

## Important Aspects of Anesthetic Management of a Patient with Hereditary Sensorial and Autonomic Neuropathy Type 4: A Case Report

Hereditör Sensöriyel Otonomik Nöropati Tip 4 olan Hastada Anestezi Yönetiminin Önemli Yönleri: Olgu Sunumu

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### ABSTRACT

Hereditary Sensorial Autonomic Neuropathy (HSAN) type IV or congenital insensitivity to pain and anhidrosis (CIPA) is a rare congenital disorder characterized by recurrences of unexplained fever, extensive anhidrosis, insensitivity to pain, hypotonia and mental retardation in some cases. These patients develop corneal scarring, teeth eruptions, multiple fractures, osteomyelitis, buccal and lower limb wounds, injuries of finger tips so they undergo surgery. In this paper we report a patient with HSAN-IV, who developed tibia fracture and undergone successful operation under monitored anesthesia care. A 7 year old patient with HSAN-IV, admitted with left tibia fracture, obviously painless. He was operated under monitored anesthesia care without any complications and discharged home after a night follow-up. No anesthetic or analgesic drugs had been used for the surgery. Anesthetic considerations for the management of these patients are adequate perioperative sedation to reduce tactile hyperesthesia and excitement, close monitoring of cardiac rhythm and blood pressure, monitoring of body temperature and observation of nausea and vomiting.

**Key Words:** Congenital insensitivity to pain with anhidrosis, hereditary sensory and autonomic neuropathy type IV, anesthetic management

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### ÖZET

Hereditör Sensöriyel Otonomik Nöropati (HSAN) tip IV, ya da konjenital ağrı duyarsızlığı ve anhidrozis (CIPA); açıklanamayan ateş atakları, yaygın anhidrozis, ağrıya duyarsızlık, hipotoni ve bazı vakalarda mental retardasyon ile karakterize, nadir görülen genetik bir hastalıktır. Bu hastalarda korneal yaralanmalar, diş çıkmaları, çoklu kırıklar, osteomyelit, bukkal ve alt ekstremitte yaraları, parmak uçları yaralanmaları gelişebilir ve sıklıkla cerrahi geçirirler. Bu makalede tibia kırığı gelişen ve monitörize anestezi bakım altında başarılı bir operasyon geçiren HSAN-IV hastasını sunuyoruz. Yedi yaşında HSAN-IV tanısı almış hasta ağrısız sol tibia fraktürü nedeni ile başvurdu. Monitörize anestezi bakımı altında, komplikasyon olmadan opere edildi. Cerrahi için herhangi bir anestezi veya analjezik ilaç kullanılmadı. Bu hastalarda taktik hiperestezi ve heyecan durumunun giderilmesi için perioperatif dönemde uygun sedasyon, kalp ritmi, kan basıncı ve vücut ısısının izlenmesi, bulantı ve kusmanın yakından izlenmesi anestezi yaklaşım açısından dikkate alınması gereken noktalar dır.

**Anahtar Sözcükler:** Konjenital ağrıya duyarsızlık, anhidrozis, hereditör sensöriyel ve otonom nöropati tip IV, anestezi yönetimi

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### INTRODUCTION

Hereditary Sensorial Autonomic Neuropathy Type IV (HSAN-IV), also known as Congenital Insensitivity to Pain with Anhidrosis (CIPA) is a rare congenital disease characterized by recurrent unexplained fever, total insensitivity to pain, anhidrosis, and mental retardation in some cases (1). Mutations of the neurotrophic tyrosine receptor kinase 1 gene (NTRK1), located on chromosome 1 (1q21-q22), which encodes a receptor tyrosine kinase (RTK) for the nerve growth factor (NGF) are responsible (2). NGF induces neurite outgrowth and promotes survival of embryonic sensory and sympathetic neurons.

Markedly decreased or absent sweating is one of the cardinal features of CIPA. The trunk and upper extremities are always affected, while other areas of the body are variably affected. In contrast to patients with Familial Dysautonomia, there is compensatory tachycardia with hypotension. Patients may have a heightened sympathetic response, as erythematous blotching of the skin with excitement has been seen in younger patients. Mental developmental milestones are frequently delayed; severe learning problems can be observed. In rare cases normal mental functions are observed. Hyperactivity and emotional lability are common (1).

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Diagnosis is generally made by clinical findings, but some laboratory studies can be helpful and confirmative. Neuropathological findings include absence of unmyelinated axons, decrease in the number of small myelinated axons and normal distribution of large myelinated axons. Sweat glands have a normal structure, except for not being innervated. Pharmacological test involves intradermal injection of 1:10000 histamine, which fails to show axon flare. Electrophysiological studies show normal motor and sensory nerve conduction. Molecular studies, demonstrating NTRK1 gene mutations, represent the ultimate step in diagnosis, and are rarely resorted to (1).

