Case Report

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Bilateral hearing impairment as an early symptom in a patient with Charcot-Marie-Tooth Type 1: the first case report from Syria

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Introduction: Charcot-Marie-Tooth (CMT) is a group of inherited neuromuscular disorders that vary clinically and genetically. It is characterized by peripheral nerve damage, leading to muscle weakness and sensory loss.

Case presentation: A 13-year-old male presented to the rheumatology department with bilateral hearing impairment since the age of 3 years, pes cavus, and difficulties walking. Some family members had Achilles tendon lengthening surgery. During physical examination, the patient had a shortened Achilles tendon, there are high arches in the feet, curled toes, loss of touch sensation in the feet, ankles, and legs, atrophy in the foot muscles. An eye examination revealed a discrepancy that needed glasses. Neurological findings included horizontal and vertical nystagmus, proprioception disorder, and demyelinating sensorimotor disorder diagnosed as CMT type 1. The audiogram showed bilateral sensorineural hearing impairment. MRI revealed spinal disc bulges. The treatment plan includes Achilles tendon lengthening surgery and physical therapy.

Clinical discussion: CMT patients need to receive supportive treatment including physical therapy, hearing aids, and glasses, to help improve their quality of life.

Conclusion: CMT disease is a genetic disorder that causes difficulties in movement, coordination, and daily activities due to muscle weakness and sensory impairments. In a few cases, patients have been documented to have bilateral hearing impairment as their first symptoms. It affects individuals in Syria and around the world, and requires proper diagnosis and treatment.

Keywords: bilateral hearing, case report, Charcot-Marie-Tooth disease, Type 1

Introduction

Charcot-Marie-Tooth (CMT) is one of the most prevalent inherited neuromuscular diseases which is thought to affect 1/2500 people worldwide[1]. CMT is divided into two major groups: demyelinating CMT type 1 (CMT1) and axonal CMT type 2 (CMT2). Other sub-classifications are based on the inheritance pattern, which can be autosomal recessive (AR), autosomal dominant (AD), or X-linked (CMTX)[1,2]. CMT1 is the most common type characterized by noticeably reduced nerve conduction velocity[1]. Clinical symptoms usually appear in the first or second decade of life. Weakness begins distally in the feet and progresses proximally in an ascending pattern. Lower motor neuron-type motor deficits combined with sensory signs and symptoms, which are indicative of sensory-motor neuropathy, are the main features of CMT. Muscle atrophy and length-dependent paresis develop in addition to areflexia. Foot deformities, such as pes cavus, can occur as a result of the chronic nature of motor neuropathy[3]. Diagnostic tests of CMT include electrophysiological studies, sural nerve biopsy, and genetic testing[3]. Herein, we presented a case of CMT type 1 with bilateral hearing impairment as a first symptoms, which is the first one documented in Syria.

HIGHLIGHTS

- Charcot-Marie-Tooth (CMT) is one of the most prevalent inherited neuromuscular diseases which is thought to affect 1/2500 people worldwide.
- The association between the development of CMT1A disease and auditory impairment is still unknown, and experiencing auditory impairment as one of the first symptoms is rare.
- The goal of treatment is to improve sensory abnormalities, motor dysfunction, and reduce disability and morbidity.

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Case presentation

A 13-year-old male presented to the Department of Rheumatology with pes cavus 3 years ago, an inability to walk properly, and bilateral hearing impairment since the age of 3 years. The child has no medication or surgery history; there are some members of his family who underwent Achilles tendon lengthening surgery. Clinical examination showed vital signs were in the normal range, awareness was good, there were no weaknesses in the hands and forearms; no wasting of muscle tissue in the lower parts of the legs; no involuntary grinding of teeth; and no scoliosis. However, there are high arches in the feet, curled toes, loss of touch sensation in the feet, ankles, and legs, atrophy in the foot muscles, and shortening of the Achilles tendon (Fig. 1). Laboratory tests were performed as follows (Table 1). An eye examination showed a deviation that required glasses. The neurological examination showed that the muscle forces and reflexes were normal, but there was horizontal and vertical nystagmus, a lack of sense of touch in the lower extremities, and a disorder in the proprioception sense. Therefore, a nerve conduction study was requested, which showed a demyelinating sensorimotor disorder, which was diagnosed as CMT type 1 (Fig. 2). An audiogram showed bilateral sensorineural hearing impairment (Fig. 3). We performed an anteroposterior radiograph and a lateral radiograph of the bilateral pes cavus (Fig. 4). MRI was performed with sagittal T1-weighted and T2-weighted, axial T2-weighted, gradient time of the cervical column, axial T1-weighted and T2-weighted, fluid-attenuated inversion recovery (FLAIR), diffusion-weighted imaging (DWI), and coronal T2-weighted and sagittal T1-weighted of the brain, and they were normal. However, MRI with sagittal T1-weighted and T2-weighted images and axial T1-weighted and T2-weighted images of the lumbar and dorsal columns showed: L4-L5: a wide central bulge touching the meningeal sac. L5-S1: mild global swelling that relatively narrows the right neural foramen (Fig. 5). In order to alleviate the problems, it was planned to perform an Achilles tendon lengthening procedure and receive physical therapy to strengthen the tendons and muscles.

