EurAsian Journal of Oral and Maxillofacial Surgery
Official publication of AÇBİD (Association of Oral and Maxillofacial Surgery Society)

CASE REPORT

Zimmermann-Laband Syndrome: A Case Report

Zimmermann-Laband Sendromu: Bir Vaka Raporu

Gurkan Rasit Bayar[1], Kerim Ortakoglu[2], H. Aykut Ozyigit[3]

[1] Professor, Department of Oral and Maxillofacial Surgery, University of Kyrenia Faculty of Dentistry, Cyprus

[2] Associate Professor, Private Clinic, Bahcelievler, Istanbul,Turkiye

[3] PhD, Department of Oral and Maxillofacial Surgery, University of Kyrenia Faculty of Dentistry, Cyprus

ABSTRACT

Zimmerman-Laband Syndrome (ZLS) is a rare genetic disorder characterized by gingival fibromatosis, craniofacial abnormalities, and limb deformities. This case report describes a 21-year-old male presenting with classical and unique features of ZLS. A male patient was referred for failure of anterior teeth eruption. Clinical examination revealed gingival fibromatosis, hypoplastic toenails, and a broad, flat nose. Additional findings included congenital curly toes and an anterior open bite (AOB). Radiographic evaluation identified multiple impacted and supernumerary teeth. The patient underwent extraction of carious and supernumerary teeth. Orthodontic and surgical interventions were planned for managing unerupted teeth and AOB. This report expands the phenotypic spectrum of ZLS, describing previously unreported findings such as curly toes and hammer toes. Comprehensive evaluation and interdisciplinary management are essential for optimizing outcomes in ZLS patients.

Keywords: Anterior open bite, congenital abnormalities, gingival fibromatosis, impacted teeth, Zimmerman-Laband syndrome.

ÖZET

Zimmerman-Laband Sendromu (ZLS), gingival fibromatozis, kraniofasiyal anormaliler ve uzuv deformiteleri ile karakterize edilen nadir bir genetik hastalıktır. Bu vaka raporu, ZLS'nin klasik ve özgün özellikleriyle başvuran 21 yaşında bir erkek hastayı tanımlamaktadır. Hasta, anterior dişlerin sürmemesi nedeniyle sevk edilmiştir. Klinik muayene, gingival fibromatozis, hipoplastik tırnaklar ve geniş, düz bir burun ile uyumluydu. Ek bulgular arasında doğuştan gelen kıvrımlı parmaklar ve anterior open-bite yer alıyordu. Radyografik değerlendirme, birden fazla gömülü ve süpernümerer dişi ortaya koymuştur. Hastanın çürük ve süpernümerer dişleri çekilmiştir. Sürmeyen dişler ve anterior open-bite için ortodontik ve cerrahi müdahaleler planlanmıştır. Bu rapor, ZLS'nin fenotipik spektrumunu genişleterek, daha önce bildirilmeyen kıvrımlı parmaklar ve çekiç parmaklar gibi bulguları tanımlamaktadır. ZLS hastalarında sonuçların iyileştirilmesi için kapsamlı bir değerlendirme ve multidisipliner yaklaşım gereklidir.

Anahtar Kelimeler: Anterior open-bite, gingival fibromatozis, gömülü diş, konjenital anomaliler, Zimmermann-Laband Sendromu

Submission Date: November 27, 2024
Acceptance Date: December 25, 2024
Corresponding author: H. Aykut Özyiğit
Address:University of Kyrenia Faculty of Dentistry Department of Oral and Maxillofacial Surgery, Şehit Yahya Bakır Sokak Karakum Girne /KKTC
Phone: +905077964306
Email: aykut.ozyigit@kyrenia.edu.tr

Gurkan Rasit Bayar 0000-0003-4119-9629
Kerim Ortakoglu 0009-0009-4325-7061
H. Aykut Ozyigit 0009-0007-8488-6564

Creative Common Attribution Licence, EJOMS Licence © 2024 by Association of Oral and Maxillofacial Surgery Society is licensed under Attribution-NonCommercial-NoDerivatives 4.0 International

