OMS

Opsoclonus-Myoclonus Syndrome

OMS life Foundation

REGISTRY POWERED BY NORD

Meet OMS Warrior ALEXA

Alexa

Alexa's battle began in the fall of 2009 at the age of 15 months. She toddled to bed one evening and did not walk again for months. During the early stages of illness, Alexa lost her ability to walk, sit up, talk, and even hold objects. Her parents took her to various doctors and specialists, but no one had a definitive answer for the rapid deterioration of Alexa's health. Despite continuous efforts, her family was unable to find any decent information on this unknown disease. After searching for answers for a month, the family reached out to a friend in Cincinnati who happened to be a doctor. He directed them to Texas Children's Hospital in Houston where, after a 500-mile drive to the facility, Alexa received her diagnosis of OMS.

Over the next 4 years, Alexa fought the battle of OMS. She endured countless scans, tests, and medical treatments. She also received speech, physical, and occupational therapies as she had to re-learn how to walk, talk, sit, grasp objects, and other developmental milestones. Alexa encountered numerous setbacks and relapses, prompting treatment dosages to be modified and adjusted. Finally, at the age of 5 years old, Alexa had her last IVIg treatment, and she remains in remission today.

While her OMS was active, Alexa led an atypical life—she rarely was able to go out in public due to her compromised immune system. Normal activities such as play dates with friends, preschool, and other activities were discouraged by her physicians. Outings with friends and relatives were in small groups and only when they were healthy, and her therapies and schooling took place at home.

Since remission, Alexa has excelled. She is an active young girl who enjoys typical pre-teen activities such as playing with friends, volleyball, learning to play guitar, dance class, Girl Scouts, and church. While the family was concerned about Alexa's future, she has shown so far that she can take on anything thrown her way. She excels in school with no classroom accommodations and she participates in many events such as the spelling bee and honor choir. Her future looks bright. She often discusses becoming a teacher someday.

It is because of Alexa's challenges at an early age that her family decided they needed to help others battling OMS. They founded the OMSLife Foundation in 2012 to provide information and be a resource; the foundation now serves more than a thousand patients throughout the world. Our mission statement is "to raise awareness of Opsoclonus-Myoclonus Syndrome, maintain a support network for patients and caregivers, and fund research."

Thank you to the OMS specialists who treat our OMS warriors, and a special thank you to NORD and Trio Health!

What is OMS?

OPSOCLONUS-MYOCLONUS SYNDROME

General Discussion

Opsoclonus-myoclonus syndrome (OMS) is an inflammatory neurological disorder, often occurring as a paraneoplastic syndrome with neurological symptoms being the first sign of an occult tumor. It is characterized by associated ocular, motor, behavioral, sleep, and language disturbances. The onset is oftentimes abrupt and can be relatively severe, with the potential to become chronic unless the appropriate diagnosis and treatment are reached in a timely manner.

Signs and Symptoms

The component features of OMS include the presence of rapid, seemingly random eye movements in the horizontal, vertical, and diagonal directions (opsoclonus); an unsteady gait or inability to walk or stand (ataxia); and brief, repetitive, shock-like muscle spasms or tremors within the arms, legs, or hands interfering with normal use (myoclonus). Behavioral and sleep disturbances, including extreme irritability, inconsolable crying, reduced or fragmented sleep (insomnia), and rage attacks are common. Difficulty articulating speech (dysarthria), sometimes with complete loss of speech and language, may occur. Additional symptoms, such as decreased muscle tone (hypotonia) and vomiting, have also been noted.

