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My46 Trait Profile

Malignant hyperthermia susceptibility

Other Names: Malignant hyperpyrexia, hyperthermia of anesthesia

Malignant hyperthermia susceptibility is a genetic condition in which individuals have a increased chance of developing a severe reaction to certain medications used during surgery. It is caused by mutations in the genes RYR1 and CACNA1S, each of which makes a protein involved in muscle contraction.

Characteristics of Malignant hyperthermia susceptibility

Individuals with malignant hyperthermia (MH) susceptibility develop a severe reaction to certain medications used during surgery. When exposed to these medications (e.g., certain general anesthetic medications and a muscle relaxant medication called succinylcholine) or in rare cases, when exposed to high environmental heat or strenuous exercise, individuals with MH susceptibility may experience a serious and severe reaction. Symptoms include, severe muscle contractions, breakdown of muscle fibers, a rapid heart rate, a fast rise in body temperature, blood clotting problems, brain injury, liver failure, kidney failure and death, if not treated quickly.

Individuals with MH susceptibility may never know they have the condition unless they have had testing or if they have experienced a severe reaction to anesthesia.

Diagnosis/Testing

MH susceptiblity can be diagnosed either by genetic testing for a change or mutation in the genes RYR1 and CACNA1S or by testing done on a skeletal muscle biopsy. Approximately 70% of MH susceptibility is caused by mutations in the RYR1 and CACNA1S genes. These genes make proteins that play an important role in muscle contraction. Mutations in these genes cause the skeletal muscles to contract abnormally in response to certain triggering-medications, which leads to severe muscle contractions and rigidity.

The Caffeine Halothane Contracture Test has been considered the standard diagnostic test for MH susceptibility since the mid-1970s. This test is performed on a freshly biopsied skeletal muscle sample from the thigh. This test can only be done at an approved testing center listed on the MHAUS website (see Resources below). This test involves measuring the contracture response of the biopsied muscle to increasing concentrations of halothane, a general anesthetic medication, and caffeine. These are two substances are known to increase contraction response in individuals with MH susceptibility.

Management/Surveillance

Every situation in which general anesthesia medications are used must be associated with a plan for treatment of unanticipated MH susceptibility. With a plan in place, prompt treatment can be lifesaving. Preparedness and quick recognition of the signs of MH susceptibility is essential to an optimal outcome.

All locations where general anesthesia is administered should contain information for the MH Hotline (1-800-644-9737 or outside the US 001-209-417-3722), be prepared to monitor for signs of MH (e.g., continuously monitor the breathing and core body temperature), and quickly treat signs of MH (e.g., discontinue the triggering-medications; give the medication dantrolene – the only medication approved to treat MH; actively cool a person).

Any family with a history of unexplained death during anesthesia anesthetia complications should make this known

to the anesthesiologist before undergoing surgery. For individuals with MH susceptibility, non-triggering medications should be used during any procedure that requires anesthesia. All closely related members of a family in which MH has occurred must also be considered MH susceptible, unless proven otherwise. It should be noted that those who have had previous anesthetic medications without problem cannot be certain they are not at risk; MH-related deaths have occurred even though MH-susceptible individuals have undergone multiple prior uneventful surgeries.

Mode of inheritance

MH susceptibility is inherited in an autosomal dominant pattern. This means inheriting one mutation increases the chance to develop MH. The mutation can be inherited from a parent with MH susceptibility or it can occur brand new (de novo) in an affected child.

Risk to family members

The risk to family members depends on whether or not the individual with MH susceptibility has a parent with MH susceptibility. If a parent also has the condition, the risk of having a child with MH susceptibility is 50% with each pregnancy. If a parent does not have MH susceptibility, the risk of other siblings being affected is very low.

Special considerations

None

Resources

Malignant Hyperthermia Association of the United States (MHAUS)
http://www.mhaus.org
Genetics Home Reference: Malignant hyperthermia
http://ghr.nlm.nih.gov/condition/malignant-hyperthermia
North American Malignant Hyperthermia Registry
http://www.mhreg.org
European Malignant Hyperthermia Group (EMHG)
http://www.emhg.org

References

Glahn, KP. et al. (2010)."Recognizing and managing a malignant hyperthermia crisis: guidelines from the European Malignant Hyperthermia Group." British Journal of Anaesthesia 105(4): 417-420.
Hirshey Dirksen, SJ. et al. (2011)."Special article: Future directions in malignant hyperthermia research and patient care." Anesthesia and Analgesia 113(5): 1108-1119.
Rosenberg H, Sambuughin N, Riazi S, Dirksen R. (Updated 31 January 2013). Malignant Hyperthermia Susceptibility. In: GeneReviews at GeneTests Medical Genetics Information Resource (database online). Copyright, University of Washington, Seattle. 1997-2013. Available at http://www.ncbi.nlm.nih.gov/books/NBK1146/. Accessed [06/26/2013].
Rosenberg, H. et al. (2007)."Malignant hyperthermia." Orphanet Journal of Rare Diseases 2: 21.

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