Discussion

CMT diseases are a diverse group of neuropathic disorders that vary clinically and genetically. They are found worldwide and affect individuals of all ethnic backgrounds. CMTs collectively represent the most common inherited neuromuscular disorder, with an estimated prevalence of 1 in 2500

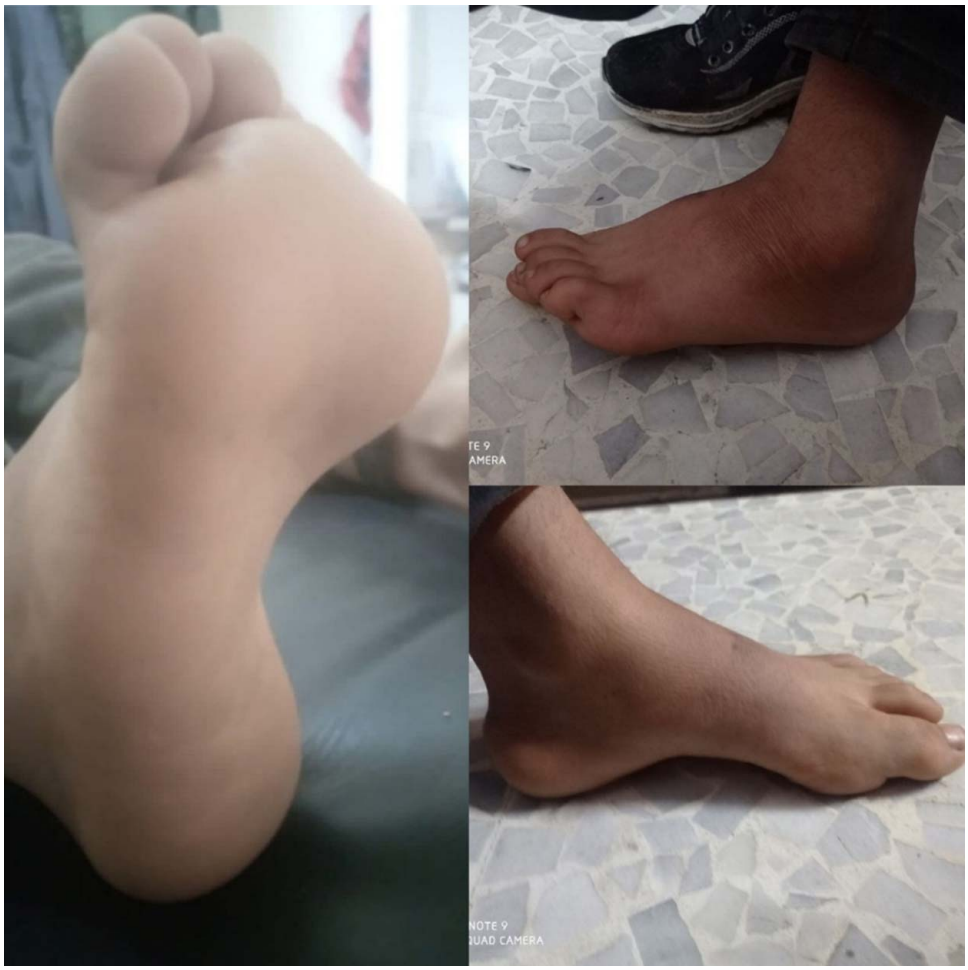

Figure 1. There are high arches in the feet, curled toes, atrophy in the foot muscles, and shortening of the Achilles tendon.

