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A New Case of Zimmermann-Laband Syndrome with Atypical Retinitis Pigmentosa

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This paper reports a case study of a 10-year-old girl exhibiting symptoms of a Zimmermann-Laband syndrome (ZLS), including an ocular involvement not previously observed. In addition to the case reported, we have also discovered 21 patients described in the literature. Major clinical findings, defined as being present in more than 75% of the cases under discussion, are presented. ***Key words: Gingival fibromatosis syndromes; Nail dysplasia; Phalanx dysplasia.***

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The Zimmermann-Laband syndrome (ZLS) is a rare genetic disorder, characterized by gingival fibromatosis with an association of soft tissue, phalangeal and nail anomalies. Two isolated cases were first described by Zimmermann in 1928 (1). The syndrome was later, in 1964, more fully delineated by Laband in a case of a mother and five of her seven children (2). Since that time a total of 22 cases, including the one under present discussion, have been reported in conjunction with other disorders including hypertrichosis, vertebral anomalies and mental retardation (3–9).

This paper sets out to present an additional case of that genetic entity, drawing attention to an ocular disorder not previously reported.

CASE REPORT

The patient, a white female, was born on 9th March 1981, after a full-term uncomplicated pregnancy. The patient's weight at birth was 4,050 kg. No neonatal problems were observed. She is the first born child of healthy, genetically unrelated parents. The parents, grandparents on both sides of the family and the subsequently born 5-year-old brother were or are all free of gingival hypertrophy, dysmorphic syndromes or skeletal malformations. Their family history does however reveal that two maternal cousins of the patient died several days after birth, having exhibited a dysmorphic syndrome which remained unexplored.

The mother of the patient was able to inform us that several members of the family, taken over three generations, had suffered significant loss of hearing. There is no evidence of consanguinity in the family.

Gingival hypertrophy appeared at the time of the breakthrough of the milk teeth. Teething was delayed as a result of the hypertrophy, which worsened over the following years. Diphenylhydantoin or cyclosporine have never been administered to parents or daughter.

At the age of 4 years, reduced visual acuity was noted for the first time and the impairment has worsened since the patient reached the age of 8 in 1989. This had led in turn to problems with accomplishing school work. No problems with social adaptation have been noted, and the patient is not mentally impaired.

During the clinical examination at the age of 8 years and 9 months a height of 144,5 cm and a weight of 30 kg were registered. The circumference of the head measured 53,8 cm. None of these measurements deviate from the norm. The patient's nose was bulbous with a soft cartilage consistency. The lips were thick and an intense overgrowth of gingival tissue prevented the patient's mouth from closing. This affected the whole of both gingivae without extending onto the hard palate (Figs. 1–2). The points of her teeth were visible through the hypertrophied gingivae.

Radiological examination showed that the patient had a full complement of teeth, with persistence of the molar and canine milk-teeth.

The finger nails of all digits except the index fingers were small and dystrophic (Fig. 3). Nails on the halluces resembled spikes set in a shallow pit. When the feet were examined, the toenails of the second and third digit were found to be very small and friable.

Radiological examination of the left hand exposed a hypoplasia of the distal phalanx of the little finger. The terminal phalanx of both the thumb and the index finger were divided; there was no epiphysis. The terminal phalanx of the third finger seemed also to be primarily bipartite but with secondary fusion of the two bone parts (Fig. 4). Bone age was compatible with chronological age. X-rays of the feet were not available.

Neurological examination of the patient revealed no pathological symptoms. Liver and spleen were not palpable. There was no pes cavus. No joint hypermobility could be detected. The skin was dry, soft and velvety. Head hair and body hair were clinically normal. A trichogram of frontal and occipital hairs was normal.

Results of routine laboratory studies including complete blood cell count, serum aminotransferases, alkaline phosphatases and total bilirubin were consistently normal. Radiological evaluations of the vertebral skeleton, skull and chest proved to be normal. An audiometric examination revealed no hearing loss. The caryotype was 46, XX.