Treatment is conservative and focused on control of hyperthermia, prevention of self-mutilation and orthopedic problems, and helping family cope with behavioral and educational issues. Careful daily inspection for unrecognized injuries is important (1). These patients occasionally develop corneal scarring, teeth eruptions, multiple fractures, osteomyelitis, buccal and lower limb wounds, and injuries of finger tips caused by self-mutilating behaviors; so they often undergo surgery. In this paper we report our experience with HSAN-IV patient developed tibia fracture, from anesthetic viewpoint.

## CASE REPORT

A 7 year-old-male patient, having clinical diagnosis of HSAN-IV from the infancy, admitted to our hospital with left tibia fracture. He had history of ulna fracture, minor burns on the finger tips and flank without sequelae. Preoperative physical examination was made, and revealed no pathology, except for lack of pain sensation and sweating. No hypotonia was observed and mental development was normal. No recurrent fever attacks were reported by the family. Preoperative blood count, blood biochemistry, coagulation studies were within normal ranges. Pediatric consultation was made, and no further evaluation was recommended. The patient was scheduled for elective operation under monitored anesthesia care (MAC) on the same day.

Preoperative 6 hour fasting was applied to achieve nil per os status. Routine monitorization was made, including electrocardiogram, pulse-oximeter, non-invasive blood pressure and body temperature measurement from axilla, in the operating room. A 22-gauge intravenous cannula was inserted into one of the left dorsal hand veins, and isotonic sodium chloride infusion was started at a rate of 100 mL h<sup>-1</sup>. No sedative, anesthetic or analgesic was used. Spontaneous breathing was maintained with O<sub>2</sub> and air in a ratio of 1:1. Closed reduction and external fixation of tibia was performed without any complications, and the surgery lasted 30 minutes. Heart rate, blood pressure and body temperature of the patient were within normal limits throughout the procedure. No complications were observed. The patient was discharged after one night uneventful follow-up.

## DISCUSSION

CIPA is an extremely rare disorder. Only few cases have been previously reported in Turkey (3, 4). Some important anesthesia implications must be considered when dealing with these patients. CIPA patients have decreased peripheral and central activity of epinephrine, norepinephrine and dopamine; and this makes them prone to cardiovascular events like hypotension, bradycardia and dysrhythmias (5, 6). Notwithstanding, their cardiovascular reflexes are preserved, and reflex tachycardia is observed as a response to hypotension (7). Although we observed no reflex tachycardia in our patient, and blood pressure was stable throughout the procedure, we prepared atropine (0.1 mg/mL) and ephedrine (5 mg/mL) ready for use. Although there is total analgesia, the patients can experience tactile hyperesthesia, which may cause unpleasant sensation during surgical manipulation. Audio-hypersensitivity can add to tactile hyperesthesia, so general anesthesia is recommended to these patients (8). We have observed no tactile hyperesthesia in our patient. Hyperthermia is another important problem, must be kept in mind. These patients are prone to hyperthermia, and 20% may die of this within the first 3 years of life. Prevention of hyperthermia requires careful monitoring of temperature and room temperature adjustment. Cooling blankets can be used if necessary. Fever may be resistant to antipyretics (9). Two site temperature monitoring may be prudent. Premedication not only calms the patient, but is also helpful in reducing excitement caused fever (6). We have not used preoperative sedation for our patient, as we were unfamiliar with this possibility of excitement induced hyperthermia risk, and clinical observation of the patient revealed no signs of excitement. Caution must be taken when using anticholinergic agents as a part of preoperative sedation due to anhidrosis, as these may result in heat accumulation.

Another problem encountered in CIPA patients is vomiting. These patients must be considered as "full stomach" regardless of the duration of nil per os status, due to autonomic nervous system abnormalities. Regurgitation and aspiration have been previously reported in patients under anesthesia (10). However, no cases of vomiting was reported in a series of 40 anesthesia records by Rozentsveig et al. (5). Although not frequent, this may be a major concern for anesthesiologists. We have not used antiemetic prophylaxis, because we were unfamiliar with the effects of antiemetics in these patients at the time of the urgent operation.

General anesthesia have been used in CIPA patients, and atropine, merperidine, fentanyl, succinylcholine, atracurium, vecuronium, ketamine, propofol, droperidol, barbiturates, benzodiazepines and inhalation agents have been safely used (7,8). As the patients have no sensation of pain to surgical stimuli, doses of anesthetic and analgesic agents must be closely titrated according to the hemodynamic. Bispectral Index (BIS) monitoring have previously been used in the patients with CIPA (3,4,6). Spinal, epidural anesthesia and deep sedation have also been used for operations. We haven't come across a patient with CIPA having operation without anesthesia or sedation in the literature. The urgency of the surgery from the surgical point of view and the unfamiliarity of the anesthesiologists with the disease was the main reason of not providing anesthesia for the patient. Although this is an alternative, we suggest a routine provision of sedo-analgesia or general anesthesia for the patients with CIPA.

## CONCLUSION

Important anesthetic implications of the patients with HSAN type IV include adequate pre- and intraoperative sedation to reduce tactile hyperesthesia and excitement, close monitoring of cardiac rhythm and blood pressure, monitoring of body temperature and observation of possible nausea and vomiting.

## Conflict of interest

No conflict of interest was declared by the authors.

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