Case Report

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Oral Manifestations in Siblings with Van Maldergem Syndrome: A Case Report

Van Maldergem Sendromu Olan Kardeşlerde Ağız Bulguları: Olgu Sunumu

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ABSTRACT

Type 1 Van Maldergem syndrome (VMLDS1) is an autosomal recessive disorder characterised by intellectual disability, typical craniofacial features, auditory malformations causing hearing loss, and skeletal and limb malformations. Two siblings, a 5-year-old boy and a 7-year-old girl with VMLDS1, presented to our clinic with complaints of early tooth loss and tooth deficiency. To the best of our knowledge, early tooth loss and tooth agenesis as prominent oral manifestations in siblings with VMLDS1 have not been previously reported. The two siblings with VMS presented with rare oral manifestations and exhibited an atypically mild clinical course, with the absence of hearing loss, and major skeletal anomalies associated with VMLDS1. No formally documented intellectual disability was reported; however, speech delay and learning difficulties requiring educational support were present. These findings point to the phenotypic variability of the syndrome and contribute to the differential diagnosis in pediatric dentistry practice.

Keywords: Van Maldergem syndrome, child, paediatric dentistry, oral findings

ÖZ

Tip 1 Van Maldergem sendromu (VMLDS1); entelektüel yetersizlik, tipik kraniyofasiyal özellikler, işitme kaybına yol açan işitsel malformasyonlar ile iskelet ve ekstremite anomalileriyle karakterize otozomal resesif bir hastalıktır. VMLDS1 tanısı bulunan 5 yaşında bir erkek ve 7 yaşında bir kız kardeş, araştırmamıza göre daha önce literatürde bildirilmemiş olan erken diş kaybı ve diş eksikliği şikayetleriyle kliniğimize başvurmuştur. Bu iki kardeşte nadir oral bulgular saptanmış ve olgular, işitme kaybı ve majör iskelet anomalilerinin bulunmaması ile karakterize atipik olarak hafif bir klinik seyir göstermiştir. Resmi olarak belgelenmiş bir zihinsel yetersizlik bildirilmemiştir; ancak konuşma gecikmesi ve özel eğitim desteği gerektiren öğrenme güçlükleri mevcuttur. Bu bulgular, sendromun fenotipik değişkenliğine işaret etmekte ve pedodonti pratiğinde ayırıcı tanıya katkı sağlamaktadır.

Anahtar kelimeler: Van Maldergem sendromu, çocuk, pediatrik diş hekimliği, ağız bulguları

Introduction

Type 1 Van Maldergem syndrome (VMLDS1) is caused by homozygous mutations in the *DCHS1* gene (OMIM no: 603057) on chromosome 11p15. VMLDS1 is an autosomal recessive disorder characterised by intellectual disability, distinctive craniofacial features, auditory malformations leading to hearing loss, and skeletal and limb anomalies. Some patients also present with renal hypoplasia. Brain magnetic resonance imaging typically reveals periventricular nodular heterotopia (1).

The VMLDS1 was first described in 1992 by Van Maldergem and colleagues in a female patient who exhibited distinct facial features, including telecanthus, epicanthus, short palpebral fissures, dental anomalies, and dysplastic ears. She also presented with camptodactyly, interdigital webbing, joint laxity, talipes, neonatal hypotonia, intellectual disability, and hyperkinetic behaviour during childhood (2). Since then, several cases with similar clinical presentations have been reported. The commonly reported features include facial dysmorphism, hand malformations (e.g., syndactyly and camptodactyly), joint laxity, hypotonia, intellectual

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disability, and brain anomalies, such as abnormalities of the corpus callosum (3-5).

Although dental anomalies have occasionally been mentioned in previously reported cases of VMLDS1, detailed dental evaluations remain limited in the literature. In most published reports, dental findings were restricted to brief references to "malocclusion", without further specification of occlusal characteristics, tooth agenesis, eruption patterns, or radiographic features. Consequently, the spectrum of oral manifestations associated with VMLDS1 has not been systematically characterised.

