Case Report

A Very Rare Syndrome of Tooth Enamel; Kohlschütter–Tönz Syndrome: A Case Report and Review

Diş Minesini İlgilendiren Nadir Bir Sendrom; Kohlschütter-Tönz Sendromu: Olgu Sunumu ve Literatür Derlemesi

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Abstract

Kohlschütter–Tönz Syndrome (KTS) is a very rare syndrome described by Kohlschütter in 1974. It is characterized by amelogenesis imperfecta, persistent epileptic seizures, spasticity and developmental delay. In this case report, we present a 9 year-old boy who was diagnosed as KTS together with a literature review. Dental history and clinical examination revealed that patient suffered from severe enamel defects of teeth, along with drug-resistant epileptic seizures and mental retardation since the age of five months. He had a dental examination and extractions under nitrous oxide sedation because of mental retardation. Literature review performed up to now indicates a total of 52 KTS patients that have been reported in the literature. This is the first reported KTS case from Turkey. For this reason, it can make a great contribution to the dental clinics in the context of raising awareness and informing the parents of such syndromic patients in proper.

Keywords: Amelogenesis imperfecta; drug resistant epilepsy; Kohlschütter-Tönz syndrome

Özet

Kohlschütter-Tönz Sendromu (KTS), amelogenezis imperfekta, ilaca dirençli epileptik nöbetler, spastisite ve gelişimsel gerilik ile karakterize olan ve 1974 yılında Kohlschütter tarafından tanımlanmış, oldukça nadir görülen bir sendromdur. Bu makalede Türkiye'den ilk KTS vakası bildirilmektedir. Bu olgu raporunda, bir yıl önce KTS tanısı konulmuş olan 9 yaşında bir erkek çocuk literatür derlemesi ile birlikte sunulmaktadır. Bu vakada alınan anamnez ve klinik muayenede hastanın dişlerinde şiddetli mine defekti olduğu ve beş aylıktan itibaren ilaca dirençli epileptik nöbetler ve mental retardasyon şikayetlerine sahip olduğu saptanmıştır. İleri derece mental retardasyon nedeniyle dental muayene ve diş çekim işlemleri nitröz oksit sedasyonu altında yapılarak hasta takip altına alınmıştır. Yapılan literatür taramalarında, tüm dünyada günümüze kadar toplam 52 KTS vakası bildirilmiş olduğu saptanmıştır. Vakamız Türkiye'den bildirilen ilk KTS vakasıdır. Bu nedenle Diş Hekimliği kliniğinde, farkındalık yaratmak ve hasta ebeveynlerinin doğru bilgilendirilebilmesi bağlamında büyük katkı sağlayacaktır.

A**nahtar Kelimeler:** Amelogenezis imperfekta; ilaca dirençli epilepsi; Kohlschütter-Tönz sendromu

Makale gönderiliş tarihi: 20.12.2020 Yayına kabul tarihi: 04.01.2021
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Table 1. KTS reported in the English literature up to now.