Causes

The most common cause of OMS in young children is an occult (ie, a small, often hidden) tumor. The symptoms of OMS, as a paraneoplastic syndrome, presumably stem from the immune system attacking the tumor, leading to secondary inflammatory effects on the central nervous system. Despite the primarily neurological status of this condition, tumors are generally not found in the brain, but rather in other areas of the body, such as the chest or abdomen. In 50% to 80% of affected young children, a tumor of the immature nerve cells (neuroblastoma or ganglioneuroblastoma) is responsible for the development of symptoms associated with OMS. There is, however, also a relatively high rate of spontaneous tumor regression in this population, meaning the tumor may be gone by the time OMS is diagnosed and investigations are done to look for it. In contrast, among older children or teens, the disorder is often attributed to various, predominantly viral infections. When OMS occurs in adults, it is often as a paraneoplastic syndrome related to other kinds of tumors; most cases are due to lung cancers or breast cancers with the tumors commonly malignant and often disseminated. This is in contrast to paraneoplastic OMS in infants and young children, whose tumors are biologically inactive and often benign.

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Meet OMS Warrior AUDREY

Audrey

Audrey's battle with OMS began in February 2010 when she was 7. She had just fought back-to-back bouts of strep throat when one morning her parents noticed her hand was shaking slightly. The next day she started waking up in the middle of the night in a screaming rage. She had a very hard time keeping her balance, even while sitting on a chair, and the rage fits became a daily event and her ability to focus was lost.

Audrey was brought to her pediatrician for evaluation. Her condition could not be clearly diagnosed, so it was labeled as "cerebral ataxia," a catch-all diagnosis. Her parents would not accept this, so they asked for a second opinion at Dartmouth-Hitchcock Medical Center in Lebanon, NH, which was where Audrey was diagnosed with "Sydenham's Chorea."

For nearly a year Audrey received IVIg treatments every few weeks, as well as daily steroid medication. Her condition did not improve and her parents were getting frustrated as their household was in complete disarray. They did not know how to handle the rage attacks and Audrey's loss of stability; to make matters worse, she also developed severe anxiety and OCD.

Audrey's parents continued to look for a solution until they found Dr. Mark Gorman at Boston Children's Hospital. He was one of the few specialists in the United States who treated OMS, and when they met with him, he knew immediately that Audrey suffered from OMS. Although her parents were relieved by finally having a correct diagnosis, their relief was bittersweet, as the treatment was rather severe.

Audrey began a course of chemotherapy that lasted nearly 18 months. She also received regular IVIg treatments, speech and physical therapy, and took numerous medications to help her function with her anxiety and OCD.

Now, 8 years later, Audrey is in a better place. She completed her chemotherapy but continues to receive IVIg treatments every 8 weeks. She is back to being in a mainstream classroom, as her anxiety and OCD are manageable. Audrey is now a sophomore in high school and is very active in social programs involving others with special needs, such as Best Buddies, NH Special Olympics, unified sports, and dance. She still struggles at times with the effects of her OMS, but she manages it quite nicely.

Audrey got involved with OMSLife shortly after being diagnosed. She started a local teddy bear drive through OMSLife and a local charity called Annie's Angels Memorial Fund. What started with 38 teddy bears is now more than 1500 teddy bears a year that Audrey gives to kids being treated at Boston Children's Hospital, and she has been recognized locally for her efforts in building the program to where it is today.

What is OMS?

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Affected Populations

OMS is a rare disorder: it affects 1 per million individuals worldwide, usually infants and young children, although it has also been known to affect adults. The peak age of onset in children is about 18 months of age, with very few cases diagnosed before 12 months. In rare instances, OMS can also occur in somewhat older children, up to approximately 6 years of age. Occurrence of opsoclonus in infants under 6 months old is quite uncommon, and opsoclonus in that age group, when isolated, is usually found to originate from another cause. OMS is thought to be slightly more common in girls than boys. While 50% of children with OMS are found to have a neuroblastoma or similar tumor, only 3% of children with such tumors present with OMS, though a small percentage more can go on to develop the condition later in their course of treatment.

Related Disorders

Several disorders present with symptoms related to those of OMS, and may serve as a useful comparison when crafting a differential diagnosis.

About 95% of children with OMS are initially diagnosed as having acute cerebellar ataxia, a much more common disorder characterized by sudden, uncoordinated movements originating from disease or injury to the cerebellum. In children with OMS, the ataxia may appear before the eye findings, leading to this particular misdiagnosis. Where present, the existence of opsoclonus is inconsistent with acute cerebellar ataxia, and OMS should be suspected as the true diagnosis. It should be noted that occurrences of opsoclonus or myoclonus may not be constant and can be subtle, making these findings harder to recognize and properly diagnose.