EurAsian Journal of Oral and Maxillofacial Surgery
Official publication of AÇBİD (Association of Oral and Maxillofacial Surgery Society)

INTRODUCTION

Zimmerman-Laband Syndrome (ZLS) is a rare genetic disorder characterized by gingival fibromatosis, craniofacial abnormalities, and other systemic manifestations. The syndrome typically includes a coarse facial appearance, hyperextensibility of small joints, hypoplasia or aplasia of toenails and terminal phalanges, hepatosplenomegaly, and intellectual deficits of varying severity. Additional features such as hirsutism and "dystrophic" finger and toenails have also been documented. The first case of ZLS was described by Zimmerman in 1928, with Laband et al. later reporting familial occurrences and suggesting autosomal dominant inheritance.[1,2]

Although ZLS is generally considered to follow an autosomal dominant inheritance pattern, recessive inheritance has been suggested in certain cases, particularly in families without parental manifestations.[3,4] To date, approximately 36 cases of ZLS have been documented in the literature, highlighting its rarity. Despite its distinctive phenotype, variability in clinical presentation underscores the importance of comprehensive case evaluations.

This report describes a new case of ZLS in a young male patient. Along with the classical features of the syndrome, unique findings such as congenital curly toes and hammer toes are presented, contributing to the expanding phenotypic spectrum of the disorder.

CASE REPORT

A 21-year-old male was referred to our clinic with concerns regarding the failure of eruption of his upper and lower anterior teeth. His medical history indicated that he was born at 39 weeks of gestation to healthy, non-consanguineous parents (29-year-old mother and 33-year-old father). Pregnancy and delivery were uneventful, and his birth weight was 3,150 g.

The patient's physical examination revealed a height of 152 cm and a weight of 55 kg, both within normal limits for his age. His head circumference measured 57 cm. Facial features included a broad, flat, fleshy nose and thick, floppy ears (Figures 1 and 2). Examination of his hands showed no abnormalities; however, the toenails were bilaterally hypoplastic, and the third toes were rudimentary (Figure 3). Additional findings included congenital curly toes involving the fourth and fifth toes of the left foot and the fifth toe of the right foot, as well as hammer toes affecting all toes except the halluces. The patient's skin was dry, soft, and velvety, with thick and bushy eyebrows. Hair growth on the scalp and body was unremarkable.

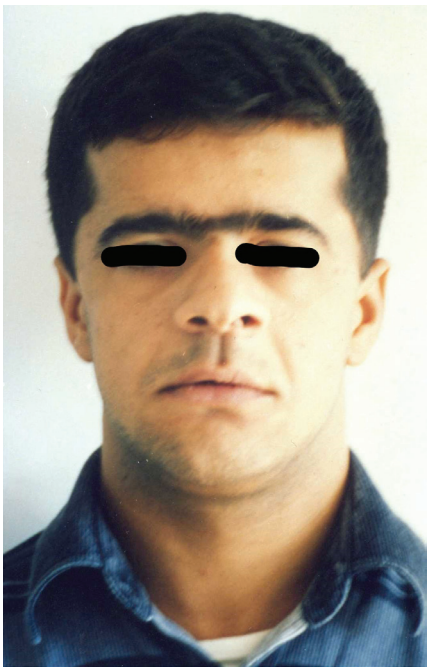

Figure 1. Front view of patient showing broad, flat and fleshy nose.

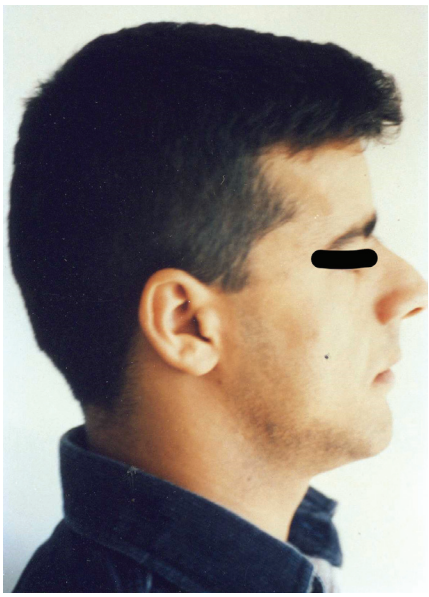

Figure 2. Lateral view of patient showing thick and floopy ears.

