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CASE REPORT

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A rare case of hereditary sensory and autonomic neuropathy type II

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Abstract

We describe the follow-up of a 29-year-old man diagnosed with hereditary sensory and autonomic neuropathy type II, including the different complications that presented since his childhood. Despite efforts to maintain an optimal quality of life, the lack of an early diagnosis led to an unfavorable prognosis and life condition.

KEYWORDS

arthrodesis, auto-amputation, electromyography, fistula, hereditary sensory and autonomic neuropathy, osteomyelitis

1 | INTRODUCTION

Hereditary sensory and autonomic neuropathy (HSAN) is a group of rare disorders affecting the sensory and autonomic neurons. It is classified into five types (type 1–5)[1,2] depending on the age of onset, clinical features, and genetic inheritance.[3] However, with the identification of several new responsible genes, this classification has further expanded to HSAN type 1–8.[4] The global prevalence of type II HSAN is unknown, and no sex predilection has been reported.[5] Its onset can occur at birth and often before puberty.

HSAN type II (HSAN2) is associated with autonomic dysfunction accompanied by severe changes in sensory function.[6] It is conventionally an autosomal recessive disorder with a mutation in the HSN2 exons of the *WNK1*, *FAM134B*, and *KIF1A* genes located on chromosome 12p13.33,[7] causing reduced pain, temperature, and touch sensations, and consequently, ulcers, burns, auto-amputations, and poor wound healing.

Therefore, diagnoses and treatment at an early age in patients with HSAN2 is essential to prevent the risk of growth disorders and auto-amputation. Here, we describe

the follow-up of a 29-year-old man diagnosed with HSAN2, as well as the different complications that presented in his life since childhood.

2 | CASE PRESENTATION

A 29-year-old man was admitted to our hospital. The patient was the third child in his family and born after a full-term pregnancy with hospital care and prolonged labor. His siblings were healthy and had no familial history of neuromuscular disease.

The patient had congenital strabismus. At the age of 8 years, he developed septic arthritis of the right ankle. When he was 14 years, he underwent surgery for prepatellar septic bursitis of the right knee. Postoperatively, he developed osteomyelitis of the patella, for which extra-articular knee resection was performed; arthrodesis of the knee joint with an external fixation device was unsuccessful. The patient's right lower limb was shortened by 10 cm because of the consecutive operations performed for osteomyelitis, and he required crutches and shoes with a 15-cm platform, leaving the patient handicapped (Figure 1).

Gradually, he developed numerous skin ulcers, experienced tooth loss, and his tongue bifurcated due to constant biting (Figure 2). Thickened palms, soles, and finger along with nail deformities were observed on both hands and feet (Figure 3). Unilateral absence of a deep tendon reflex, reduced heat sensitivity, lack of pain sensation throughout the body, hyporeflexia, dysphagia with preservation of gag and palatal reflexes, no abnormalities in cardiovascular reflexes, and casual sweating were observed.

In April 2021, the patient developed choking and ingestion of the contents of the oral cavity; an intraoral examination revealed fistula formation in the left upper jaw. The fistula had been established through the maxillary sinus and was repaired through soft-tissue reconstruction. Laboratory results, including those for uric acid, were within normal limits. Brain magnetic resonance imaging also yielded normal results, yet electroneurography revealed generalized axonal sensory neuropathy.

The patient was subsequently referred for genetic analysis. The presumptive diagnoses were Moebius syndrome or HSAN, considering the age of onset, clinical symptoms, and electroneurography results. A novel homozygous pathogenic mutation, c.1426del (p.Gln476Argfs*57), in the FAM134B gene was identified, and a final diagnosis of HSAN2 was made.

3 | DISCUSSION

In this case, progressive insensitivity to pain was observed, and the alterations in pain perception indicated

FIGURE 1 The patient's right lower limb was shortened by 10 cm and used shoes with a 15-cm platform.

HSAN, which can present at an early age. HSAN2 is characterized by a generalized loss of superficial and deep sensations, loss of heat and touch sensitivity, urinary incontinence, decreased sweating, and slow pupillary reaction to light.[8–10] This neuropathy is expressed in childhood through self-inflicted injuries that are severe and potentially mutilating. The absence of pain entails a lack of protective mechanisms, causing repetitive microtrauma and consequent gross damage to the joint surface and subchondral bone and, ultimately, joint deformity.

Patients present with poor orthopedic treatment responses and frequent post-surgical complications, as well as pseudarthrosis, osteomyelitis, septic arthritis, among others.[8] In this case, the patient had recurrent ulcers, leading to osteomyelitis of the patella.

Dental and oral complications in patients with HSAN2 begin with the growth of teeth in the form of biting of the tongue, lips, and oral mucosa; dislocation of dental organs; oral self-injury; and dental attrition.[11] Our patient experienced tooth loss, tongue bifurcation, dysplasia of the phalanges of the hands, and fistula formation in the upper jaw. Rehabilitation for dental and oral complications is imperative for these patients.[12]

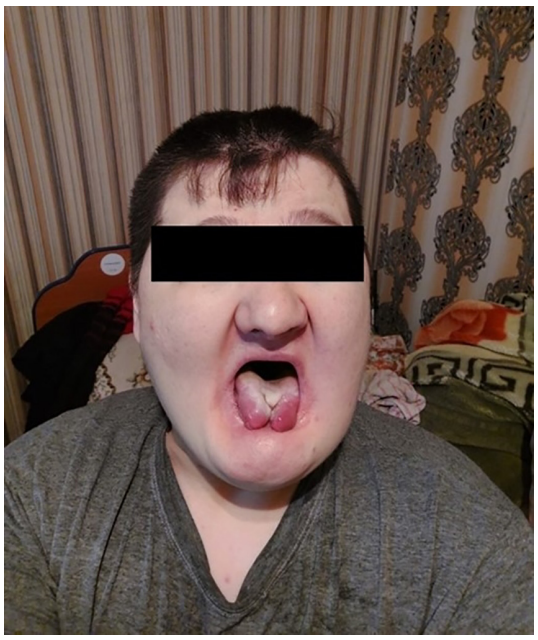

FIGURE 2 The patient developed a tongue bifurcation due to constant biting.

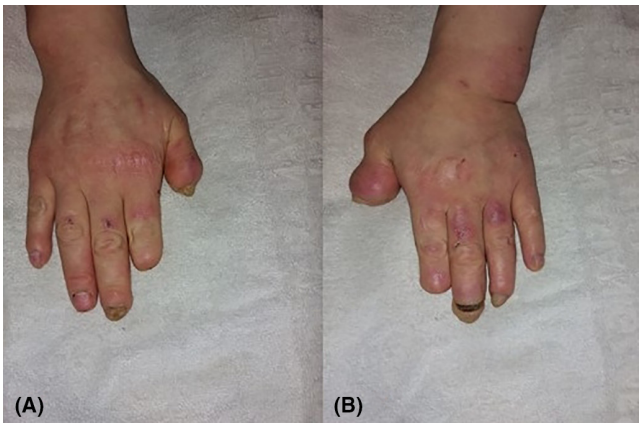

FIGURE 3 Photograph showing thickened palms and soles and finger and nail deformities of both hands.

Previously, tooth extraction was considered to prevent damage to oral tissues and the auto-amputation of limbs; however, a treatment that can better preserve the quality of life is needed.[10]

For diagnosis, three tests are relevant: electrophysiological, histopathological, and genetic tests. Electrophysiology reveals reduced or absent sensory nerve action potentials, preserved or reduced nerve conduction velocities, and reduced compound muscle action potentials. There is no definitive diagnosis for HSAN2, and only symptomatic treatment is provided for associated complications.[13] Currently, the treatment plan entails special attention toward the use of dentures and patient education.[14]

The mechanism of mutations in the FAM134B gene causing HSAN2 is not known. An in vivo study on mice models demonstrated that a depletion in FAM134B protein levels lead to structural alterations in the Golgi apparatus, interfering with multiple cellular pathways necessary for the survival of sensory and autonomic ganglion neurons.[15]

Our patient reported foot ulcers. Similarly, HSAN2 should be considered in the differential diagnosis of chronic leg ulcers in patients with a healthy immune system.[16]

4 | CONCLUSIONS

Despite efforts to maintain an optimal quality of life, this case shows that the absence of early diagnosis leads to an unfavorable prognosis and life condition in patients with HSAN2. To our knowledge, this study is the first to report a case of HSAN2 in central Asia. No specific and deterministic treatment exists for HSAN2, and only supportive and preventive measures are available to reduce complications. Therefore, educating patients and their families to prevent ulcer formation is necessary.

AUTHOR CONTRIBUTIONS

Elmira Mamytova: Conception, design of the work, manuscript preparation, and data acquisition. Asel Jusupova: Design of the work, manuscript preparation, and data acquisition. Anara Toktomametova: Conception, manuscript preparation, and data acquisition. Kunduz Karbozova: Design of the work, manuscript preparation, and data acquisition. Begimay Kadyrova: Design of the work, manuscript preparation, and data acquisition. Yethindra Vityala: Design of the work, manuscript preparation, and data acquisition. Tugolbai Tagaev: Manuscript preparation, and data acquisition.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data are available from the corresponding author upon reasonable request.

ETHICAL APPROVAL

The patient gave her informed consent prior to her inclusion in the study.

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