Author/Year	G	AI	DD	Seizure	OE	Spasticity	Ref	Author/Year	G	AI	DD	Seizure	OE	Spasticity	Ref
Current case/2021	M	Yes	Yes	Yes	9 y	Yes		Mory/2012	F	Yes	Yes	Yes	9 m	X	13
Morscher/2017	F	Yes	Yes	Yes	9 m	Yes	16	Mory/2012	F	Yes	Yes	Yes	9 m	X	13
Aswath/2017	F	Yes	Yes	Yes	10 m	Yes	17	Mory/2012	M	Yes	Yes	Yes	9 m	X	13
Huckert/2014	F	Yes	Yes	Yes	3 w	yes	15	Mory/2012	M	Yes	Yes	Yes	11 m	X	13
de Souza/2014	F	Yes	Yes	Yes	40 d	Yes	4	Haberlandt/2006	M	Yes	Yes	Yes	8 m	No	3
de Souza/2014	M	Yes	Yes	Yes	6 h	Yes	4	D.donnai/2005	M	Yes	Yes	Yes	5 w	No	12
Mory/2014	F	Yes	Yes	Yes	12 m	X	13	D.donnai/2005	F	Yes	Yes	Yes	11 w	No	12
Mory/2014	M	Yes	yes	Yes	7 m	X	13	Wygold/1996	M	Yes	Yes	No	?	No	11
Alejandro/2013	M	Yes	Yes	Yes	8 y	Yes	18	Musumeci/1995	M	Yes	Yes	Yes	2 m	Yes	10
Tucci/2013	M	Yes	Yes	Yes	7 m	No	14	Musumeci/1995	F	Yes	Yes	Yes	10 m	Yes	10
Tucci/2013	M	Yes	Yes	Yes	8 m	Yes	14	Guazzi/1994	F	Yes	Yes	Yes	?	Yes	9
Tucci/2013	M	Yes	Yes	Yes	?	No	14	Petermöller/1993	M	Yes	Yes	Yes	8,5 m	No	8
Tucci/2013	F	Yes	Yes	Yes	18 m	No	14	Petermöller/1993	F	Yes	Yes	Yes	8 m	No	8
Schossig/2012	M	Yes	Yes	Yes	4 m	No	8	Zlotogora/1993	M	Yes	Yes	Yes	3 m	Yes	7
Schossig/2012	F	Yes	Yes	Yes	12 m	No	8	Zlotogora/1993	F	Yes	Yes	Yes	12 m	No	7
Schossig/2012	M	Yes	Yes	Yes	11 m	No	9	Christodoulou/1988	M	Yes	Yes	Yes	11 m	No	6
Schossig/2012	F	Yes	Yes	Yes	6 m	No	10	Christodoulou/1988	M	Yes	Yes	Yes	18 m	No	6
Mory/2012	F	Yes	Yes	Yes	13 m	X	13	Christodoulou/1988	M	Yes	Yes	Yes	13 m	No	6
Mory/2012	F	Yes	Yes	Yes	12 m	X	13	Christodoulou/1988	F	Yes	Yes	Yes	11 m	No	6
Mory/2012	M	Yes	Yes	Yes	9 m	X	13	Christodoulou/1988	F	Yes	Yes	Yes	22 m	No	6
Mory/2012	F	Yes	Yes	Yes	12 m	X	13	Christodoulou/1988	M	Yes	Yes	Yes	7 m	No	6
Mory/2012	M	Yes	Yes	Yes	6 m	X	13	Kohlschütter/1974	M	Yes	Yes	Yes	19 m	Yes	2
Mory/2012	M	Yes	Yes	Yes	3 y	X	13	Kohlschütter/1974	M	Yes	Yes	Yes	21 m	Yes	2
Mory/2012	M	Yes	Yes	Yes	9 m	X	13	Kohlschütter/1974	M	Yes	Yes	Yes	4 y	Yes	2
Mory/2012	F	Yes	Yes	Yes	9 m	X	13	Kohlschütter/1974	M	Yes	Yes	Yes	18 m	Yes	2
Mory/2012	F	X	X	Yes	Birth	X	13	Kohlschütter/1974	M	Yes	Yes	Yes	11 m	Yes	2
Mory/2012	M	Yes	Yes	Yes	10 m	X	13								

AI:Amelogenesis imperfecta; DD:Developmental delay; OE:Onset of Epilepsy;
G:Gender;Ref:Reference; y:year; m:month; w:week

INTRODUCTION

Kohlschütter-Tönz Syndrome (KTS) is an uncommon disease that has been associated with an autosomal recessive inheritance on ROGDI gene.[1,2] Syndrome is characterized by amelogenesis imperfecta, persistent epileptic seizures, spasticity and developmental delay.[1] It also has other clinical findings such as ventricular enlargement, dry skin and myopia. In this case, there was none of this clinical signs.[3]

This syndrome was first described by Kohlschütter *et al.* in 1974.[1] Until now, there are only 52 KTS cases reported in the literature (Table 1). In the present case, it was aimed to report a case of this very rare syndrome in order to take dental practitioners' attention for the early diagnosis of the syndrome as it may be helpful for both patient and family to handle the situation better.