EurAsian Journal of Oral and Maxillofacial Surgery
Official publication of AÇBİD (Association of Oral and Maxillofacial Surgery Society)

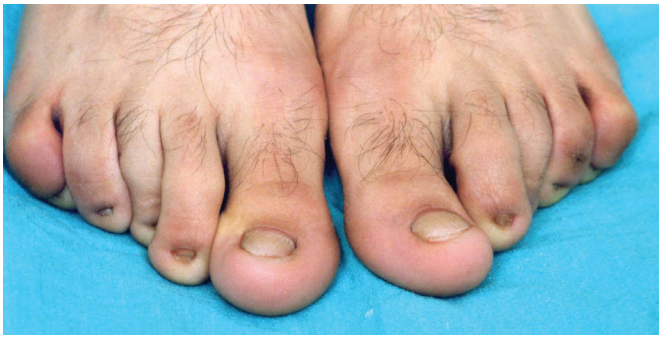

Figure 3. Toes view of patient showing bilaterally hypoplastic nails and other features of toes.

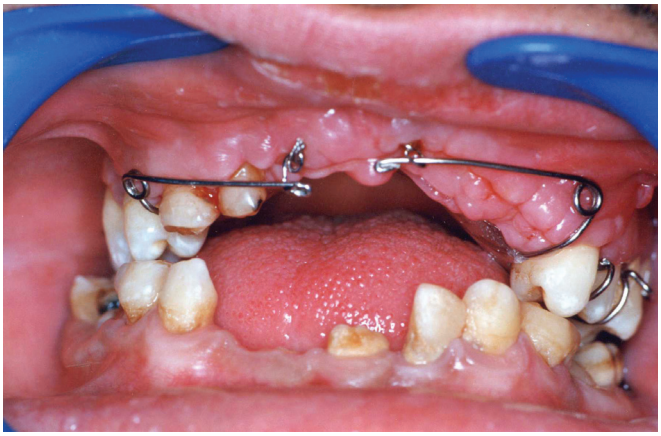

Figure 4. Intraoral view showing an anterior openbite and the condition of teeth.

Neurological and ophthalmological evaluations revealed no pathological findings. Intelligence appeared normal upon subjective assessment. Joint hypermobility was noted in the metatarsophalangeal and knee joints. Liver and spleen were non-palpable, and routine hematological and karyotyping analyses (46, XY) were normal. Since there is no specific gene associated with ZLS yet and it was not possible to establish contact with the patient's relatives, further genetic testing could not be performed.

Oral examination revealed pronounced gingival fibromatosis, which contributed to the failure of tooth eruption. The patient was in the permanent dentition phase, but most permanent teeth were unerupted. Teeth present in the oral cavity included: maxillary deciduous lateral incisors, canines, and primary molars, mandibular deciduous canines, primary molars, and partially erupted permanent central incisors and second premolars. Several unerupted teeth, including maxillary central and lateral incisors, canines, and mandibular lateral incisors and canines, were confirmed via radiography (Table I).

The patient also exhibited an anterior open bite (AOB) (Figure 4), despite no history of thumbsucking or tongue thrusting. There was no evidence of macroglossia.

A panoramic radiograph revealed multiple unerupted permanent teeth and five supernumerary teeth, one located in the maxillary right posterior region and four in the maxillary anterior region (Figure 5). No abnormalities were observed in the vertebral skeleton, skull, or chest.

The patient was admitted for extraction of carious and supernumerary teeth and for the management of unerupted teeth. The informed consent of the patient was obtained regarding the planned procedures. Further orthodontic and surgical interventions were planned to address the AOB and facilitate the eruption of impacted teeth. Since the patient was performing military service during the treatment, long-term follow-up could not be conducted after the patient was discharged.