The aim of this report is to describe the oral and dental findings observed in two siblings with VMLDS1 and to discuss their clinical relevance within the context of paediatric dentistry.

Case Reports

Two siblings (a 5-year-old boy and a 7-year-old girl) previously diagnosed with VMLDS1 presented with early tooth loss and missing teeth (Figures 1 and 2). Both exhibited telecanthus, bilateral epicanthus, short palpebral fissures, a broad and flat nasal bridge, dental agenesis affecting both primary and permanent dentitions, and malocclusion (Supplementary Figures 1 and 2). The diagnosis was confirmed by molecular genetic testing demonstrating a homozygous *DCHS1* mutation. Written parental consent for publication of clinical data and images was obtained. Apart from the characteristic facial findings, neither patient had microtia or external auditory canal atresia, and no intellectual disability, digital contractures or skeletal anomalies were identified. The patients did not exhibit severe intellectual disability, although mild neurodevelopmental findings, including speech delay and learning difficulties, were noted. Talipes equinovarus and joint laxity were also absent (Supplementary Figures 3 and 4). Detailed growth chart data were not available at the time of dental evaluation; however, no prior pediatric assessments had documented growth retardation.

Case 1

A 5-year-old boy was referred to our clinic with complaints of early tooth loss and missing teeth. He was born at term following an uncomplicated pregnancy. There was no parental consanguinity, and the family history was negative for congenital anomalies or known genetic disorders. VMLDS1 was genetically confirmed in 2024 by molecular analysis demonstrating a homozygous mutation in the *DCHS1* gene. Extraoral examination revealed telecanthus, bilateral epicanthus, short palpebral fissures, and a broad nasal bridge. Intraoral examination demonstrated dental agenesis affecting both primary and permanent dentitions, midline deviation, crowding of the primary incisors, and supernumerary mandibular primary incisors (Figure 1). Panoramic radiography confirmed complete absence of the primary second molars. Teeth 81 and 82 were extracted due to clinical indication. Restorative treatments were completed on the remaining teeth, and regular follow-up was recommended.

