



CASE REPORT

Anesthetic management of two siblings with congenital insensitivity to pain with anhidrosis syndrome

Konjenital ağrı duyarsızlık ve anhidrosis sendromu olan iki kardeşin anestezi yönetimi

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Summary

Congenital insensitivity to pain with anhidrosis (CIPA) is a rare syndrome characterized by a lack of sensitivity to pain due to congenital sensory and autonomic neuropathies, anhidrosis, an inability to regulate body temperature, growth retardation, mental retardation at different levels of severity, and inadvertent self-harm. It is an autosomal recessive disorder that is result of a mutation in the neurotrophic receptor tyrosine kinase 1 gene, which encodes neurotrophic tyrosine kinase. CIPA patients are frequently admitted to hospitals with unrecognized traumatic fractures and unhealed wounds due to the lack of a pain response. Presently described is the method of anesthetic management used for 2 siblings, aged 17 and 14 years, with a generalized lack of pain, anhidrosis, mental retardation, and septic arthritis. Sedation with midazolam alone provided satisfactory surgical comfort without causing hemodynamic instability in these 2 patients with CIPA syndrome.

Keywords: Congenital insensitivity to pain syndrome with anhidrosis; pain insensitivity.

Özet

Konjenital ağrıya duyarsızlık sendromu, konjenital duysal ve otonomik nöropatiye bağlı gelişen ağrıya duyarsızlık, anhidrozis, epizodik ateş, gelişme geriliği, farklı düzeylerde mental retardasyon ve kendine zarar verme ile karakterize nadir görülen bir sendromdur. Nörotrofik tirozin kinazın kodlandığı nörtrofik tirozin kinaz-1 genindeki mutasyon sonucu meydana gelen otozomal resesif bir sendromdur. Çoğu hasta hastaneye ağrısız iyileşmeyen yaralar ve farkedilmeyen travmatik kırıklar ile başvurmaktadır. Bu yazımızda on yedi ve on dört yaşında ağrıyı hissetmeme, anhidrosis, mental retardasyon ve septik artriti olan iki kardeşi sunmaktayız. Konjenital ağrıya duyarsızlık sendromu olan hastalarda, tek başına midazolom ile sedasyon, tatminkar bir cerrahi konforu, herhangi bir hemodinamik bir instabilite yaratmadan sağlamaktadır.

Anahtar sözcükler: Ağrıya duyarsızlık; CIPA; konjenital ağrıya duyarsızlık sendromu.

Introduction

Pain is an important protection mechanism for the body.^[1] Loss of pain sensation can lead to serious problems. Congenital pain insensitivity syndrome with anhidrosis (CIPA) was first described by Dearborn in 1932.^[2] Although there is no data about the prevalence of the syndrome, it is a very rare entity. The Syndrome consist of the pain insensitivity due to congenital sensory and autonomic neuropathies, anhidrosis, increase of episodic body temperature, growth retardation, mental retardation at different levels and self-harm. Dick et al.^[3] (1993) classified CIPA as 5 subgroups. CIPA syndrome type IV hereditary sen-

sorial and autonomic neuropathy (HSAN-IV), is one of the most common type of these subgroups.^[4] It is thought that the mutation of neurotrophic tyrosine kinase receptor 1 (NTRK1) gene, which is autosomal recessive inheritance and responsible for the effects of the nerve growth factor in the embryonic period causes the syndrome.^[5-6] In these patients pain sensation is lost, and heat insensitivity and autonomic function are impaired while touch and pressure sensations are intact. An increase in body temperature, seen in episodes of early ages, can be the first symptom of the disease.^[7] Additionally fingers and lip bites, painless fractures, joint deformities causing chronic osteomyelitis, and neurogenic arthropathy (charcot joint) can

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be seen in the patients.^[8] Despite patients are insensitive to pain, general anesthesia or sedation may be necessary because of disturbing conditions such as tactile hyperesthesia during the surgical procedure.^[9]

Experience on anesthesia management of these patients is limited due to few number of cases. We aimed to present our experience about the anesthesia management of two siblings with CIPA syndrome.

Case Report

Here we report sixteen and thirteen years old two siblings who were diagnosed with CIPA syndrome. Patients were consulted to anesthesiology clinic for preoperative evaluation due to chronic and acute septic arthritis in ankles (Fig. 1).

The older sister diagnosis was made in infancy period while being investigated for fever etiology. Her medical history revealed episodic increase in body temperature, self-harming behaviours, recurrent surgical procedure from knees, hands, fingers and heels in ortopedia clinics due to traumatic and none traumatic reasons. Moderate mental retardation diagnosis had been made by pediatric psychiatry. Physical examination revealed, retardation in mental function, dry skin, thickening of the palms of both hands,



Figure 1. Chronic septic arthritic image of sixteen years old patient.

and old scars with new wounds on their fingers. Also we learned from medical history a failed surgical attempt to close chronic fistula which was located on left foot ankle about one year ago. Because of the fact that she had CIPA diagnosis, after the birth of her brother, genetic analysis was done and he was also diagnosed with CIPA syndrome. And his medical history and physical examination have shown similar findings with his sister. Other systemic examinations of both patients were normal. The mallampati scores were II in their airway assessments.