Myoclonus and tremor may also occur in other conditions without opsoclonus, both with or without ataxia. Myoclonus, in particular, may accompany a number of neurologic diseases, including seizure disorders, brain injuries, hereditary brain disorders, viral infections, metabolic disorders, and toxicological illness. (More information on these disorders can be found by searching for "general myoclonus" in the Rare Disease Database.)

SYNONYMS OF OPSOCLONUS-MYOCLONUS SYNDROME

- Dancing eyes-dancing feet syndrome
- Dancing eye syndrome (term usually used in UK)
- Kinsbourne syndrome
- Myoclonic encephalopathy, Kinsbourne type
- OMAS (opsoclonus-myoclonus ataxia syndrome)
- Opsoclonic encephalopathy

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Meet OMS Superhero BRAEDEN (SUPERBUB)

Braeden

Braeden's OMS first became obvious in March 2007. At just shy of 2 years old, he went to bed one night seemingly fine. The next morning he was unable to stand without falling and unable to walk without crashing into things. The changes were sudden and terrifying. Searching for answers led his parents to a pediatric neurologist who miraculously knew just what he was seeing. He felt Braeden's abdomen, found his tumor, explained what OMS and neuroblastomas are, and sent the family to Helen DeVos Children's Hospital. This began an almost 2-year journey of hope, joy, and despair. Braeden's family treated his cancer at their local children's hospital and traveled to an OMS specialist for confirmation and a treatment plan.

Braeden underwent so much treatment and so many tests in an effort to treat his diseases. He had essentially two teams—one to treat his OMS and another to treat the cancer that had caused the OMS. Everything his doctors did for one illness had to take into account the other. It was incredibly difficult for all involved, but Braeden was almost always spunky and smiling. Although his OMS quickly went into remission during chemotherapy treatment, his neuroblastoma proved more difficult to treat. Despite multiple treatments and surgeries, Braeden relapsed twice and began hospice care in February 2009. He died at home on April 18, 2009, just a few weeks before his 4th birthday.

Our journey didn't go at all the way we had hoped, but during those 23 months we got to know so many amazing people and see so much compassion and dedication on the part of so many medical professionals, we will be forever grateful.

What is OMS?

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Diagnosis

The diagnosis of OMS is clinical; there is no single diagnostic test that serves as a specific marker of the disease, as the exact immunological factors responsible for causing the syndrome remain unidentified. The combined presence of the "dancing eyes," the shock-like muscle spasms, and the gait impairment, especially if accompanied by irritability, are highly reliable indicators of this syndrome. To detect a tumor in children, either a CT scan or an MRI with contrast of the neck, chest, abdomen, and pelvis should be done. An MRI with contrast of the brain should be performed in all patients. MIBG or PET scanning should also be done in all patients with OMS as an important second investigation looking for occult tumors. In addition, a spinal tap to detect neuroinflammation is necessary. Besides routine tests for infection, recommended cerebrospinal fluid (CSF) studies include oligoclonal bands (with paired serum sample), to see if there are antibodies secreted by B-cells in the CSF. If available at the institution, CSF lymphocyte subset analysis (flow cytometry) using immunophenotyping may identify increased frequency of CSF CD 19+ B-cells, an important biomarker of OMS disease activity. Various nonspecific autoantibodies in some children with OMS have also been detected in research laboratories.

Standard Therapies

TREATMENT

Early and aggressive treatment for OMS is recommended, as some evidence suggests this better achieves the goal of a durable and more complete neurological remission. If a tumor is present, surgical resection is standard. The tumors in young children are usually low-stage neuroblastomas or ganglioneuroblastomas (stage I or II), and chemotherapy or radiation therapy is generally not indicated. Tumor resection does not typically provide sufficient clinical benefit for OMS.