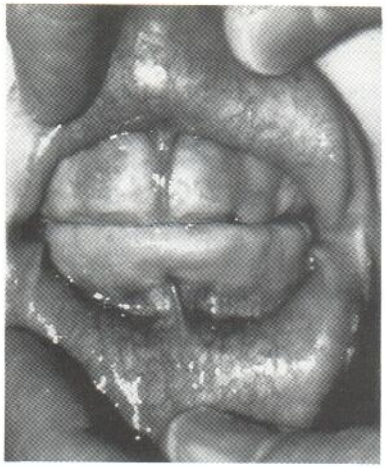
Ophthalmological investigations were carried out to investigate the rapid deterioration of vision. On examination, visual acuity was 6/40 and intraocular pressure was 12 mm Hg for both eyes. The fundus examination showed localized peripapillar yellow patches, an optical disc and a macular region that appeared normal. The atypical retinitis pigmentosa was confirmed by performing electro-oculography and electro-retinography. Nuclear magnetic resonance and computed tomography of the brain were normal.

In August 1990 a gingivectomy was performed by the oral surgery department of the University of *Münster*. All redundant tissue which covered the teeth and interfered with mastication and normal speech was removed. Histological examination was consistent with a diagnosis of gingival fibromatosis with an increase in the number of collagen fibres. As of June 1991 no relapse has been observed.

DISCUSSION

The first report of two affected children in Zimmermann's review article on abnormalities of ectodermal structures is almost certainly not the first observation of that genetic entity. Earlier examples of the syndrome, as indeed suggested by Zimmermann himself and Witcop (10), are very probable.

* Presented in part as a poster at the Journées Dermatologiques de Paris which took place between 6th March and 9th March 1991.



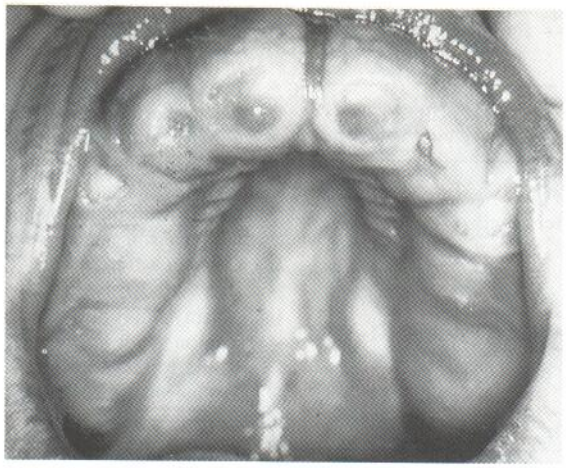


Fig. 1. Overgrowth of gingival tissue on the upper and lower gums.

Fig. 2. Crowns of teeth can be seen through the upper hypertrophied gingivae.

This author related a publication of Hopson (11) who discusses the occurrence of gingival fibromatosis in the case of a father and two children, stating that it was "peculiar that they did not show clubbing defects of the fingers in conjunction to large soft noses so frequently seen in association with gingival fibromatosis".

Humphry (12) describes a girl with unilateral hypertrophy of the gums, nail defects and apparently without terminal phalanx of the right thumb and the second digit of the left foot, a combination of symptoms suggesting the ZLS.

Among the cases discussed by Laband (2) is a mother of seven children, five of whom were affected. Alavandar (4) investigates an affected mother with three affected sons and an 8-month-old affected grandson. The syndrome was apparently transmitted as an autosomal dominant trait. The other observed patients, including two brothers and a spontaneous case reported in Russia by Il'ina et al. (9) are possibly the result of a new germ cell mutation.

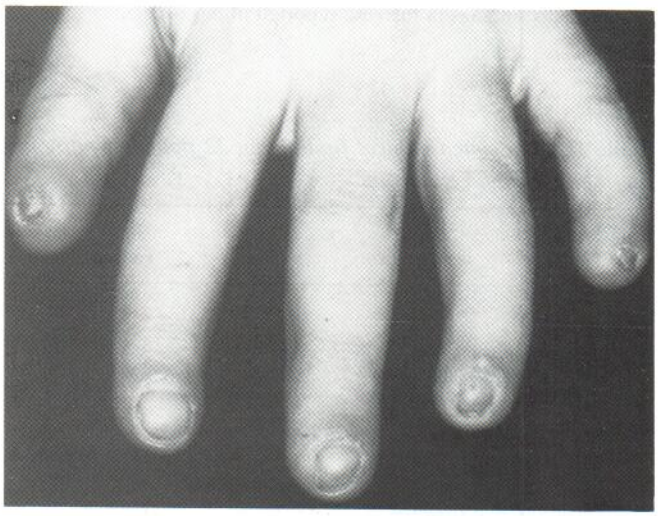
A constant feature of the ZLS is gingival fibromatosis (1, 2, 7, 8), or in cases not histologically examinated, gingival hypertrophy (1–6, 9), appearing in early childhood, associated with enlargement of the soft tissue of the nose and ears, absence or dysplasia of the nails and absence, hypoplasia or dysplasia of the terminal phalangeal bones (Table I).