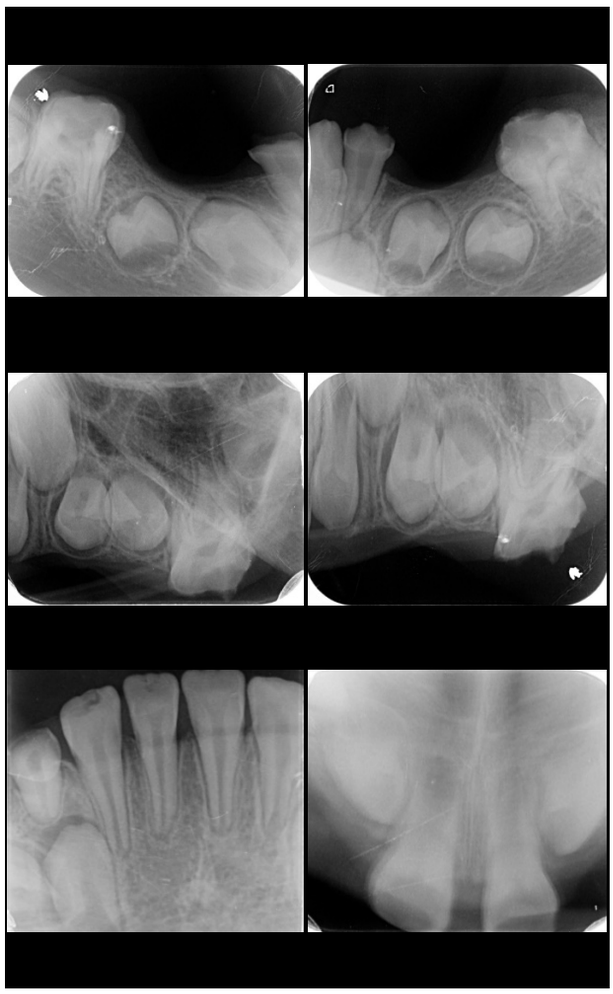

Figure 1. Radiological examination reveals the number of teeth exist in total.

