NTRK1 Gene Analysis in Congenital Insensitivity to Pain with Anhidrosis (CIPA)

DISORDER ALSO KNOWN AS:
congenital insensitivity to pain with anhidrosis; CIPA; congenital sensory neuropathy with anhidrosis; hereditary sensory and autonomic neuropathy type IV; HSAN IV

CLINICAL FEATURES:
Congenital insensitivity to pain with anhidrosis is a rare form of hereditary sensory and autonomic neuropathy. Characteristic features are indifference to painful stimuli, self-mutilating behavior, anhidrosis (inability to sweat), corneal ulcers, and sometimes hypogammaglobulinemia and recurrent infections, skin changes, osteomyelitis, bone fractures, and cognitive impairment[1,2]. The patients' inability to sweat usually leads to recurrent episodes of unexplained fever and can be fatal due to hyperthermia, especially in infants and small children. The lack of pain sensation is thought to stem from the absence of the dorsal root ganglia responsible for pain sensation, while anhidrosis is due to the loss of innervation of eccrine sweat glands by sympathetic neurons.

GENETICS:
Autosomal recessive

TEST METHODS:
Using genomic DNA obtained from the submitted biological specimen, bi-directional sequence of the coding region and intron/exon boundaries of the NTRK1 gene (exons 1-16) is analyzed. If sequencing identifies a variant on only one allele of the NTRK1 gene, and if clinically indicated, reflex deletion/duplication testing (ExonArrayDx) will be performed at no additional charge to evaluate for a deletion/duplication of one or more exons of this gene. Variants found in the first person of a family to be tested are confirmed by repeat analysis using sequencing, restriction fragment analysis, or another appropriate method

TEST SENSITIVITY:
Over 98% of CIPA patients tested were found to have variants in the NTRK1 gene, including patients of more then 50 unrelated families from Japan, the Middle East, the Mediterranean, Northern Europe and the USA[3].

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