Table I. Conditions of the teeth of the patient

Fully Erupted Teeth	52,53,14,15,17,62,63,24,25,26,27,83,85,46,72,73,75,36
Partially Erupted Teeth	41,31,45,35
Unerupted Teeth	11,12,13,18,21,22,23,28,32,33,34,35,42,43,44,48
Extracted Teeth	16,47,37,38

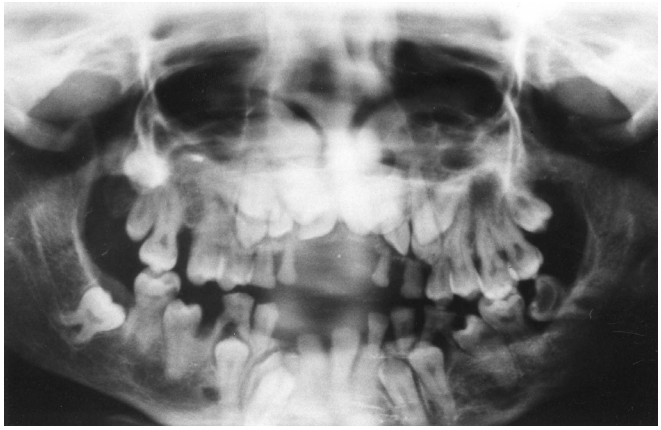

Figure 5. Panoramic radiograph showing unerupted teeth and supernumerary teeth.

EurAsian Journal of Oral and Maxillofacial Surgery
Official publication of AÇBİD (Association of Oral and Maxillofacial Surgery Society)

Table II Laband syndrome:Summary of reported findings (Adapted from data in Chadwick et al)