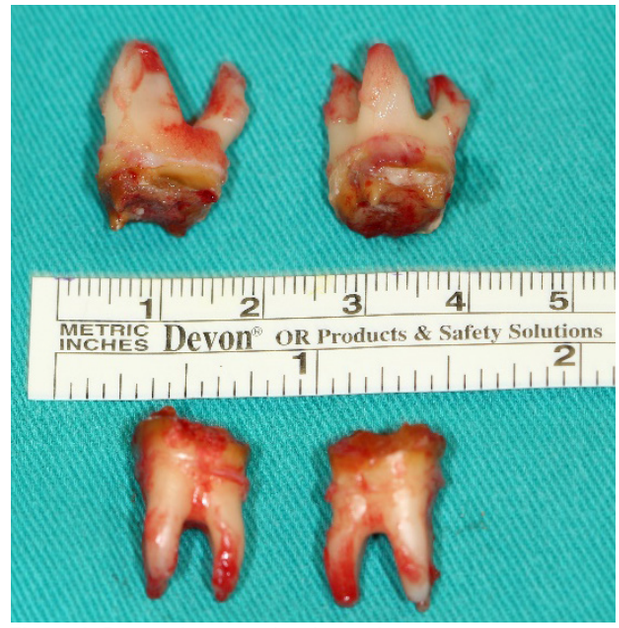

Figure 2. Decayed extracted molar teeth

CASE REPORT

A 9 years-old boy was admitted to Gazi University Dental School, Department of Pediatric Dentistry by the complaint of pain on his left face and restlessness for two weeks because of decayed teeth. The patient was examined and found that he had all the symptoms of KTS which are amelogenesis imperfecta, persistent epileptic seizures, spasticity and developmental delay. Therefore, patient was referred to Department of Oral and Maxillofacial Surgery in order to carry on his treatment under nitrous oxide sedation. During dental and medical history was taken, his family shared his medical history in detail that he started to have epileptic seizures when he was 5-months-old. His mother affirmed that he was having seizures attack once a day everyday; until he became 7 years-old then he started to take Clobazam 10mg capsule per day by the prescription of Pediatrician working at Hacettepe University, Medical School, Department of Genetic Diseases and Early Childhood. Since then his convulsions has reduced to once a year. At the same centre, he was also diagnosed to have spasticity and developmental delay. Following that, his intraoral clinical and radiological examination done at Gazi University, Dental School revealed that he had 10 permanent and two deciduous teeth which are; tooth number 11, 16, 21, 26, 31, 32, 73, 36, 41, 42, 83, 46 as displayed in Figure 1.

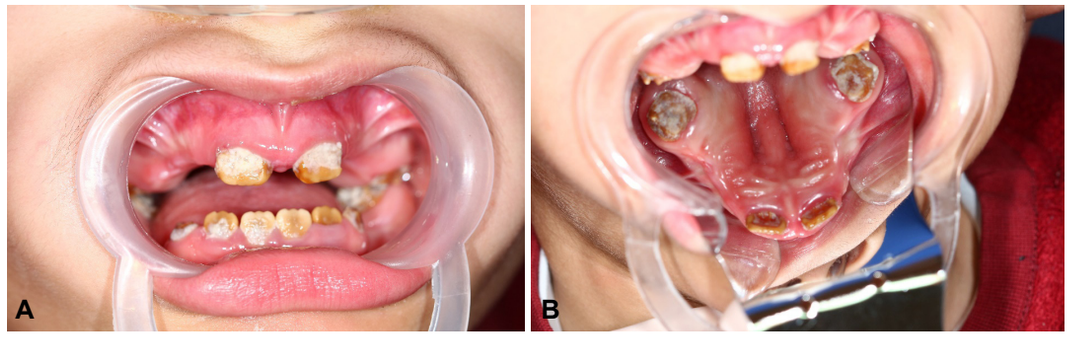

Figure 3. A.Yellowish decayed teeth B. Palatal deformity

Nevertheless, all the molar teeth were decayed (Figure 2) and the rest were yellowish and soft in texture when probed (Figure 3A). It was also noticed that there was a palatal deformity (Figure 3B). Informed consent form was obtained from patient's custodians before all the dental procedures were performed. Molar teeth were extracted and the rest were left for the scaling and fluoride application. Dental examination was performed under nitrous oxide sedation because of the communication inabilities.

The family history revealed that his mother was 21 years-old when she gave a birth to him and father was 25. His parents were medically healthy and no close family tie existed to cause any genetic disorder. Both parents were originally coming from a same province called as Cubuk near to Ankara. The father revealed that he has got an elder daughter from his first marriage being also epileptic but not diagnosed as KTS by the genetic tests run following our patient's diagnosis.

Patient's mother declared that she had a normal pregnancy and spontaneous vaginal delivery and there was no abnormal situation that she noticed until the 5th months after his birth. He had his first convulsive seizure when he was only 5-months old. His previous dental records revealed that he had a total of 9 teeth extracted previously in 2016 under the consultation of Pediatrics which lead to diagnosis of KTS by the identification of the causative gene ROGDI homolog at the Hacettepe University, Medical School in the same year.

At the moment, he is being seizures free while he is being unverbal, disoriented and profoundly mentally retarded. He is having difficulty during chewing and swallowing. Therefore, he has been feeding by baby food. Following his dental treatment, dental advices were given to his family and made a next appointment in 3 months time in order to keep him under close follow up.

Histopathological examination

Pathological examination revealed the extracted teeth had normal crown and root formation. Both pulp chamber and dentin structure were within normal limits and all of the teeth consisted of dentin tubules parallel to each other. The enamel structure observed in the decalcified and undecalcified sections is amorphous and displayed locally globular/nodular structure; however the enamel prism that usually seen in the normal enamel structure was not exist (Figure 4).

