Successful Pain Management in a Child with SCN9A Mutation Characterized by Alternating Insensitivity to Pain and Paroxysmal Extreme Pain

Matthew J. Rabito, MD; Thomas M. Morgan, MD; Andrew D. Franklin, MD, MBA; Stephen R. Hays, MS, MD, FAAP

VANDERBILT SCHOOL OF MEDICINE
DEPARTMENT OF ANESTHESIOLOGY

INTRODUCTION

- The Nav1.7 neuronal voltage-gated sodium channel is found in nociceptors throughout the nervous system.
- Nav1.7 mutations are associated with pain indifference and/or paroxysmal extreme pain disorder (1).
- Concomitant congenital insensitivity to pain and paroxysmal extreme pain disorder has not previously been described.

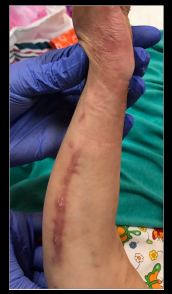
CASE PRESENTATION

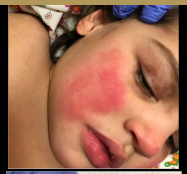
- 4-year-old female for re-fixation of a right Monteggia fracture with bilateral upper extremity spica casting to prevent patient access to the surgical site.
- History of progressively worsening, intermittent, painful erythema of hands & feet consistent with erythromelalgia since age 3 months.
- At times indifferent to painful stimuli, at other times in extreme pain without apparent inciting factors.
- Longstanding self-injurious behavior, particularly biting hands, causing infection of surgical wounds.
- Pain and behaviors refractory to empiric gabapentin.
- Pediatric pain service consulted for assistance with perioperative analgesia by geneticist when preoperative genetic testing noted to indicate I234T mutation in SCN9A gene encoding Nav1.7 α-subunit.

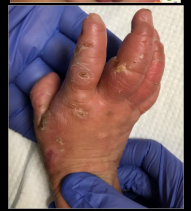
PAIN MANAGEMENT

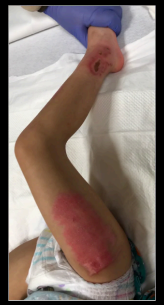
- I234T mutation has been mapped to the active site of carbamazepine (CBZ) on the Nav1.7 α-subunit.
- Carbamazepine restores normal function in neuronal preparations with I234T mutation (3,4,5).
- Began carbamazepine 65 mg (5 mg/kg) PO BID.
- Began nortriptyline 5 mg (0.5 mg/kg) PO QHS for sleep.
- Patient slept well for one of the first times in her life.
- Patient still doing well 2 months later.
- CBZ increased to 100 mg (7.5 mg/kg) PO BID.
- Continues to do well on this regimen.

IMAGES









DISCUSSION

- Congenital insensitivity to pain is a rare condition (~20 cases) rendering patients incapable of perceiving pain:
  - Loss-of-function SCN9A mutations produce dysfunctional Nav1.7 α-subunit impairing nociception (2).
- Paroxysmal extreme pain disorder is a rare condition (~80 cases) characterized by intermittent erythema, warmth, and severe pain lasting seconds to minutes:
  - Gain-of-function SCN9A mutations produce aberrant Nav1.7 α-subunits causing channels to close incompletely when deactivated, enhancing nociception (2).
- I234T mutation maps to the active site of CBZ.
- Use of CBZ, suggested by reverse pharmacogenomics, ameliorated both indifference to pain and paroxysmal extreme pain in this patient with I234T mutation.

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