The clinical findings observed in less than half of all reported cases demonstrate the morphological variability of the syndrome (Table II).

The association between the four major symptoms is not constant but is nevertheless found in 14 of the 22 cases. All of the published cases manifest at least three of the anomalies justifying the diagnosis of the syndrome.

The constant presence of gingival hypertrophy differentiates the ZLS from the tricho-rhino-phalangeal syndromes, associated with a bulbous nose, hair rarification, teeth dysplasia and mental retardation.

Twelve distinct and frequently inherited groups of disorders include gingival fibromatosis as a constant manifestation com-



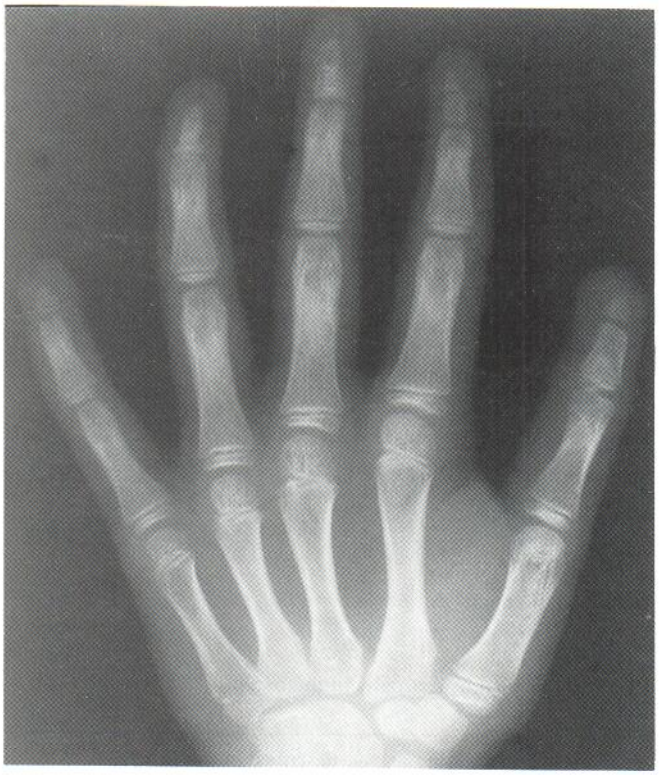


Fig. 3. A view of the left hand shows the small and dystrophic fingernails of the digits.

Fig. 4. Radiography of the left hand. (See text for description).

Table I. *Major clinical findings in 22 patients with Zimmermann-Laband syndrome*

Finding		No of cases and source	
Gingival fibromatosis or gingival hypertrophy		21,+	1–9
Dysplasia, hypoplasia or absence of the terminal phalanx	– Hands	20,+	1–9
	– Feet	12,?	1,3–9
Enlargement of soft tissues of the face			
	– Bulbous soft nose	18,+	1–3, 5–9
	– Thick ears	17	1–3, 5–9
	– Thick lips	4,+	1,5,6,8
Dysplasia, hypoplasia or absence of nails		15,+	1–9

Major clinical findings are defined as those symptoms identified in more than 75% of all reported cases (n = 22).
+ represents findings in the case reported in this article.

Table II. *Associated clinical findings in 22 patients with Zimmermann-Laband syndrome*