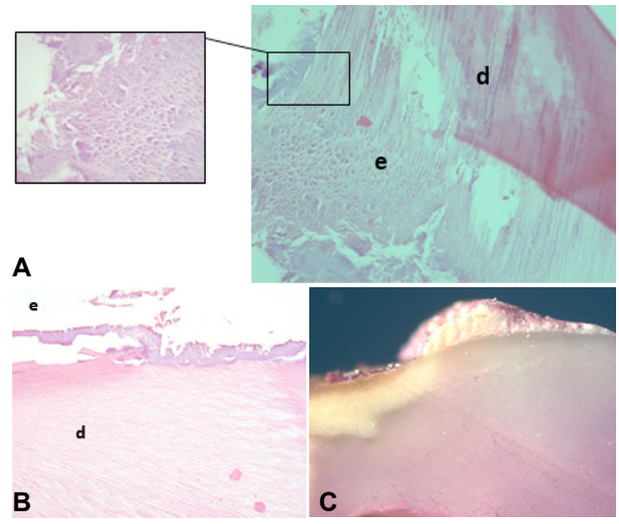

Figure 4.
A. Amorphous structured enamel matrix unified with tubular dentin, no prismatic structure was seen (HEX20) and locally globular enamel matrix in the amorphous structure (HEX40) (e:enamel, d:dentin)
B. Amorphous structured enamel matrix unified with tubular dentin; no prismatic structure was seen (HE X20)
C. Undecalcified sections, tooth surface displays a discontinuous enamel structure (HE X20)

DISCUSSION

KTS is a rare syndrome and there have been only 52 cases reported in the literature until now. This has been the first KTS case reported from Turkey, specifically from the part of central Anatolia. The typical characteristics of this syndrome (amelogenesis imperfecta, early onset seizures and progressive mental retardation) have been observed in all the reported cases, but with a variable expressivity as displayed in Table 1. Dental abnormalities may be seen during both primary and secondary dentitions.[4] However in this case, patient's mother declared that there was no abnormality during primary dentition.

Amelogenesis imperfecta occurs as a result of deformation in tooth formation that starts at the beginning of organic matrix stage and continues during the calcification stage. It can exist as an isolated feature or in syndromic forms.[4] Inheritance pattern is variable and X-linked and autosomal cases have been detected.[5] Total of eight different subtypes of amelogenesis imperfecta are described depending on the histology of tooth. KTS is usually accompanied by the hypoplastic type, as found in our patients.[6,9] Generally, this disorder is diagnosed during childhood around the age of 0-4 years-of age when they had the first convulsion attack.[3] Our patient had his first seizure when he was only 5-months old.

A series of KTS cases was reported by Guazzi *et al.* in 1994 suggesting an autosomal dominant inheritance suggesting either a different entity or possibly etiologic heterogeneity for KTS.[9,10] In their case series, there may be a variant of KTS showing difference with described recessive mutation. Seizures typically seen in this disorder are usually treatment resistant to various anti-epileptic agents, and the patient presents psychomotor delay or regression in infancy, associated to spasticity of the lower and upper limbs.[1,4] Our patient had also treatment resistant seizures till he was diagnosed as KTS with his dental findings. Therefore, it is quite important to be aware of such kind of syndromic patients in order to let them to get a proper treatment while it is not too late.

Previously, differential diagnosis of KTS has been reported to be very limited including Rud syndrome, tuberous sclerosis, mucopolysaccharidosis, oculodentodigital dysplasia and isolated or syndromic amelogenesis imperfecta.[9,13] KTS can be easily distinguished by two distinctive sign, it displays; amelogenesis imperfecta and seizure.[14,18] When the disorder is diagnosed patient should be kept under the routine control of the neurologist for seizures and mental retardation and also by the dentist because of the high risk of caries in order to improve the quality of life for both patient and the parents.

This present case is the first report of KTS in a patient from central Anatolian part of Turkey with a confirmed loss of mutation in the ROGDI gene followed by the existence of two very distinct clinical and neurological sign which are amelogenesis imperfecta and seizure. And it seems new reports are needed for a better clinical and genetic search of this disorder.

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