Malignant Hyperthermia vs. Neuroleptic Malignant Syndrome vs. Serotonin Syndrome

Malignant hyperthermia, neuroleptic malignant syndrome, and serotonin syndrome are all conditions that may present in a similar way. For instance, autonomic instability and muscle rigidity are common in the presentation of these conditions. However similar these conditions may seem, they also have fundamentally different causes, clinical features, and approaches to treatment that distinguish them apart from each other.



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Autonomic Instability
Unstable Atomic-automobile
All three diseases feature autonomic instability, which can include signs like fever, tachycardia, hypertension, and diaphoresis.

Muscle Rigidity
Muscle-man of Stone
All three diseases also present with muscle rigidity, although the extent varies by disease. For example, the rigidity in neuroleptic malignant syndrome is often severe and “lead pipe”, while the rigidity in serotonin syndrome is less so.

Malignant Hyperthermia

Ryanodine Receptor 1 Mutation
Rihanna Receptor (1) Wand Mutant
Malignant hyperthermia patients have a genetic predisposition due to mutations in skeletal muscle ion channels. Ryanodine receptor 1, coded by the RYR1 gene, is a commonly affected calcium channel that controls calcium release from the sarcoplasmic reticulum. Mutations in this channel result in excessive calcium accumulation within muscle cells after exposure to anesthetics or succinylcholine.

Inhaled Anesthetics
A-Nest of Inhaled Anesthesia
A common trigger for malignant hyperthermia is inhaled anesthetics given during surgery, such as halothane and isoflurane. Therefore, suspect malignant hyperthermia if a post-surgical patient develops the acute onset of autonomic symptoms and muscle rigidity.

Succinylcholine
Sucker-in-cola
Succinylcholine is a depolarizing neuromuscular blocking agent often used during procedures to paralyze muscles and facilitate intubation. In myocytes with mutated calcium channels, however, succinylcholine will trigger excess calcium release and lead to malignant hyperthermia.

Dantrolene
Denture-lion
Dantrolene is the treatment for malignant hyperthermia. It directly inhibits the ryanodine receptor in myocytes, thereby preventing calcium release from the sarcoplasmic reticulum of muscle cells.

Neuroleptic Malignant Syndrome

Antidopaminergic Medications
Ant-Tie Doberman
Neuroleptic malignant syndrome occurs after prolonged exposure to antidopaminergic medications. This dopamine blockade can lead to both nervous system and musculoskeletal dysfunction. Antipsychotics like haloperidol, fluphenazine, clozapine, and risperidone are common causes. Antiemetics that are dopamine antagonists can also cause it, like metoclopramide or promethazine.

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Hyporeflexia

Hippo-reflex-hammer

Neuroleptic malignant syndrome (NMS) presents with extreme muscle rigidity and hyporeflexia. The decreased reflexes are key in differentiating between NMS and serotonin syndrome since serotonin presents with increased reflexes. Additionally, the muscle rigidity in NMS is often extreme and “lead pipe”, whereas rigidity is less severe in serotonin syndrome.

Myoglobinuria

Mayo-globe-urinal

Because NMS is associated with such extreme muscle rigidity, muscle breakdown often occurs, releasing creatine kinase and myoglobin into the bloodstream. Myoglobinuria occurs when the kidneys filter myoglobin into the urine and can lead to acute renal failure. Labs will show increased creatine kinase.

Dantrolene

Denture-lion

Similar to its use in malignant hyperthermia, dantrolene can treat NMS by directly acting on skeletal calcium channels and preventing release of calcium from the sarcoplasmic reticulum. Bromocriptine, a dopamine agonist, is another medication used to directly counteract the effects of antidopaminergics. Lastly, the causative medications should be discontinued.

Serotonin Syndrome

Serotonergic Medications

Silver-tonic

Serotonin syndrome is caused by excess serotonin levels from serotonergic medications that increase the levels of the neurotransmitter. There are many medications that can cause this, and combining them increases the risk. Implicated medications include psychiatric meds like SSRIs (eg., sertraline, escitalopram), MAOIs (eg., selegiline, phenelzine), SNRIs, or tricyclic antidepressants (TCAs). Other serotonergic medications include ondansetron, triptans, and linezolid.

Hyperreflexia

Hiker-reflex-hammer

Serotonin syndrome patients will exhibit fast, brisk reflexes, termed hyperreflexia. This is in contrast to neuroleptic malignant syndrome, which has hyporeflexia.

Clonus

Clown

Serotonin syndrome is characterized by neuromuscular hyperactivity, which differentiates it from neuroleptic malignant syndrome and malignant hyperthermia, which lack these features. Neuromuscular hyperactivity can include clonus (involuntary muscle twitches), as well as ataxia and tremors.

Cyproheptadine

Zippo-head

Cyproheptadine is a direct antiserotonergic agent with antihistamine and anticholinergic properties as well. It will provide antagonism at serotonin receptors, counteracting the effects of the serotonergic medications that caused the syndrome.

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