Congenital Insensitivity to Pain and Anhidrosis (CIPA) and Anesthesia

Abdulrahman Abdullah Al Sulaiti, BSc, MD* Ahmed Abdelgawad MSc, EDRA, EDAIC**
Ali Habib Almoumen, MBBS***

Hereditary sensory and autonomic neuropathy type IV, also known as congenital insensitivity to pain with anhidrosis CIPA, is a rare hereditary syndrome. The syndrome is one of the inherited disorders grouped under Hereditary Sensory and Autonomic Neuropathies (HSAN). The syndrome affects the ectodermal structures such as skin, nervous system and bone. The presentation of the syndrome is unique as it can cause marked sweat gland dysfunction, episodic hyperpyrexia secondary to high environmental temperature, insensitivity to pain, self-inflicted injury and intellectual disability. The anesthetic management of the CIPA is challenging, which could lead to preoperative complications.

We present a case of rare hereditary sensory and autonomic neuropathy syndrome type IV related to anesthesia. An eighteen-year-old female, diagnosed as a case of congenital insensitivity to pain and anhidrosis syndrome was admitted electively for external fixation of a fracture of the right elbow. The patient was diagnosed on genetic testing at 10 months and confirmed the presence of mutations in neurotrophic tyrosine kinase receptor type 1 (NTRK1) gene.

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Congenital insensitivity to pain and anhidrosis syndrome is an autosomal recessive disorder characterized by insensitivity to pain and temperature, and decrease or absent sweating which leads to variable injuries. The disorder is one of other five congenital syndromes of hereditary sensory and autonomic neuropathies which are classified according to the age of onset, mode of inheritance and clinical features[1]. In 1932, hereditary sensory and autonomic neuropathy was first described by Deadborn as congenital pure analgesia[2].

The aim of this presentation is to report the management of a rare case of hereditary sensory and autonomic neuropathy syndrome type IV related to anesthesia.

THE CASE

An eighteen-year-old female diagnosed as a case of congenital insensitivity to pain and anhidrosis syndrome was admitted for external fixation of a fracture of the right elbow under general anesthesia. The patient was diagnosed with the syndrome based on genetic testing at the age of 10 months and confirmed the presence of mutation in neurotrophic tyrosine kinase receptor type 1 (NTRK1) gene. The patient had multiple surgeries in upper and lower limb mainly due to osteoporotic bone fractures and septic arthritis. The parents were first cousins and she had one affected sister who was deceased. On general examination, the patient was wheelchair bound due to multiple operations in both of her lower limbs; she was oriented, alert with mild intellectual disability.

On examination, the patient had nail dystrophy. Mallampati score was 3, short neck, oligodontia, and thyromental distance were more than 3 fingers. The patient had impaired sensation to pain over all the dermatomes. No evidence of spinal deformity was found.

In theatre, no premedications were prescribed, basic monitoring devices were attached including non-invasive blood pressure, pulse oximetry, three leads electrocardiography and temperature probe. Invasive arterial line insertion was performed prior to induction for close monitoring of blood pressure. Supraclavicular brachial plexus block was performed before the induction of general anesthesia (GA) to minimize the anesthetic requirements and to avoid narcotic analgesics. The brachial plexus was identified in the supraclavicular region and the needle entry point was numbed with 3 ml of lidocaine 1% then 20 ml of bupivacaine 0.25% was injected via 5 cm 22 gauge Pajunk nerve block needle. First 5 ml was injected in the corner pocket below the plexus and the remaining 15 ml was injected inside the plexus. There was no pain during skin puncture but the patient complained of severe pain with the start of injection below the plexus.

GA was started immediately after the block. Preoxygenation was performed for 3 minutes; the patient was induced with propofol 1.5 mg/kg and fentanyl 2 mcg/kg. Intubation was performed using cuffed endotracheal tube size 7 by direct laryngoscope without muscle relaxant. Paracetamol 1 g, ondansetron 4 mg, ketamine 0.3 mg/kg (subanesthetic dose) and dexamethasone 8 mg were given via intravenous route. Anesthesia was maintained by using sevoflurane with nitrous 50:50. Despite minimal fluctuations of blood pressure between 90/66 to 110/70, the patient continued to be hemodynamically stable throughout the surgery with normal body temperature. Forced air warming was avoided due to heat intolerance. The patient received 2 liters of ringer's lactate solution.

The operation duration was 2 hours with an estimated blood loss of around 100 ml. The patient was transferred to the recovery room, and then to the ward. A complete motor and sensory (to her baseline) recovery were achieved after 10 hours. The

* Senior House Officer
** Specialist Anesthesiologist
*** Consultant Anesthesiologists and Interventional Pain Management
Dammam Medical Complex
E-mail: Abdulrahman.ALSulaiti@khuh.org.bh

pain was perceived as poorly localized dull aching pain which responded well to paracetamol 1 gm IV injection. Her blood pressure continued to fluctuate within the same range as it was preoperatively.

DISCUSSION

Congenital insensitivity to pain and anhidrosis syndrome is a rare autosomal recessive disease which was first described by Swanson in 1963[3]. The incidence of this syndrome is 1 in 25,000 population[4]. Evidence has shown that the causative genetic mutation is in the gene NTRK1[2]. It encodes for one of the receptors for nerve growth factor located in chromosome 1. The nerve growth factor is essential for the formation of autonomic neurons and small sensory neurons. NTRK1 is expressed in neurons that sense temperature and noxious stimuli[5]. The diagnosis of congenital insensitivity to pain and anhidrosis depends on the clinical presentation, pharmacological testing, neuropathological biopsy and genetic analysis[6].

The clinical presentation of this syndrome includes unexplained fever due to impaired thermoregulation, which occurs in early infancy and can lead to seizure, anhidrosis and loss of pain sensation. Both insensitivity to pain and intellectual disability lead to self-mutilation of lips, fingers and tongue. Corneal laceration and Charcot arthropathies are commonly present. Joint deformities lead to osteomyelitis and septic arthritis. Those patients typically undergo multiple orthopedic procedures. The lack of a normal axon flare in the skin after intradermal injection of histamine is a pharmacological test for CIPA[6]. Skin biopsy shows a deficiency in C and A-delta fibers in the epidermis, and hypoplastic or absence of sweet gland innervations[7].

A retrospective study of 35 patients revealed that autonomic dysfunction in the syndrome could lead to preoperative complications such as regurgitation, bradycardia, hypotension, and hyperthermia, as well as postoperative complications of bradycardia and hypotension[8].

Due to the unique characteristics of the syndrome, the requirement for opioids during the induction and maintenance is less than the dosage used for normal patients. Opioids are usually used to blunt the stress response of airway manipulation[8]. The muscle relaxants in CIPA can be safely used and it does not increase the risk of malignant hyperthermia[9].

The use of peripheral nerve block for postoperative analgesia was interesting in this patient as there was no pain during skin puncture but the patient complained of severe pain with start of injection below the plexus. Few cases of CIPA were reported in consanguineous marriage[10]. Parental screening is the only way to prevent the birth of affected children. No cure for this syndrome had been identified, and early recognition can prevent accidental injuries from orthopedic complications.

CONCLUSION

Congenital insensitivity to pain with anhidrosis (CIPA) is a rare syndrome and is a challenge for anesthesiologists during intraoperative and postoperative periods. Care should be sought in dealing with this type of patient during operation and recovery with regards to autonomic dysfunction complications. Insensitivity to pain, anhidrosis and hyperthermia are cardinal signs. Genetic test is required for definitive diagnosis. Regular ophthalmology and dental follow up are advisable.

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