OMS treatment, which is usually continued for at least 1 to 2 years, should involve combined immunotherapies. While evidence is limited, the expert consensus for treatment involves a 3-agent protocol, with initial use of intravenous immunoglobulin IVIg, rituximab, and either high-dose corticosteroids (IV methylprednisolone followed by pulse oral dexamethasone) or ACTH (corticotropin) appearing to have the best-documented outcomes for moderate and severe cases. Most children respond initially to treatment with high-dose steroids or ACTH, showing at least partial improvement. Those treated with steroids or ACTH alone, however, tend to promptly relapse when treatment is stopped. Over time, it is worth noting that treatment with corticosteroids or ACTH may have substantial cortisol-related adverse effects that should be monitored carefully, including weight gain, hypertension, and reduction in bone density. For OMS relapse, low-dose IV cyclophosphamide (3 to 6 cycles) or repeated courses of rituximab (1 to 2 cycles) may be given. Oral weekly methotrexate may be a useful steroid-sparing agent in chronic relapsing-remitting disease.

Along with the above noted pharmacological agents, all children should receive appropriate physical, occupational, and speech therapy services. Formal neurodevelopmental and neurocognitive assessments should be performed over time to help develop individual educational accommodations.

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Meet OMS Warrior CHLOE

Chloe

Chloe, born a healthy baby girl in 1992, developed normally and met the child development milestones until 18 months. After a fever and flu-like symptoms following her 18-month vaccination against MMR, her eyes started to dart back and forth. This was followed by a loss of coordination—Chloe had lost her ability to walk, talk, and sit up, and also manifested choking and sleep disorders. She had months of testing to determine what was wrong with her, as well as three "second opinions." Testing included an MRI, X-ray, eye tests, CT scan, spinal tap, electrodes glued to her head, needles placed in her muscles—more tests than most people have in their entire life. She was initially misdiagnosed with cerebellar ataxia. Once it was determined that Chloe had OMS, she started on an oral steroid protocol, taking a high dose of prednisone twice daily. Her symptoms would subside as long as she remained on steroids, while it kept her immune system "in check." When the prednisone was tapered too quickly, however, her symptoms would reappear. To keep the OMS at bay, she received monthly IVIg infusions along with the very slow reduction of prednisone dosages. While on the steroids, Chloe retained water and had high blood pressure, followed by a loss of appetite and weight loss. She reacted negatively to the IVIg infusions, experiencing headaches, vomiting, and the inability to stay awake. The extremely slow reduction of prednisone meant that Chloe stayed on steroids for 6 years.

To help Chloe regain her lost coordination, she had speech therapy from 3 years old until 6 years old, and physical and occupational therapies from 5 years old until 11 years old. She also took karate, ballet, and horse-back riding lessons. As a result of the OMS attacking Chloe's brain, she was left with learning disabilities. Though she participated in special education programs while in school, Chloe was mainstreamed into regular classrooms throughout her school career. Her Individual Education Plan (IEP) was essential to receive the accommodations to which she was entitled; these included audio books, extended testing times, additional learning methods (Lindamood-Bell), and modified assignments. Because of her parents advocating for Chloe and meeting with her teachers regularly, Chloe was able to excel during her academic career. She graduated with honors from college with an Associate Degree in Early Childhood Education and is currently a full-time teacher and living independently.

Chloe has not relapsed since her last dose of steroids at 7 1/2 years old. As an adult, she still tires easily, and becomes shaky when ill. She has some lasting side effects from long-term steroid use, but due to her determination and perseverance, Chloe is fully recovered from OMS. She has a great sense of humor, a positive outlook, and a strong personality. She continues to amaze and delight all who meet her and hear her story.

What is OMS?