Table 1

Laboratory test results.

Test	Result	Normal range
White blood cell (WBC)	5.85	4.4–11 × 10^3/µl
Neutrophil	60	40–70%
Lymphocyte	38	20–40%
Monocyte	0	2–8%
Eosinophil	2	0–4%
Basophil	0	0–1%
Red blood cell (RBC)	4.84	4.5 - 6.2 × 10^6/µl
Hemoglobin (Hb)	12.60	12–14 g/dl
Hematocrit (Hct)	41.00	37–42%
Mean corpuscular volume (MCV)	84.7	80–96 fl
Mean corpuscular hemoglobin (MCH)	26.0	27–32 pg
Mean corpuscular hemoglobin concentration (MCHC)	30.7	31–35%
Red cell distribution width (RDW)	12	11.5–14.5%
Platelet count	151	150–450 × 10^3/µl
Erythrocyte sedimentation rate (ESR)	3	Up to 0.5 mm/h
Vitamin D	24.76	30–100 ng/ml
Glucose (Glu) (Fasting)	83	70–110 mg/dl
Creatinine (Cr)	0.80	0.6–1.2 mg/dl
Sodium (Na)	136	135–140 mEq/l
Potassium (K)	4.21	3.5–5 mEq/l
Calcium (Ca)	8.1	8.6–10.0 mg/dl
Phosphorus	2.61	2.5–4.5 mg/dl
Alkaline phosphatase (ALP)	468	Up to 936 U/l
Creatine phosphokinase (CPK)	147	30–370 U/l
Lactate dehydrogenase (LDH)	219	Up to 248 U/l
Albumin (Serum)	4.46	3.4–4.5 g/dl
C-reactive protein (CRP)	3.5	Up to 5.0 mg/l

individuals[4]. The prevalence of CMTs varies globally, ranging from 9.7 per 100 000 in Serbia to 82.3 per 100 000 in Norway[5]. Population-based studies have shown differing frequencies of CMT in various countries, such as Libya (8 per 100 000), Nigeria (10 per 100 000), South Wales (17 per 100 000), Northern Sweden (20 per 100 000), and Northern Spain (28 per 100 000)[6]. There are no accurate statistics on the spread of this disease in Syria. Perhaps consanguineous marriage is one of the factors in the spread of this disease. CMTs are broadly classified into demyelinating (CMT1) and axonal (CMT2) subtypes, with CMT1 accounting for 37.5 to 84% of cases and CMT2 for 12 to 35.9%[5]. The typical clinical features seen in all types of CMT diseases include weakness, muscle wasting, reduced reflexes, and skeletal abnormalities that primarily affect the distal parts of the body, especially the lower limbs. Symptoms commonly reported by patients include difficulty walking quickly or running, frequent tripping or falls, and ankle sprains. Individuals with CMT may experience delays in reaching motor milestones during childhood and may struggle with coordination in sports activities. As the condition progresses, patients may develop a high-stepping gait and foot drop, along with challenges in tasks like buttoning clothes, zipping, and writing due to hand weakness. While sensory symptoms are less prominent, some patients may experience musculoskeletal pain rather than neuropathic pain. Physical examination often reveals characteristic foot deformities like pes cavus, hammertoes, and clawed hands in individuals with long-standing CMT. Leg and thigh muscle wasting can resemble an inverted champagne bottle shape, and spinal deformities such as scoliosis may also be present[7]. Gait abnormalities and balance issues result from a combination of proprioceptive loss and skeletal deformities like pes cavus and hammertoes[8]. These clinical manifestations are primarily due to axonal loss, even in demyelinating forms of CMT, as nerve conduction velocities are already reduced before visible symptoms appear[9]. Hearing impairment is a relatively common symptom of CMT1A because the cochlear nerve is a peripheral nerve, CMT patients can exhibit sensory peripheral nerve deficit, the association between the development of CMT1A disease and auditory impairment is still unknown[10]. CMT can be diagnosed through three distinct types of tests: estimation of the speed of nerve impulses (nerve conduction study), a biopsy of the nerve, and DNA testing. DNA testing can give a conclusive finding, yet not every one of the genetic markers for CMT are known. CMT is first most seen when somebody creates lower leg weakness, for example, foot drop, or foot disfigurements, including hammertoes and high curves, yet signs alone do not prompt the diagnosis. To see indications of muscle weakness, the neurologist might request that patients to walk on their heels or to move part of their leg against a contradicting force. To recognize sensory loss, neurologist tests for profound ligament reflexes, for example, the knee jerk, which are diminished or missing in CMT. The specialist may ask the patient's family history since CMT is genetic but the absence of family history does not preclude CMT[11]. The goal of treatment is to improve sensory abnormalities, motor dysfunction, and reduce disability and morbidity. Specific treatments for CMT are unknown[12,13]. There is still no effective drug treatment for CMT; none of the drugs examined over the last 25 years, including oral creatine