Author and case#	Country of origin	Sex	a	b	c	d	e	f	g	h	i	j	k
Zimmerman 1	Germany	M	+	N	+	N	?	Spina Bifida	+/+	?	+	?/?	-
Zimmerman 2	Germany	F	+	(M.retard)	+	+	?	N	+/+	?	+	?/?	MG
Jacoby et al 1	U.K.	F	+	N	N	N	+	Spina Bifida	+/+	?	N	N/N	-
Laband et al 1	Trinidad	F	+	IQ70	N	+	+	N	+/+	+	N	+/+	-
Laband et al 2	Trinidad	M	+	IQ70	N	+	+	N	+/+	+	N	+/+	-
Laband et al 3	Trinidad	F	+	IQ70	N	+	+	N	+/+	+	N	+/N	-
Laband et al 4	Trinidad	M	+	IQ70	N	+	+	Kyphosis	+/+	+	N	N/N	-
Laband et al 5	Trinidad	F	(+)	IQ70	N	+	+	N	+/+	+	N	+/+	-
Laband et al 6	Trinidad	F	+	IQ70	N	+	+	N	+/+	+	N	N/N	-
Alavandar 1	S. India	F	+	N	N	+	+	N	+/+	+	?	N/N	-
Alavandar 2	S. India	M	+	N	N	+	+	N	+/+	N	?	+/N	-
Alavandar 3	S. India	M	+	N	N	+	+	N	+/+	+	?	+/+	-
Alavandar 4	S. India	M	(+)	N	N	+	+	N	+/+	+	?	N/N	-
Alavandar 5	S. India	M	(+)	N	N	N	N	N	+/+	+	?	N/N	-
Anatasov 1	Bulgaria	F	+	N	+	?	?	?	?/+	?	?	?/?	-
Anatasov 2	Bulgaria	M	+	(M.retard)	?	?	?	?	+/+	?	?	?/?	-
Oikava et al 1	U.S.A.	F	+	(M.retard)	+	+	+	Kyphosis	+/+	N	Thick eyelashes	+/N	-
Chodirker et al 1	Canada	M	+	M.retard	+	+	+	Scoliosis	+/+	+	N	N/N	MG
Pino Neto et al 1	Brazil	F	+	(M.retard)	N	+	+	N	+/+	+	+	+/+	MG
Beemer 1	Holland	F	+	N	+	+	N	N	+/+	N	?	N/N	MG/ AOB
Ili˙na et al1	Ukraine	F	+	(M.retard)	+	+	+	Scoliosis	+/?	N	N	N/N	AOB
Bazoupoulou et al 1	Greece/ Albania	F	+	(M.retard)	+	+	+	N	+/+	+	Synophrys	N/N	AOB
Bakaeen and Scully 1	Jordan	F	+	N	N	+	N	N	+/?	+	N	N/N	-
Bakaeen and Scully 1	Jordan	M	+	N	N	+	N	N	+/+	+	N	N/N	-
Pfeiffer et al 1	Germany	M	+	M.retard	+	+	N	Spondylodyplasia	+/?	?	+	+/N	-
Pfeiffer et al 1	Germany	M	+	N	N	+	+	N	+/+	?	+	+/+	-
Chadwick et al	U.K.	F	+	N	+	+	N	N	+/+	N	+	+/N	AOB
Chadwick et al 2	Pakistan	M	+	(M.retard)	+	+	+	N	+/+	N	+	N/N	AOB
Koch et al 1	Germany	F	+	N	+	+	?	N	+/+	N	N	N/N	ARP
Lacombe et al 1	S. India	+	+	? Slightly delayed motor development	+	+	+	?	+/+	(+)	+	+/N	-
Van Buggenhout et al 1	Holland	M	+	M. retard	N	+	+	Scoliosis	+/+	+	Bushy eyebrows	N/N	RI
Robertson et al 1	Australia	M	+	M. retard	+	+	+	?	+/+	+	Thick eyebrows, synophrys, hirsutism	N/N	CVC
Dumic et al 1	Croatia	F	+	?	?	+	+	?	+/+	+	+	+/?	MG
Katz et al 1	USA	F	+										
Stefanova et al 1	Bulgaria	F											
Stefanova et al 1	Bulgaria	F											
Holzhausen 1	Brasil												
Davalos et al 1	Mexico	F											
Davalos et al 1	Mexico	M											
Atabek et al 1	Turkey	M											
Kim et al 1	USA	M											
Kissi et al 1	France	F											
Douzgou et al 1	Italy												
Ortakoglu et al 1	Turkiye	M	+	N	N	+	+	N	N/+	+	Thick eyebrows	N/N	AOB
Shrian et al 1	Iran	F	+	N					+/N		+	+/+	VSD, telecanthus
Kshirsagar et al 1	India	F	+	Impaired intellectual and adaptive function	+	+							AOB, MG

List of Abbreviations
a: Gingival fibromatosis
b: Mental development
c: Thick lips
d: Broad nose
e: Large Ears
f: Spine
g: Aplasia or hypoplasia of nails or terminal phalanges of hands / feet
h: Hyperextensibility of joints
i: Hypertrichosis
j: Hepatomegaly / splenomegaly
k: Other
M: Male
F: Female
N: Normal
?: Not reported
MG: Macroglossia
AOB: Anterior open-bite
(...):Mild manifestation
IQ Intelligence quotient
ARP: Atypical retinitis pigmentosa
CVC: Cardiac and vascular complications
RI: Retrognathia inferior
VSD: Ventricular septal defect

EurAsian Journal of Oral and Maxillofacial Surgery
Official publication of AÇBİD (Association of Oral and Maxillofacial Surgery Society)

DISCUSSION

A total of 36 cases of ZLS have been reported in the literature. Laband et al. described six individuals from a single family, Alavandar documented five cases within a pedigree, and Bakeen et al., along with Shirian et al., reported two affected siblings.[2-4,22] Additionally, 21 isolated cases without familial involvement have been identified.[1,5-19,23] This article presents a further isolated case of ZLS, where no other family members exhibited symptoms of the syndrome.

ZLS is a rare genetic disorder characterized by gingival fibromatosis, nasal and/or ear abnormalities, and hypoplasia or absence of the nails or terminal phalanges of the hands and feet. Other clinical manifestations may include joint hyperextensibility, hepatomegaly, splenomegaly, hypertrichosis, mental retardation, thick lips, macroglossia, AOB, and occasional spinal abnormalities. The features of reported cases, summarized in Table II, show overlapping characteristics but also variability. Despite phenotypic similarities to known storage disorders, no definitive biochemical defect has been identified

The diagnosis of ZLS in our patient was based on hallmark clinical findings, including a coarse facial appearance with a broad nose, thick and floppy ears, gingival fibromatosis, and hypoplasia or absence of toenails.

