molar and a retained primary mandibular molar. Multiple permanent teeth were congenitally absent, including all permanent canines and one mandibular premolar. Several deciduous teeth were retained beyond the expected age of exfoliation. Severe crowding, ectopic eruption, palatal displacement of premolars, and labially positioned incisors resulted in significant malocclusion. Oral hygiene was poor, likely influenced by cognitive limitations and lack of prior dental care. Dental anomalies such as hypodontia, malocclusion, and delayed eruption have been frequently reported in LGS and may serve as early diagnostic indicators.

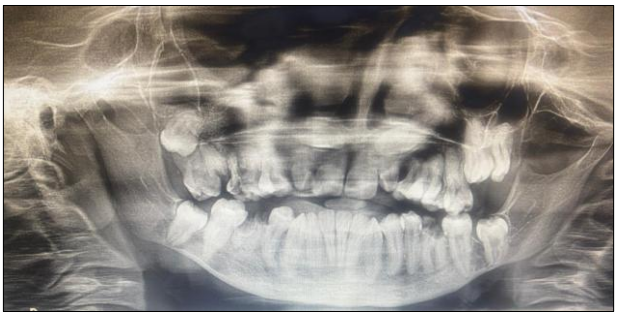

Figure 4: Orthopantomogram demonstrating hypodontia, impacted teeth and retained root stumps.

Radiological findings

Radiographic evaluation demonstrated multiple enchondromas involving the metaphyseal regions of long bones and small tubular bones. Cone-shaped epiphyses of the phalanges were evident, a radiological hallmark of trichorhinophalangeal syndromes. These findings supported the clinical diagnosis of Langer–Giedion syndrome and reflected abnormal cartilage and bone development resulting from combined *TRPS1* and *EXT1* gene deletion.

Diagnosis and differential considerations

The diagnosis of Langer–Giedion syndrome was established on clinical and radiological grounds based on the characteristic constellation of craniofacial dysmorphism, multiple osteochondromas, cone-shaped epiphyses, dental anomalies, and neurodevelopmental impairment. Trichorhinophalangeal syndrome type I was excluded due to the presence of multiple exostoses, while multiple hereditary exostoses was considered unlikely because of the associated intellectual disability and facial dysmorphism. Other chromosome 8q deletion syndromes were considered but did not fully account for the observed phenotype.

Management and follow-up

Management required a multidisciplinary approach involving dental, orthopedic, psychiatric, and genetic services. Dental care focused on extraction of non-restorable teeth, restoration of carious lesions, preventive strategies, and long-term orthodontic and prosthodontic planning. Orthopedic surveillance was advised to monitor the progression of osteochondromas and joint function. Psychiatric intervention emphasized supportive psychotherapy, caregiver education, and adaptive skills

training to improve functional independence. Genetic counseling was provided to explain the nature of the disorder, its autosomal dominant inheritance pattern, and reproductive implications, including the low recurrence risk for parents and a 50% transmission risk for affected individuals.

DISCUSSION

LGS, also known as trichorhinophalangeal syndrome type II, is a rare contiguous gene deletion disorder characterized by craniofacial dysmorphism, multiple osteochondromas, intellectual disability, and dental abnormalities. The present case demonstrates the classical phenotypic features of LGS while also highlighting the often-overlooked psychiatric and adaptive functioning impairments that significantly influence long-term outcomes.

The craniofacial features observed in our patient, including microcephaly, a bulbous nasal tip, prominent ears, long philtrum, and short stature, are consistent with those described by Schinzel et al and George et al, who identified these findings as characteristic clinical markers of LGS.[4,6] Similarly, the presence of multiple osteochondromas, brachydactyly, and cone-shaped epiphyses corresponds with the skeletal manifestations reported in previous studies and reflects the consequences of EXT1 gene deletion on endochondral bone development.[9,11]

Dental abnormalities represented one of the most striking features in the present case. Hypodontia, retained deciduous teeth, malocclusion, delayed eruption, and extensive dental caries were observed. Similar oral findings have been reported by Katge et al and Machuca et al, who emphasized that dental anomalies may constitute an important early diagnostic clue, particularly when patients initially present to dental services rather than genetic clinics.[7,16] Our case further supports the importance of oral examination in facilitating syndromic diagnosis in resource-limited settings where genetic testing may not be readily available.

An important aspect of this case is the presence of neurodevelopmental and psychiatric manifestations. The patient exhibited borderline intellectual functioning, social immaturity, impaired adaptive functioning, emotional dysregulation, and poor problem-solving abilities. Although cognitive impairment has been described in LGS, psychiatric and behavioural manifestations remain relatively underreported in the literature. Schinzel and colleagues reported behavioural abnormalities and social difficulties in individuals with rare chromosomal disorders, while more recent genotype–phenotype studies suggest that larger deletions involving genes such as RAD21 may contribute to greater neurodevelopmental impairment.[13,17] The findings in our patient support these observations and highlight the need for routine psychiatric assessment as part of comprehensive care.

The diagnosis in this patient was established primarily through clinical and radiological findings. This is particularly relevant in low- and middle-income countries where molecular genetic testing may not be universally accessible. Previous studies have emphasized that recognition of the characteristic combination of craniofacial dysmorphism, multiple exostoses, and dental abnormalities can facilitate an accurate clinical diagnosis even in the absence of genetic confirmation.[15]

Management of LGS requires a multidisciplinary approach involving dentistry, orthopedics, psychiatry, rehabilitation services, and genetic counseling. While orthopedic and dental complications often receive clinical attention, psychosocial functioning and adaptive skills are frequently neglected. Early intervention programs, caregiver education, and psychiatric support may substantially improve quality of life and social functioning. Our case underscores the importance of integrating psychiatric assessment into the routine evaluation of individuals with LGS.

CONCLUSION

In conclusion, this case adds to the limited literature on LGS and reinforces the value of oral and psychiatric findings as important diagnostic clues. Greater awareness among dentists, psychiatrists, and primary care physicians may facilitate earlier recognition, timely referral, and comprehensive multidisciplinary management of affected individuals.

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