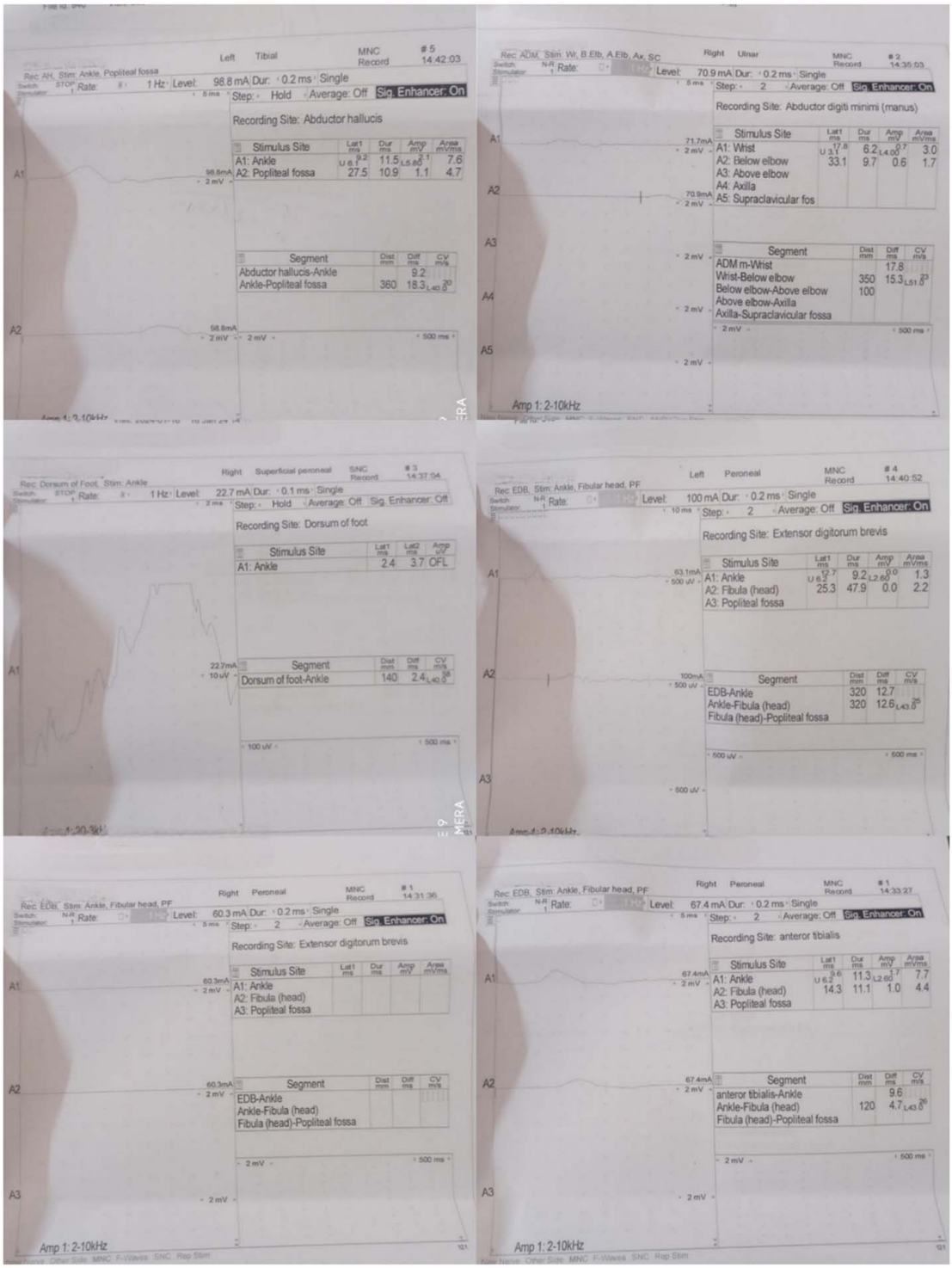

Figure 2. A nerve conduction study showed a demyelinating sensorimotor disorder, which was diagnosed as Charcot-Marie-Tooth type 1.