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OUTCOME

Almost all children with neuroblastoma and OMS survive their tumor, which usually does not behave aggressively, though larger tumors may pose difficulties for resection. In contrast, the tumors associated with OMS in adults are often aggressive and can be fatal. The OMS relapse rate in children treated with only conventional agents is 50% to 75%. Increased immuno-suppression has, however, improved neurodevelopmental outcomes in OMS. With more aggressive initial therapies in children, the relapse rate appears to be much lower. OMS onset in the first 2 years of life is particularly damaging to expressive speech and language development, and may result in a higher incidence of residual cognitive impairment. The best outcomes appear to be those involving early combination therapy and mild-to-moderate OMS severity. Failure to achieve complete neurological remission and multiple relapses may result in chronic-progressive OMS, with permanent deficits, such as attention deficient disorder (ADD) attention-deficit/hyperactivity disorder (ADHD), obsessive-compulsive disorder (OCD), and irreversible cognitive impairment (low IQ). Children in the chronic state may become oppositional, depressed, or aggressive, and attention to these issues can help improve quality of life (QoL). Parents with a severely ill infant or child may develop "fragile child syndrome" and have difficulty ever seeing their child as a normal, thriving individual, with "ordinary" behavioral issues of childhood misinterpreted to represent a relapse of OMS. These parents may benefit from counseling to gradually adjust the management of their child's ongoing behavioral and developmental challenges.

Investigational Therapies

Information on current clinical trials is posted on the Internet at www.clinicaltrials.gov. All studies receiving US government funding, and some supported by private industry, are posted on this government web site.

For information about clinical trials being conducted at the NIH Clinical Center in Bethesda, MD, contact the NIH Patient Recruitment Office:

Toll free: (800) 411-1222
TTY: (866) 411-1010
Email: prpl@cc.nih.gov

Current clinical trials are also posted on the NORD website:

www.rarediseases.org

For information about clinical trials sponsored by private sources, contact:

www.centerwatch.com

For information about clinical trials conducted in Europe, contact:

www.clinicaltrialsregister.eu

Meet OMS Warrior COLE

Cole

Cole was diagnosed with a neuroblastoma and OMS in July 2011, when he was 15 months old. His symptoms started with a viral infection and fever, and he went from a happy, playful baby to an irritable toddler who could not sleep and could no longer crawl or sit up. His neurological symptoms continued to worsen over the next few days as he also started having hand tremors, body tremors, ataxia, and erratic eye movements. He feared any kind of motion and would cling to you while carrying him down the stairs or while riding in his car seat. It was devastating and heartbreaking to watch. He had even quit babbling in the mornings and rising to greet us in his crib.

Our world came crashing down as we were given his diagnosis. We were told that most children with OMS develop cognitive disabilities and behavioral issues. Our son and family would be facing a long and challenging road with long-term deficits and relapses. We were also told that OMS is a rare condition that did not have much funding or research and no well-studied treatment protocol to follow. With the support of the staff and doctors at Dell Children's in Austin, Texas, however, Cole was diagnosed and treated quickly. He was started on a series of immunomodulating therapies and immunosuppressants that would continue over the next 7 years. He is still currently receiving IVIg treatments due to side effects from his aggressive treatments at diagnosis.

This has been a long journey with many ups and downs and it has given him an old soul with a heart of gold. He is cautious and empathetic and puts others before himself. He doesn't look for the thrill of things. He prefers to keep his feet planted solidly on the ground. He doesn't ride roller coasters or go down tall water slides. He doesn't like to ride bikes or roller blades. Sometimes we question if it is because of what he has gone through or if it is just who he is.

After many years of speech, occupational, and physical therapies, together with periods of isolation due to being immunocompromised, Cole is leading an amazing life. He is in a public school in a regular class with no accommodations and is at level or even above level in some of his classes. He is loved by all who know him and has many friends. Cole is involved in many activities, such as Cub Scouts, golf, and basketball. He dreams of one day going to his father's alma mater, University of Kentucky, and playing basketball. We still hold our breath if we hear him cough or notice him tripping or that he is too quiet, but we have never lost hope. With every sad tear we have shed, we have also shed tears of happiness; happiness for watching our son do some of the simplest things in life that many others take for granted. Never lose faith. Never lose hope.

I tell you therefore: Everything you ask and pray for, believe that you have it already, and it will be yours.
Mark 11:22-25.

