



# Guide to *CACNA1A*-related Severe Hemiplegic Migraine (CSHM)

*for families*

Dear *CACNA1A* Caregiver,

You may be reading these resources because your child has experienced, or may be at risk for experiencing, a severe hemiplegic migraine related to their *CACNA1A* variant. This type of event is a medical emergency and has the potential to cause permanent damage, or even death. You are better able to protect your child from damage from these types of events by knowing what initial signs to look for and having a written emergency plan from your provider. This information was compiled from published case studies and data from affected *CACNA1A* families, who wished to prepare other families for these types of emergencies. We hope this document empowers you to be prepared in case of a CSHM. The contents of this guide are not intended to substitute for professional medical advice, diagnosis or treatment. Please consult your physician for personalized medical advice.

The CACNA1A Foundation  
[www.cacna1a.org](http://www.cacna1a.org)  
[www.cacna1a.org/hemiplegic-migraine](http://www.cacna1a.org/hemiplegic-migraine)

## What is CSHM?

In some patients with a *CACNA1A* variant there is a condition that has been labeled as hemiplegic migraine but can be progressive and severe, resulting in uncontrolled seizures, and potentially life-threatening brain swelling. Similar to more traditional hemiplegic migraine, the dysfunction of the calcium channels leads to cortical spreading depression. This can lead to temporary changes in perception including other aura symptoms like visual changes, sensory changes, speech changes, and weakness. It also can trigger a headache. However, in addition to this dysfunction, some patients can also experience changes in the blood vessels of the brain causing narrowing and reducing blood flow to certain regions of the brain as well as swelling that can lead to the longer lasting weakness as well as change in level of awareness along with seizures.

## What is going on in the brain during a hemiplegic migraine?

Hemiplegic migraine is triggered by the start of an electrical phenomenon called cortical spreading depression. Cortical spreading depression is a wave that spreads across the surface of the brain that first activates and then briefly inactivates the nerve cells and then leads to an inflammatory response. When the brain is activated you can have “positive” symptoms like seeing extra things like sparkles/waves, or feeling a tingling. When it deactivates the brain, you can have “negative” symptoms like a blind spot or numbness. When the wave hits the part of the brain that controls movement it deactivates those nerve cells so it is hard to move.



## Who is at risk for CSHM?

It appears these events are linked with certain variants in the *CACNA1A* gene including: p.S218L, p.R1349Q, or p.V1396M. Please see our website for more variants. Those with gain-of-function variants are more susceptible. These types of attacks often start in early childhood, including as young as the first year of life.

## What are CSHM symptoms to look for?

**The most distinguishable feature is stroke-like symptoms with one-sided weakness and/or paralysis.**

<p>Some may also experience:</p> <ul style="list-style-type: none"><li>● Eye deviation</li><li>● Increased nystagmus (more than the patient's baseline nystagmus).</li><li>● Decreased responsiveness and/or altered consciousness</li><li>● Vomiting</li><li>● Development of a fever</li></ul>	<p>Triggers may include:</p> <ul style="list-style-type: none"><li>● Minor head trauma</li><li>● Seizures</li><li>● Emotional or physical stress,</li><li>● Viral infections</li><li>● Lack of sleep</li><li>● Menstrual period</li><li>● Can occur without identified trigger</li></ul>
<p>Patients who are susceptible to CSHM often have co-morbidities like seizures, dystonia, ataxia, nystagmus and other eye movement disorders. It can be difficult to recognize the differences for caregivers and doctors, especially the first time a CSHM occurs. To better recognize a potential CSHM, refer to <a href="http://www.cacna1a.org/hemiplegic-migraine">www.cacna1a.org/hemiplegic-migraine</a> for caregiver-provided videos.</p>	

Note on minor head trauma: Typically, within an hour of the injury a child might develop a headache, vomiting or a fever.

Note on SCHM with seizures: The weakness on one side of the body becomes evident after seizures are controlled. If a patient requires sedation to control seizures, a CSHM may not be detectable and should be treated if at all suspected. For those whose CSHM is triggered by seizures, it can be difficult to differentiate when seizure has stopped and CSHM begins due to some similarities in presentation (eye deviation).

Note on one-sided weakness: It may last for weeks or even months.

## CSHM emergency treatment

**It is imperative to seek emergency treatment at the first sign of symptoms.**

Rapid administration of treatment medications should be administered prior to obtaining imaging. Patients should receive a 3-5 day round of treatment to ensure the CSHM has resolved.

<p>First line treatments for CSHM:</p> <ul style="list-style-type: none"> <li>● Verapamil</li> <li>● Acetazolamide</li> <li>● Ketamine</li> </ul> <p>For cerebral edema:</p> <ul style="list-style-type: none"> <li>● Steroids (methylprednisolone)</li> <li>● Hypertonic saline</li> <li>● Mannitol</li> </ul> <p>Pain management and nausea:</p> <ul style="list-style-type: none"> <li>● Motrin</li> <li>● Ketorolac</li> <li>● Zofran</li> </ul>	<p>Medications to avoid:</p> <ul style="list-style-type: none"> <li>● Standard migraine medications, which can reduce blood flow like ergotamine and dihydroergotamine</li> <li>● Triptans</li> </ul> <p>*Newer migraine rescue medications (CGRP antagonists and ditans) do not have as much concern for changing blood flow and may be considered in the future for those with hemiplegic migraine, but they are too new to offer any information at this time.</p>
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### Imaging

A CSHM can lead to cerebral edema and stroke. Similar symptoms can be seen in other conditions like seizure, infection, and brain tumors. It is important to make sure these conditions are evaluated for. Head imaging should be obtained. MRI is the preferred test, but it is not always immediately available. In order to ensure timely identification of stroke, CT may be performed first. A MRI is recommended after having a CT, even if the CT is normal. In addition, a blood vessel study like a MR angiogram (preferred) or CT angiogram should be done. Lastly, an EEG may be ordered as well as bloodwork to check for infection. All of this testing does not need to be completed every time someone has a hemiplegic attack. If you have a known history of hemiplegic migraine, especially with a known genetic mutation, typically no testing need be repeated with every attack. In a child with a history of these types of attacks, it is recommended to go to the ER unless there is a very rapid resolution of all symptoms with a home treatment plan. It is recommended that observation be considered at least overnight in the hospital because even prior history of mild attacks cannot fully predict severity of current attack. These parameters should be advised by the treating physician.

### Prophylactic options

- Verapamil
- Flunarizine
- Acetazolamide (be aware of acidosis risk)
- Topamax
- Supplements to consider: Riboflavin, CoQ10
- If minor head trauma is a known trigger, a protective helmet may be worn