monohydrate, have proven efficacy. Surgical correction and rehabilitative therapy are the most common types of treatment CMT for bone malformations and soft-tissue anomalies. It has been demonstrated that mild to moderate exercise significantly improves lower limb strength and walking abilities in patients with CMT and is safe and effective. Skeletal abnormalities are treated in various ways, especially in the foot[14]. Although numerous surgical reconstructive procedures for CMT disease-related cavovarus foot deformity have been published, a few authors have reported long-term results[15]. Our patient initially had a bilateral hearing impairment. Nine years later, he developed a pes cavus foot deformity. He uses glasses and

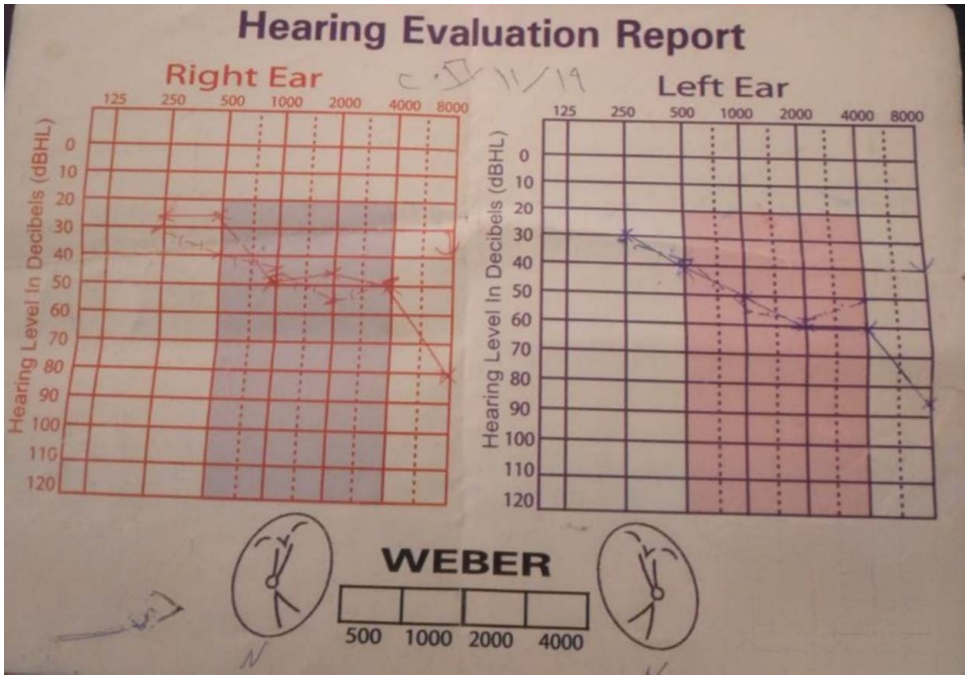

Figure 3. An audiogram showed bilateral sensorineural hearing impairment.

hearing aids, receives rehabilitative therapy, and eventually has his Achilles tendon lengthened operatively to reduce the symptoms of the pes cavus.

Conclusion

CMT disease is a genetic disorder that affects individuals worldwide, including those in Syria. It is known that CMT occurs in all ethnic groups and populations. In Syria, individuals with CMT may face similar challenges to those in other countries, including difficulties with mobility, coordination, and daily activities due to muscle weakness and sensory impairments. However, in a few cases, the patient's first symptoms have been documented as having bilateral hearing impairment. Access to healthcare services, including specialized care for rare genetic disorders like CMT, can vary depending on the region and resources available in Syria. Patients with CMT in Syria may benefit from multidisciplinary care involving neurologists, physical therapists, orthopedic specialists, and genetic counselors to manage their symptoms and provide support. It is important for individuals with CMT in Syria to receive proper diagnosis, treatment, and support to help improve their quality of life.