Who we are: OMSLIFE FOUNDATION

About

Founded in 2012, the OMSLife Foundation focuses on enhancing collaborative efforts between medical experts, researchers, caregivers, and patients. These individuals each have unique contributions to offer to the OMS community. Our objective is to be the glue that brings these individuals and teams together to build a stronger, better-aligned community of experts on OMS.

Our stated mission is to raise awareness of Opsoclonus-Myoclonus Syndrome, provide a support network for patients and caregivers, and fund research for a cure. In short, we want to see every patient experience as normal a quality of life as possible. With a median age of 18 months at onset, we recognize that these OMS warriors have so much to experience in life. Enabling these young patients in their battle to have a strong quality of life is the ultimate measure.

Our strategy is to take a holistic approach to addressing the needs of the OMS warriors' quality of life challenges. Like many nonprofit organizations, we offer funding for research. We also host two very important conferences: the OMS Caregivers Conference and the International OMS Medical Workshop. We have a very active social media presence, with over 1,000 patients from approximately 60 countries currently participating. We are also assisting Boston Children's Hospital as it builds its clinical registry and virtual biorepository, and we hope to continue funding similar endeavors.

Lastly, we have focused our attention on being a strategic partner with NORD. We are one of the original 20 organizations that received a grant to build a patient-reported registry. In addition to this book, we have also collaborated with NORD on an animated medical video about OMS.

The OMSLife Foundation wants to thank our medical advisory team who has helped us with this book and so many other initiatives; Drs. Wendy Mitchell, Tim Lotze, Mark Gorman, and Marc Tardieu. Finally, thank you to Dr. Michael Pranzatelli for his guidance to OMSLife over the years.

We thank the wonderful people at NORD and at Trio Health for the great opportunities they have provided to OMSLife. We appreciate the confidence you have in our organization.

For more information about the OMSLife Foundation, please go to our website at www.omslifefoundation.org or follow us on Facebook at www.facebook.com/OMSLifeinformation.

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Meet OMS Warrior LAUREN

Lauren

In January 2009, our normally developing 21-month-old daughter began having difficulty balancing and within a couple days had regressed to a 6- to 7-months-old level. She could no longer walk and was barely able to sit due to tremors and ataxic dysarthria that left her unable to function. After 3 days of tests, a differential diagnosis of acute post-infectious cerebellar ataxia/cerebellitis and a seizure disorder was given. She began medication for seizures and 3 days of IV steroids to help with the cerebellar ataxia; her symptoms included ataxia, tremors, eye movements, sleep disturbances, and rages/outbursts. She also had difficulty regulating her loudness at times (whether too loud or too soft), which indicated cerebellar involvement.

Lauren showed mild improvements and began physical and occupational therapies. After she relapsed in April 2009 and May 2009, we were told she had elevated HVA/VMA catecholamine levels, possibly indicating neuroblastoma. Six months after her symptoms initiated, Dr. Mark Gorman diagnosed her with OMS, with treatments including high-dose daily steroids and IVIg (rituximab and dexamethasone) every 3 weeks.

Lauren's journey took a drastic turn on November 3, 2011. An MRI found a tumor in her upper abdominal cavity. It was removed, but she was re-hospitalized with complications for 5 1/2 months, unable to eat or drink by mouth. She was on total parenteral nutrition (TPN) and lipids for nutrition and received physical therapy.

In March 2012 she underwent an 8-hour surgery to hopefully bypass the complications she was having and spent 2 1/2 weeks in the PICU on a ventilator due to further complications. Lauren finally returned home in April 2012. As of 2013, she had fully recovered from the complications and surgery.

Lauren continued her battle with OMS with the help of IVIg and CellCept®. This allowed her to wean off steroids in November 2014 and to gradually wean IVIg to 4 and then 5 weeks after receiving it every 3 weeks for 6 years. Currently we are trying to wean the IVIg to every 6 weeks and wean her off the CellCept. Lauren is on her second port and her veins have not recovered from the excessive use when she was first diagnosed.