Finding	No of cases and source	
Cutaneous		
– Skin soft and velvety	3,+	1,6,7
– Generalized hypertrichosis	2	7,9
– Hypertrichosis of the face	1	5
Skeletal		
– Hyperextensibility of joints	11	2, 4, 6, 7
– Vertebral abnormalities	7	
. Kyphosis	3	2,5,9
. Scoliosis	2	6,9
. Spina bifida	2	1,3
– Pes cavus	6	2,4
– Hallux valgus	3	2,5
– Genu valgum, cubitus valgus	1	5
– Clubbed fingers	1	6
– Flexion contractures (hips and knees)	1	6
– Asymmetry of the lower limbs	1	7
Cranio-Facial		
– Large tongue	4	1,6–8
– Tongue furrowed	2	5,8
– High-arched palate	2	5,9
– Macrocephaly	2	9
– Partial anodontia	1	7
– Prognathia	1	1
Hepatomegaly	8	2,4,5,7
Splenomegaly	6	2,4,7
Mental retardation		
– Profound	3	1,6,9,
– Mild	2	5,7
Neurological anomalies		
– Epilepsy	1	6
– Tremor	1	9
Recurrent virginal hypertrophy of the breasts	1	8
Retinitis pigmentosa	+	

+ represents findings in the case described in this article.

Table III. *Gingival fibromatosis syndromes*

Isolated generalized gingival fibromatosis affecting all the gingivae.
Isolated symmetrical gingival fibromatosis (Rushton).
Gingival fibromatosis with hypertrichosis, oligophrenia and epilepsy.
Gingival fibromatosis with macrocephaly, brachydactily and genital dysplasia.
Gingival fibromatosis-phacomatose syndrome.
Gingival fibromatosis with progressive deafness.
Cowden syndrome.
Cross-Mc Kusick-Breen syndrome.
Murray syndrome.
Ramon syndrome.
Rutherford syndrome.
Zimmermann-Laband syndrome.

ponent with an overlapping of the clinical features between them, but no association with the major clinical findings of the ZLS (Table III). These genetic entities were reviewed in part by Witcop (10). The familial gingival fibromatosis associated with progressive deafness was described later by Jones et al. (13) and Hartsfield et al. (14).

The family history of our patient reveals several individuals with hearing loss but without gingival hypertrophy, who have appeared over three generations, but a parallelism to the observed ZLS can at best be inferred.

The retinitis pigmentosa to our knowledge not previously described, may represent another unusual clinical feature of the syndrome.

REFERENCES

1. Zimmermann. Über Anomalien des Ektoderms. Vierteljahresschrift für Zahnheilkunde 1928; 44: 420–434.
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 1964; 17: 339–351.
3. Jacoby NM, Ripman HA, Munden JM. Partial anonychia (recessive) with hypertrophy of the gums and multiple abnormalities of the osseous system: report of a case. Guy's Hospital Report 1940–41; 90: 34–40.
4. Alavandar G. Elephantiasis gingivae. Report of an affected family with associated hepatomegaly, soft tissue and skeletal abnormalities. Journal of the All India Dental Association 1965; 37: 349–353.
5. Oikawa K, Cavaglia AMV, Lu D. Laband syndrome: report of a case. J Oral Surg 1979; 37: 120–122.
6. Chodirker BN, Chudley AE, Toffler MA, Reed MH. Zimmermann-Laband syndrome and profound mental retardation. Am J Med Genet 1986; 25: 543–547.
7. Pina Neto JM de, Soares LRM, Souza AHO, Petean EBL, Velludo MASL, Freitas AC de, Ribas JP. A new case of Zimmermann-Laband syndrome with mild mental retardation, asymmetry of limbs, and hypertrichosis. Am J Med Genet 1988; 31: 691–695.
8. Beemer FA. "New syndromes", Part II: "European" syndromes. Am J Med Genet 1988; Suppl. 4: 71–84.
9. Il'ina EG, Lur'e IV, Vasiljanskene IP. Analysis of phenotypical variability of the Zimmermann-Laband syndrome. Pediatriia 1988; 4: 86–89.
10. Witcop JW. Heterogeneity in gingival fibromatosis. Birth Defects 1971; VII(7): 210–221.
11. Hopson MF. Three cases of general hypertrophy of the gums. Transactions of the Odontological Society of Great Britain 1899–1900; 32: 34–41.
12. Humphry GM. Unilateral hypertrophy of the gums associated

with other abnormalities, chiefly hypertrophic and unilateral. Ann Surg 1886; 3: 1–8.

13. Jones G, Wilroy RS, McHaney V. Familial gingival fibromatosis associated with progressive deafness in five generations of a family. Birth Defects 1977; XIII (3B): 195–201.

14. Hartsfield JK, Bixler D, Hazen RH. Gingival fibromatosis with sensorineural hearing loss: an autosomal dominant trait. Am J Med Genet 1985; 22: 623–627.