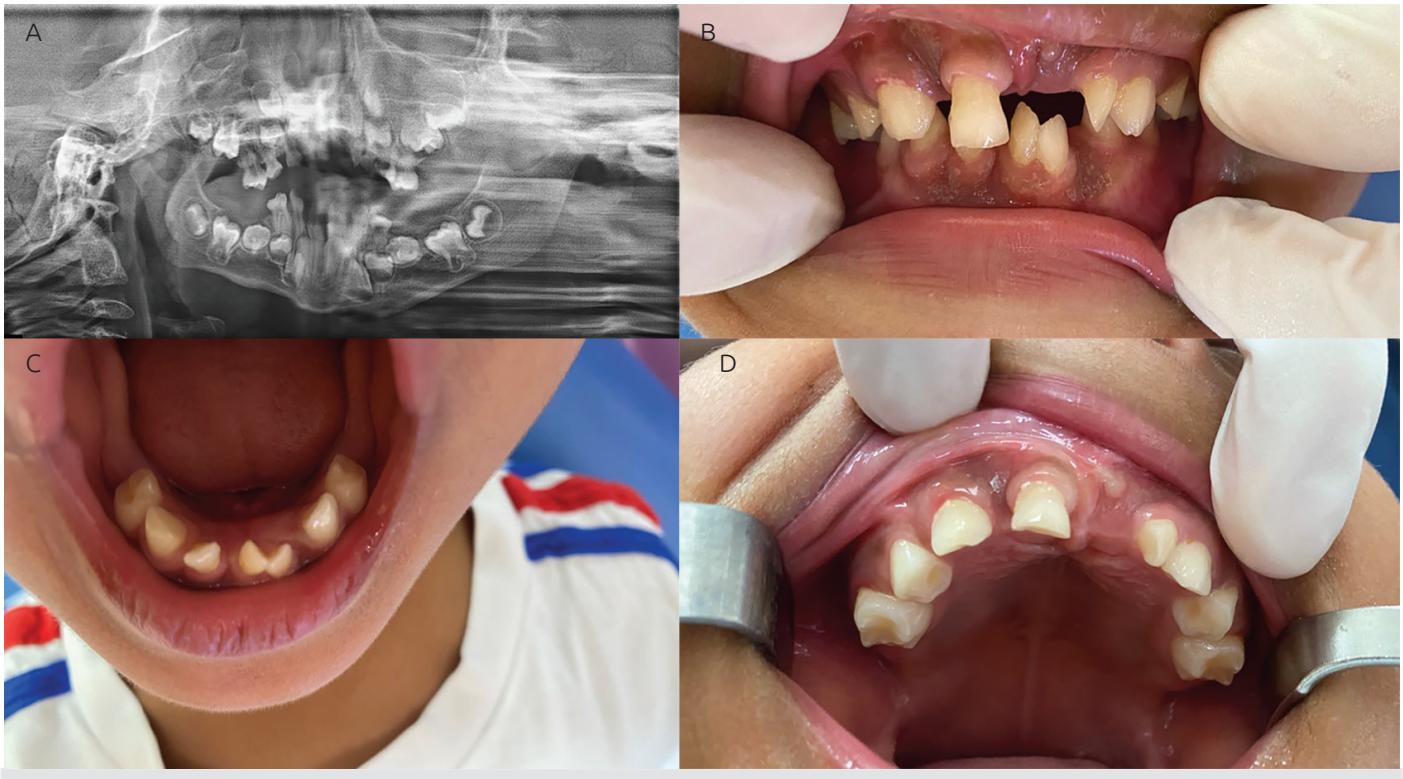

Figure 1. Radiographic and intraoral images of the male patient reveal dental agenesis affecting both the primary and permanent dentitions (A), as well as dental malocclusion (B-D)

Case 2

A 7-year-old girl presented with early tooth loss and occlusal irregularities. She was born at term following an uncomplicated pregnancy, and no significant prenatal or perinatal history was reported. There was no parental consanguinity. Although clinical features suggestive of VMLDS1 had been observed earlier, a definitive diagnosis was established in 2025 through molecular genetic testing revealing the same homozygous *DCHS1* mutation identified in her brother. She has been under multidisciplinary follow-up. Developmental assessments indicated speech delay and learning difficulties requiring educational support. No intellectual disability, hearing impairment, or systemic organ involvement was documented. Extraoral examination demonstrated telecanthus, bilateral epicanthus, short palpebral fissures, a broad and flat nasal bridge, and unilateral blepharophimosis. A history of camptodactyly was reported by the parent and had resolved spontaneously over time. Intraoral examination revealed dental agenesis involving both primary and permanent dentitions, maxillary hypoplasia-related posterior crossbite, dental malformations, and caries lesions (Figure 2). Panoramic radiography confirmed agenesis of the mandibular permanent second premolars. Tooth 51 was extracted due to clinical indication. Restorative treatment was completed, and orthodontic consultation was recommended.

Discussion

Although VMLDS1 was first described in 1992, its molecular basis was not clarified until 2013, when biallelic variants in *DCHS1* and *FAT4* were identified. Since then, additional reports have expanded the phenotypic spectrum of the disorder, underscoring marked clinical variability. To the best of our knowledge, the present report is the first to address VMLDS1 manifestations within the scope of paediatric dentistry. Previous cases have described variable combinations of core features, including facial dysmorphism, hand malformations (e.g., syndactyly and camptodactyly), joint laxity, hypotonia, intellectual disability, and brain anomalies such as abnormalities of