Despite her OMS, Lauren is a well-adjusted child who enjoys swimming, horseback riding, art, and basketball. She is in a regular education classroom but was held back one year. She is on grade level for academics and social and emotional development, and mostly struggles with fatigue and side effects after every IVIg treatment.

Lauren appears to be doing well but inside, her body is continuing to wage a war against itself, and long-term effects of treatments remain to be seen. Her prognosis is unknown, as every child's battle is a little different.

Her family started the Lauren Mantz OMS Research Fund in 2010 at Boston Children's Hospital with the hope that the research will benefit every child with OMS.

Who we are: OMSLIFE FOUNDATION *cont'd*

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How you can help

Since OMS attacks the cerebellum of the pediatric patient during his or her formative years, prompt diagnosis of the disease and proper treatment is imperative to ensure the best outcome. While a new treating physician who has never seen a patient presenting these symptoms may easily misdiagnose the disease, the greater issue is when that physician chooses to take a "wait and see" approach in treatment of the disease.

Once accurately diagnosed, in almost all cases the treatment protocol outlined previously will present the best outcomes. Leading specialists in treating OMS across the United States agree this therapy produces the best results known at this time. Use of only one or two of these options, or administering all of them at sub-therapeutic doses, will typically deliver sub-optimal results.

The treatment protocol should be accompanied by nonpharmaceutical modalities, including

- **Speech therapy**
- **Occupational therapy**
- **Physical therapy**
- **Behavioral therapy**

Long-term cognitive and physical issues are likely with delayed treatments and therapies. It is therefore highly recommended that physicians who are inexperienced in treating OMS coordinate the protocol with known specialists. Severity of the disease and time for proper treatment are directly correlated with long-term QoL for the patient.

Our call-to-action is straightforward:

CLINICIANS – Align your efforts with a specialist in OMS to ensure best results. Be aggressive with treatments and therapies, and if in doubt, direct the patient to the specialist.

RESEARCHERS – Align efforts with the International OMS Steering Committee, and collaborate with the committee to coordinate bio samples.

CAREGIVERS AND PATIENTS – Get educated about OMS in order to understand the disease and its treatment protocols. Consider a second opinion if the prescribed protocol is outside of typical trends by those specializing in OMS. Pay your knowledge forward by participating in the NORD/OMSLife Patient Registry as well as in other patient clinical registries and bio-banks.

Meet OMS Warrior MICHELLE

Michelle

Michelle's journey with OMS began in 2010 when she was a 24-year-old graduate school student. Starting suddenly, it began as vertigo but progressed over the following weeks to dancing eyes, full body shaking, nausea/vomiting, and extremely painful and contorting muscle spasms. Despite months of ER visits and specialist visits, she did not receive a diagnosis. Michelle continued school but was clearly emotionally labile and socially withdrawn. She lived with her symptoms while she and her husband searched for an answer.

Throughout the following years she saw a handful of neurologists and had an array of tests, including MRIs, yet everything appeared normal. Specialists remained stumped and they would blame it on stress or say she was exaggerating symptoms. A spinal tap later identified anti-glutamic acid decarboxylase (GAD) autoantibodies in her CSF, thus indicating an autoimmune component to her mysterious symptoms.

Michelle connected with an adult diagnosed with OMS who recommended she see the same provider. When she traveled from her home in Oregon to New York, the neurologist diagnosed her with OMS and started her on 5 days of IVIg treatment. Although she had great improvements with the IVIg, her symptoms slowly returned in the following months.

During this time she continued to connect with other adults and parents of OMS warriors. Through this support network it became obvious how challenging it is for other adults with OMS to receive ongoing treatment due to provider and insurance resistance. Over the following 7 years Michelle experienced ups and downs fighting insurance denials for IVIg and Rituximab. Moving their home required establishing new physician relationships, and the process of educating them and ruling out other conditions began yet again.

While Michelle continues to receive IVIg therapy along with Rituximab infusions, her symptoms are well managed. She is passionate about mentoring teens and young adults with OMS, as well as sharing her experience with parents of children too young to verbalize what they may be feeling.

Thankfully, