Congenital Insensitivity to Pain Syndrome with Hidrosis in a 17-year-old female

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ABSTRACT

Congenital Insensitivity to Pain Syndrome with Hidrosis is an extremely rare phenotype where individuals lack the ability to perceive pain and temperature. Theis syndrome was initially described by Dearborn in 1932[1] and further classified into the Hereditary Sensory and Autonomic Neuropathies (HSAN) by Dyck in 1993[2]. This case report presents a 17-year-old female with HSAN-V, detailing her history of recurrent injuries and the challenges associated with diagnosis, treatment, and rehabilitation. This case highlights the importance of early recognition, proper management, and patient education to prevent complications and improve long-term outcomes.

INTRODUCTION

- HSANs are a group of clinically and genetically diverse disorders characterized by axonal atrophy in the sensory and autonomic neurons. They often manifest with peripheral neuropathies, lack of nociception, hyporeflexia, and varying degrees of autonomic dysfunction. HSANs are a group of conditions characterized by progressive sensory loss, varying degrees of autonomic dysfunction, and axonal atrophy of sensory neurons.
- Among the five recognized HSAN subtypes, HSAN Type V (HSAN V) is particularly rare, caused by mutations in the NGFB gene, which encodes nerve growth factor beta (NGFβ)—a critical protein for the development and maintenance of nociceptive neurons[8].
- HSAN V is characterized by severe loss of pain perception while retaining autonomic function, including partial sweating ability[9]. This distinction is clinically important, as HSAN IV patients experience complete anhidrosis and cognitive impairments, whereas HSAN V patients generally have normal cognition and only partial autonomic involvement[6].
- Individuals within the HSAN classification system commonly present with traumatic fractures, burn injuries, non-healing ulcers, malunions resulting in Charcot joints, bone infections, and self-mutilation behaviors.

CASE DESCRIPTION

- A 17-year-old female patient presents with swelling of the left middle finger, presumptively stating that it was caught in her wheelchair six days prior. The patient has a past medical history of Congenital Insensitivity to Pain Syndrome with Hidrosis, HSAN-V, recurrent episodes of osteomyelitis, recurrent extremity ulcers, primary teeth removal due to self-lip biting, and multiple distal digit amputations.
- The patient is wheelchair bound due to limitations in ambulation most likely stemming from Charcot joint changes of the mid-feet on both sides. Patient also has a history of right tibia fracture when she was 3, left humerus fracture when 9, and left hip and bilateral wrist fractures in her teens. Patient has had bilateral corneal transplants and lip surgery for excessive lip biting.
- On Review of Systems the patient did not report any pain with the open middle finger wound or the ulcer on her foot. The patient denied all other ROS questions, with the patient's mother stating they came to the hospital after seeing pus leaking from the open wound.
- Physical exam revealed pustular discharge from the finger and an open wound on the right foot, actively being managed by the wound care team. The patient was febrile and showed leukocytosis (33.09) and anemia (8.7 HGB) on CBC. Patient was hyponatremic (130) and mildly hypokalemic (3.3). X-rays on admission showed soft tissue swelling of the left middle finger, and previous fractures of the distal tibia and fibula with Charcot change of the midfoot.
- The patient has had prior genetic testing for *NRTK1* (HSAN-IV), *PRDM12* (CIP), *TRPV4* (CMT & dSMA). The patient and her guardian are actively following up with their pediatric neurologist regarding further genetic testing for identification of a possible gene mutation.

RESULTS

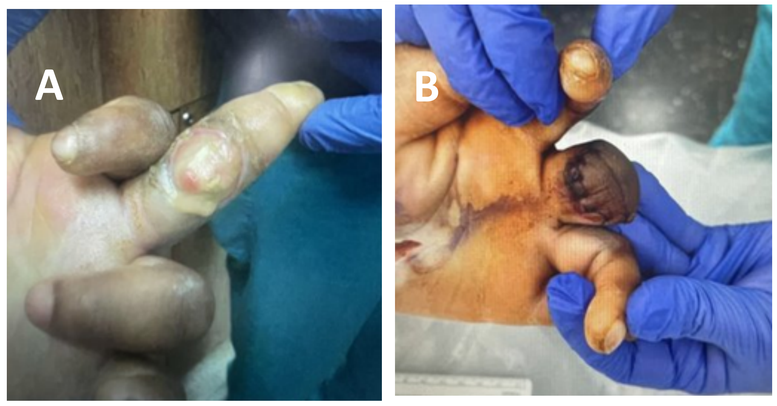

Figure 1. *Preoperative and postoperative images of left middle finger cellulitis. The preoperative image (A) shows a circular wound on the volar proximal interphalangeal joint with purulent discharge and swelling. The postoperative image (B) shows the left middle finger post-amputation and tenosynovectomy as was needed to control spread of infection.*