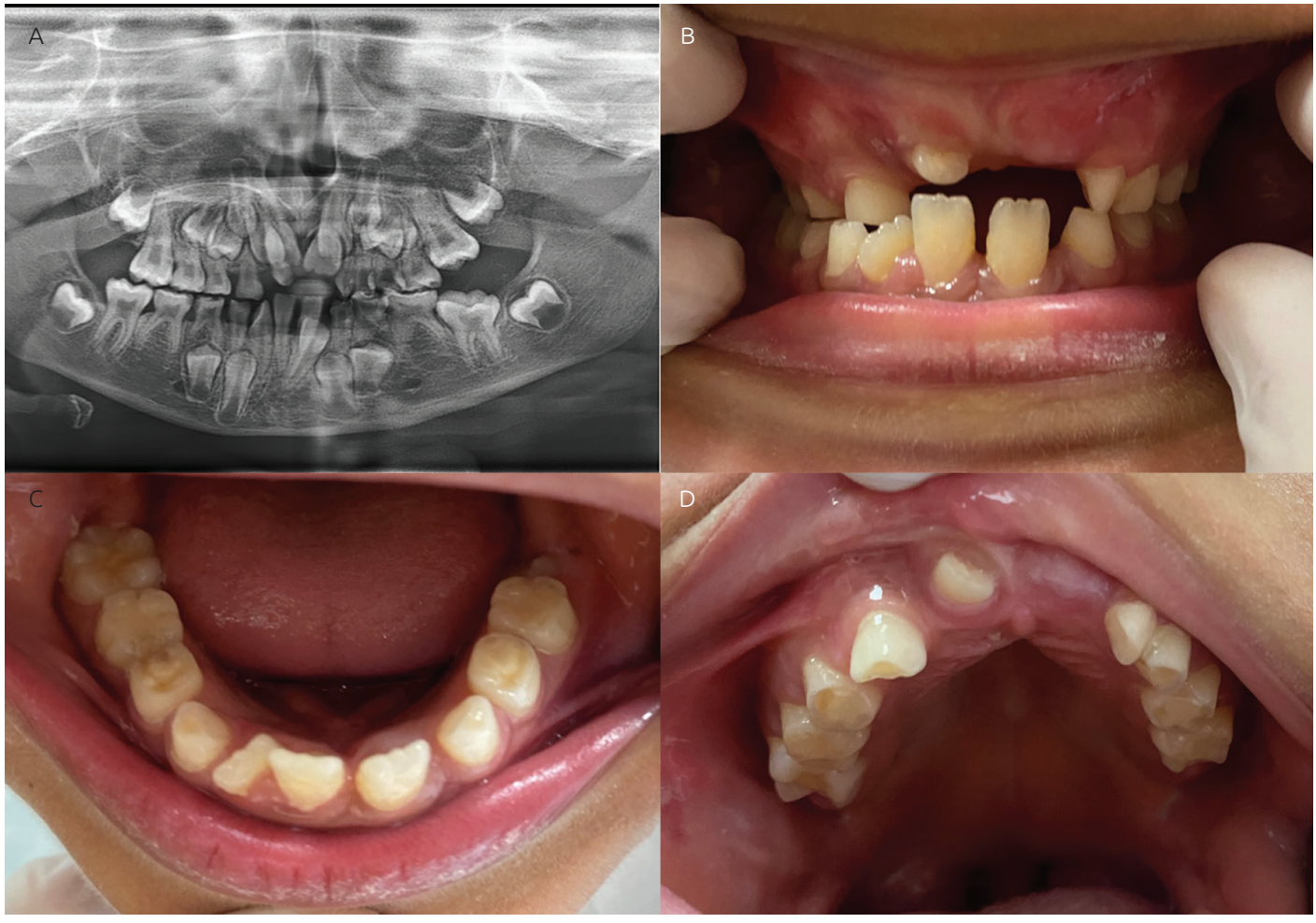

Figure 2. Radiographic and intraoral images of the female patient reveal dental agenesis affecting both the primary and permanent dentitions (A), as well as dental malocclusion (B-D)

the corpus callosum. More recent evidence, including a 2025 case report, further supports variable expressivity associated with DCHS1-related disease (1-6). In the present cases, only a subset of these findings was observed. Apart from facial dysmorphism, dental anomalies, and corpus callosum hypoplasia, other commonly reported systemic manifestations were absent. Notably, corpus callosum hypoplasia did not result in severe neurological impairment in either patient (Supplementary Figures 5 and 6). Since diagnosis, both children have received supportive interventions including special education, cognitive rehabilitation, and speech therapy. No major communication difficulties were observed.