Methods

The work has been reported in line with the SCARE criteria[16].

Ethical approval and consent to participate

Ethical approval was not required.

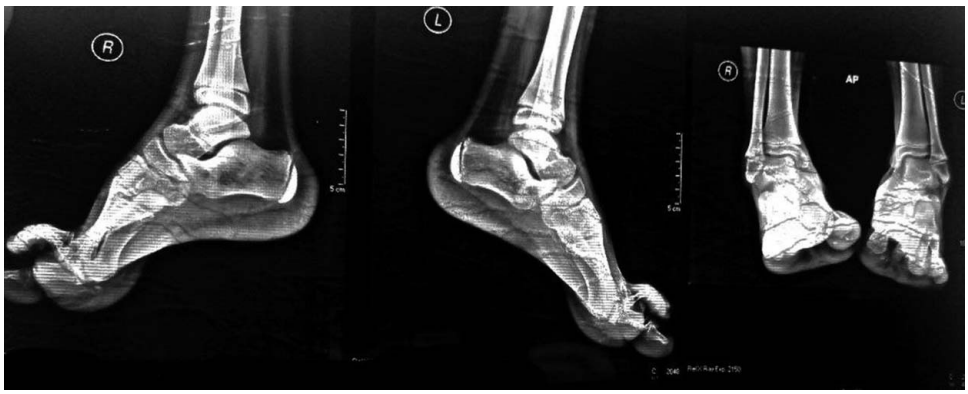

Figure 4. An anteroposterior radiograph and a lateral radiograph of the bilateral pes cavus.

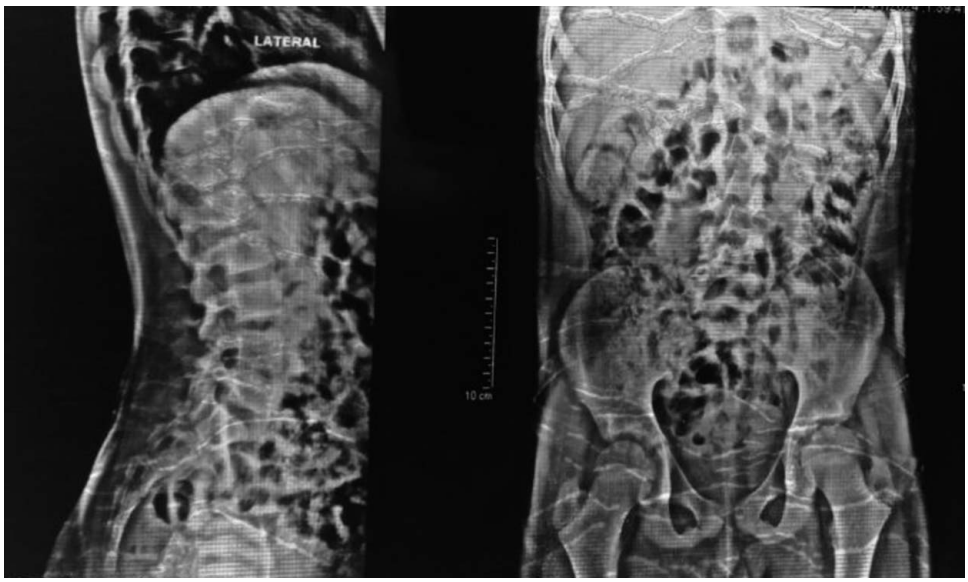

Figure 5. T1-weighted and T2-weighted images of the lumbar and dorsal columns showed: L4-L5: a wide central bulge touching the meningeal sac. L5-S1: mild global swelling that relatively narrows the right neural foramen.

Consent for publication

Written informed consent was obtained from the patient's parents for publication and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

A.M.: collected the patient's data and drafted the manuscript; H.H.: collected the patient's data and drafted the manuscript; Y.S.: collected the patient's data and drafted the manuscript; E.S.: collected the patient's data and drafted the manuscript; S.H.: collected the patient's data, drafted the manuscript, performed the procedure, revised the manuscript, and supervised the study; W.K.: revised the manuscript and supervised the study; Y.S.: revised the manuscript, and supervised the study.

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The authors report no conflicts of interest to declare.

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During the preparation of this work the authors used ChatGPT in order to paraphrase some sentences. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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