AOB has been widely reported in ZLS cases, including those by Ili'na et al., Beemer, Bazoupoulou-Kyrkanidou et al., and Chadwick et al.[5-8] These authors proposed that AOB is caused by the combined effects of a macroglossia and gingival fibromatosis. In our patient, AOB was also observed; however, macroglossia and digit-sucking habits, often associated with AOB, were absent.

Supernumerary teeth have been previously reported by Chadwick et al.[5] In our case, this finding was also noted, suggesting that supernumerary teeth may represent a secondary but less common feature of ZLS.

Congenital curly (varus) toes and hammer toes have not been described in the literature to date and may represent a novel clinical manifestation of ZLS.

Laband et al. reported a mother with seven children, five of whom were affected, while Alavandar described an affected mother, three affected sons, and an affected grandson.[2,3] These cases support an autosomal dominant inheritance pattern. Although a complete family pedigree was unavailable for our case, the observed data are consistent with autosomal dominant transmission

Genetic investigations into ZLS remain inconclusive. Stefanova et al. identified a candidate locus in the 3p14.3 region of the chromosome, while Hoogendijk et al. found an insertion in the 8(10) chromosomal region. Shirian et al. and Kshirsagar et al. conducted genetic analyses that failed to detect any DNA sequences associated with known genetic diseases or nonsyndromic conditions.[20-23] These findings underscore the need for further research to elucidate the genetic basis of ZLS and its underlying pathophysiology.

This case contributes to the expanding phenotypic spectrum of ZLS and highlights the necessity for ongoing genetic and clinical studies to better understand this complex syndrome.

CONCLUSION

ZLS is a rare genetic disorder with a wide spectrum of clinical manifestations. This case report documents a 21-year-old male presenting with both classical features of ZLS, such as gingival fibromatosis, impacted teeth, and craniofacial abnormalities, and novel findings, including congenital curly toes and hammer toes. These observations expand the phenotypic spectrum of the syndrome and highlight the variability in its presentation.

The dental and systemic challenges associated with ZLS require a multidisciplinary approach involving oral surgeons, orthodontists, geneticists, and other specialists to optimize patient outcomes. Comprehensive evaluation and early intervention are essential for addressing dental and skeletal abnormalities, improving quality of life, and preventing complications

Further research and genetic studies are necessary to confirm the inheritance patterns and underlying genetic mutations associated with ZLS. This case underscores the importance of documenting rare syndromes to enhance understanding and guide the development of tailored management strategies. As the existing studies to date have not identified a specific treatment for the disease, the current treatment approach focuses on managing the abnormalities associated with the condition. In the case presented here, the aim was not the treatment of the disease itself but rather its diagnosis and a comparison of the symptoms reported in other studies.

EurAsian Journal of Oral and Maxillofacial Surgery
Official publication of AÇBİD (Association of Oral and Maxillofacial Surgery Society)