Although intellectual disability and auditory anomalies are frequently reported as core features of VMLDS1, phenotypic variability has been documented (3,6). The absence of cognitive impairment and hearing loss in our patients does not contradict the diagnosis, as both cases were molecularly confirmed. Rather, these findings support the concept of variable expressivity associated with *DCHS1* mutations and suggest that VMLDS1 may present with a broader clinical spectrum than initially recognised (5,6).

From a paediatric dental perspective, the combination of primary and permanent tooth agenesis, early loss or resorption of primary teeth, maxillary constriction-related posterior crossbite, and dental malformations represents an uncommon presentation in VMLDS1. While such findings may occur in other syndromic conditions, their coexistence in genetically confirmed VMLDS1 expands the known orodental phenotype of the disorder and highlights the importance of dental evaluation in multidisciplinary management.

The differential diagnosis of VMLDS1 includes several syndromes with overlapping craniofacial characteristics. Hennekam syndrome represents a particularly relevant differential diagnosis due to its phenotypic and genetic overlap with VMLDS1. Mutations in *FAT4* have been reported in both conditions, and Hennekam syndrome has been described as allelic to VMLDS1 in certain cases. Detailed clinical comparisons have demonstrated substantial phenotypic overlap between these entities. However, Hennekam syndrome is characteristically defined by generalized lymphatic dysplasia, including intestinal lymphangiectasia and peripheral lymphedema, features that were not observed in our patients. Furthermore, molecular genetic testing in both siblings confirmed homozygous *DCHS1* mutations, supporting a diagnosis of VMLDS1 rather than a *FAT4*-related disorder. Winter-Tsukahara syndrome and other neuronal migration disorders, including those associated with *DCX* or *LIS1*, were also considered due to overlapping cortical and craniofacial findings. Nevertheless, these conditions lack the specific constellation of craniofacial, digital, and dental findings observed in our patients and are not typically associated with biallelic *DCHS1* variants (7,8). Taken together, the combination of characteristic craniofacial features, dental agenesis involving both primary and permanent dentitions, absence of lymphatic involvement, and molecular confirmation of *DCHS1* mutations supports the diagnosis of VMLDS1 and allows exclusion of clinically overlapping syndromes (3,5,7,8).

By documenting the rare co-occurrence of early tooth loss and dental agenesis in a patient with VMLDS1, the study contributes valuable clinical insight to the existing body of literature. Furthermore, it underscores key oral and craniofacial characteristics of the syndrome, thereby equipping both paediatric and general dental practitioners with essential knowledge to aid in the accurate diagnosis and appropriate management of this rare condition.

Conclusion

In rare genetic disorders such as VMLDS1, accurate diagnosis relies on close collaboration between medical genetics and paediatric subspecialties. While the diagnosis in our patients had been molecularly established, this report contributes by delineating previously underrecognised dental manifestations of VMLDS1. Recognition of these orodental findings may facilitate earlier multidisciplinary referral, improve diagnostic awareness, and refine phenotypic characterisation of this rare condition.

Ethics

Informed Consent: Both written and verbal informed consent were obtained from the parent for the publication of this case report and any accompanying images.

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Footnotes

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Supplementary Figures: https://d2v96fxpocvxx.cloudfront.net/beb8919b-f013-4ea1-b1c8-40332e840fe1/content-images/cd414008-6621-4648-b8fb-d4a555963fa8.pdf

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