Laboratory values and chest X-rays were normal except leukocytosis, and elevation of values of C-Reactive Proteins and erythrocyte sedimentation rates.

Routine monitoring with electrocardiography, non-invasive arterial blood pressure, pulse oximetry and temperature were performed in the patients. Vital signs were normal.

The response of the patients to touch and painful stimuli were evaluated. It was decided to start with sedation since patients did not feel any pain and were cooperative. During the perioperative period, preparations were made for general anesthesia if needed. Before the surgical procedure, the patients did not feel any pain during the vascular access. Midazolam was administered intravenously as a bolus dose of 0.06 mg/kg. Oxygen was given at 3 L/min with face mask and end-tidal CO₂ (ETCO₂) levels were followed. The operation room temperature was kept at around 24°C. In surgical procedures, ankles were inserted with a 4 cm incision. The skin and subcutaneous tissues were passed through bluntly by paying attention to the tendons, veins and nerve packs. There were no sensation of pain in patients in the meantime. After reaching the ankle joint, all infected looking tissues were debrided (Fig. 2). The ankles were washed with plenty of saline and closed in each patient. Short leg splint were performed. There were no sensation of pain in patients in the meantime. Operation times were approximately 45 and 70 minutes.

In both cases there were no increase in heart rate and blood pressure, no decrease in oxygen saturation, no alterations in ETCO₂ and body temperature throughout the operation. No additional anesthetic inter-



Figure 2. Debridement image of sixteen years old patient.

vention was required. At the end of the operation, the patients were observed in the postoperative unit for 20 minutes and then, were sent to the orthopedic clinic for further follow-up and treatment. There were no analgesic requirement in the postoperative period. Before the preoperative period, the parents of the patients were informed about our anesthesia methods that could be applied and their written informed consent was obtained.

Discussion

Congenital pain insensitivity syndrome is a rare syndrome characterized by pain insensitivity, mental and growth retardation, impaired sweat secretion, and temperature regulation. In a study, Bar-On et al.^[10] investigated 13 patients with congenital pain insensitivity syndrome and reported that type-IV, was the most common CIPA syndrome. Our cases were congenital pain insensitivity syndrome type IV and had mental retardation, pain insensitivity and absence of sweat.

Pain is a very important sensation that allows people to protect themselves, and various problems arise in its absence. Today the pathophysiology of these diseases is not fully understood and there is no treatment. However, the diagnosis of disease with genetic testing can be done at the beginning of pregnancy by 98%.^[11] In our cases, the family had a genetic test for the infant born after the sick child, and the CIPA was diagnosed.

These patients are susceptible to numerous anesthetic complications such as hemodynamic instabil-

ity and risk of hyperthermia because of autonomic dysfunction. For this reason, determining the method of anesthesia, choosing the anesthetic drugs and adjusting the dose of the drugs is important for the anesthetist. The experience of anesthesia management is also limited due to the rare occurrence of the syndrome. Although general anesthesia was preferred in most of the studies,^[12] there were case presentations which only sedation was performed.^[13] Even though general anesthesia provides surgical comfort for surgeon, it increases the susceptibility to anesthesia complications due to hemodynamic instability and hyperthermia because of autonomic dysfunction. Therefore, we decided to performed sedation first.

Zlotnik et al.^[14] examined 358 operations performed under general anesthesia in 35 CIPA patients. The ratio of the anesthetic agents used in these operations was; thiopental 4%, ketamine 27%, propofol 71%, opioid 8%, muscle relaxants 27%. Özmete and colleagues administered propofol for depth sedation after premedication with midazolam, atropine, and ketamine for endoscopic intervention in CIPA syndrome patient.^[13] Only midazolam administration was enough in our cases.

In some studies, bispectral index (BIS) monitoring was used to evaluate the depth of anesthesia.^[13-14] We could not monitor the BIS because the conditions in our clinic were not appropriate.

Although the cardiovascular reflexes are protected in CIPA syndrome, the levels of epinephrine and norepinephrine levels are reduced. Tomioka et al. reported hypotension and bradycardia in the perioperative period due to decreased catecholamine levels.^[15] In our cases, hypotension and bradycardia were not observed during the operation.

Conclusion

To our knowledge this is the first case presentation in the literature which were only used midazolam for sedation. According to the mental level of the patient and the type and size of the surgical procedure, we think sedation with midazolam alone is provides satisfying surgical comfort without causing any hemodynamic instability in patients, under the mandatory monitorization.

Informed Consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

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