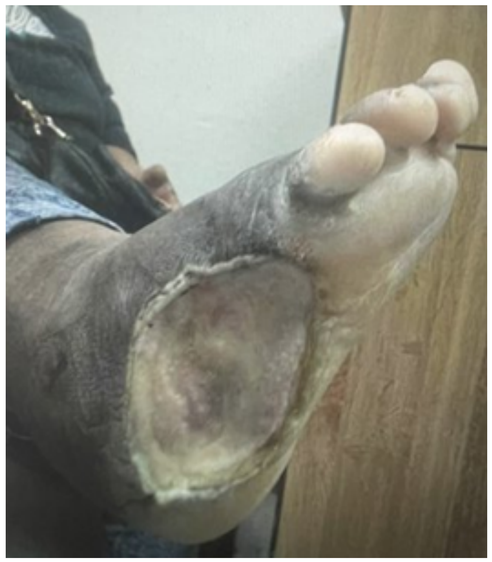

Figure 2. *Ulceration found on the plantar surface of the right foot showing exposed tissue and significant swelling.*

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REFERENCES

TREATMENT & REHAB

- The patient was started on Vancomycin empirically for cellulitis of the left middle digit.. Orthopedic surgery was consulted and opted to amputate the left middle finger. Tissue cultures on day 2 in the hospital were positive for *MRSA* and *Strep B*, and the patient was continued on her course with Vancomycin and Ceftaroline was added per ID for duration of hospital stay.
- Subsequent secondary wound closure and a tenosynovectomy were performed by her surgical team to remove residual infected tissue and restore mobility in the wrist. The remainder of her hospital stay was uneventful, and the patient was discharged on four weeks of Bactrim.
- The patient was seen by OT/PT in the hospital and noted severe limitations in the patient's ability to perform ADLs. The patient was referred to outpatient rehab to strengthen her upper and lower extremities.
- Patient education was a pertinent point of discourse during the patient's hospital stay. The patient and her mother were informed of the risks associated with the syndrome, due to the patient's lack of sensory perception. Timely and routine daily skin checks are necessary for the patient, as well as consistent dental care. A discussion was had regarding patient safety with bath-water checks, using protective gear such as padded gloves and braces, and the importance of consistent follow ups with the patient's primary care physician.

DISCUSSION

- Hereditary Sensory and Autonomic Neuropathies are rare and infrequently discussed in the current literature, as well as the medical school curriculum. The unique and diverse symptoms present in the various HSAN subtypes create challenges for proper medical management.
- The patient’s presentation aligns with classic HSAN-V features, including recurrent painless injuries, impaired wound healing, but still self-reported hidrosis. No genetic link has still been identified for the patient currently. She is negative for the NTRK1 gene mutation commonly seen in HSAN-IV, and no link has been identified with the NGFβ gene.
- Compared to other hereditary sensory neuropathies, HSAN-V primarily affects small-diameter sensory neurons responsible for pain and temperature sensation, while sparing motor function. This distinguishes it from conditions such as Charcot-Marie-Tooth disease or diabetic neuropathy, where motor involvement is more prominent. This patient was negative for the PMP22 gene in Charcot Marie Tooth.
- While there is no definitive treatment for HSAN-V, multidisciplinary care involving physical therapy, orthotic interventions, and vigilant monitoring for injuries is crucial. Emerging research on nerve growth factor-based therapies and potential gene-targeting approaches offers hope for future treatment options.
- This case underscores the need for increased awareness of HSAN-V among clinicians, as early recognition and intervention can significantly impact patient outcomes. Further studies are needed to explore targeted therapies that could address the underlying pathophysiology of the disease.

CONCLUSIONS

- The purpose of this case report is to present the findings of a patient with Congenital Insensitivity to Pain Syndrome with Hidrosis and to further the discussion of an uncommon medical diagnosis.
- Patients with Congenital Insensitivity to Pain with Hidrosis often need work-ups for peripheral sensory neuropathies, rehabilitation management for various infections and bone fractures, and proper education on the syndrome itself.