REFERENCES

1. Zimmermann KW. Über anomalien des ektoderms. Vierteljahresschrift für Zahnheilkunde. 1928;44:419-434.
2. Laband PF, Habib G, Humphreys GS. Hereditary gingival fibromatosis – Report of an affected family with associated splenomegaly and skeletal and soft-tissue abnormalities. Oral Surg Oral Med Oral Path. 1964;17:339-351.
3. Alavandar G: Elephantiasis gingivae: Report of an affected family with associated hepatomegaly, soft tissue and skeletal abnormalities. J All Ind Dent Assoc. 1965;37:349-353.
4. Bakaeen G, Scully C. Hereditary gingival fibromatosis in a family with the Zimmermann-Laband syndrome. J Oral Pathol Med 1991;20:456-459.
5. Chadwick B, Hunter B, Hunter L, Aldred M, Wilkie A. Laband syndrome: Report of two cases, review of the literature, and identification of additional manifestations. Oral Surg Oral Med Oral Pathol. 1994;78:57-63.
6. Ili'na JG, Lurie JV, Vaslianskene JP. Analysis of phenotypic variability of Zimmermann-Laband syndrome. Pediatriia. 1988;4:86-88.
7. Beemer FA. New syndromes: Part II: "European" syndromes. Am J Med Genet Supp. 1988;4:71-84.
8. Bazoupoulou-Kyrkanidou E, Papagianoulis L,Papanicolaou S, et al: Laband syndrome: A case report. J Oral Pathol Med. 1990;19:385-387.
9. Jacoby NM, Ripman HA, Munden JM. Partial anonychia (recessive) with hypertrophy of the gums and multiple abnormalities of the osseous system: Report of case. Guys Hosp Rep. 1940;90:34-40.
10. Anatasov D, Kavlakov P, Penev P. Congenital idiopathic gingival fibromatosis combined with anichia. Stomatologija (Sofija). 1979;61:29-33.
11. Oikawa K, Cavaglia MV, Lu D. Laband syndrome: Report of a case. J Oral Surg. 1979;37:120-122.
12. Chodirker BN, Chudley AE, Toffler MA, Reed MH. Zimmermann-Laband syndrome and profound mental retardation. Am J Med Genet. 1986;25:543-547.
13. Pina Neto JM, Soares LMN, Souza AHO. A new case of Zimmermann-Laband syndrome with mild mental retardation, asymmetry of limbs, and hypertrichosis. Am J Med Genet. 1988;31:691-695.
14. Pfeiffer RA, Seemanova E, Süss J, Müssig D, Tietze HU. Das syndrom von Zimmermann-Laband. Klin Pediatr. 1992;204:1-5.
15. Koch P, Wettstein A, Knauber J, Zaun H. A new case of Zimmermann-Laband syndrome with atypical retinitis pigmentosa. Acta Derm Venereol (Stockh). 1992;72:376-379.
16. Lacombe D, Bioulac-Sage P, Sibout M, Daussac E, Lesure F, Manchart JP et al. Congenital marked hypertrichosis and laband syndrome in a child: Overlap between the gingival fibromatosis-hypertrichosis and laband syndromes. Genet Counsel. 1994;5:251-256.
17. Van Buggenhout GJCM, Brunner HG, Trommelen JCM, Hamel BC. Zimmermann-Laband syndrome in a patient with severe mental retardation. Genet Counsel. 1995;6:321-327.
18. Robertson SP, Lipp H, Bankier A. Zimmermann-Laband syndrome in an adult. Long-term follow-up of a patient with vascular and cardiac complications. Am J Med Genet. 1998;78:160-164.
19. Dumic M, Crawford C, Ivkovic I, Cvitanovic M, Batinica S. Zimmermann-Laband syndrome: An unusually early presentation in a newborn girl. Croat Med J. 1999;40:102-103.
20. Stefanova M, Atanassov D, Krastev T, Fuchs S, Kutsche K. Zimmermann-Laband syndrome associated with a balanced reciprocal translocation t(3;8)(p21.2;q24.3) in mother and daughter: molecular cytogenetic characterization of the breakpoint regions. Am J Med Genet A. 2003;15;117A(3):289-294.
21. Hoogendijk CF, Marx J, Honey EM, Pretorius E, Christianson AL. Ultrastructural investigation of Zimmermann-Laband syndrome. Ultrastruct Pathol. 2006;30(6):423-6.
22. Shirian S, Shahabinejad H, Saeedzadeh A, Daneshbod K, Khosropanah H, Mortazavi M et al. Zimmermann- Laband Syndrome: Clinical and Cytogenic study in Two Related Patients. J Clin Exp Dent. 2019;11(5):e452-6.
23. Kshirsagar JT, Dharani K, Thangavel P. Zimmermann–Laband syndromeassociated hereditary gingival fibromatosis. J Indian Soc Periodontol 2023;27:645-50.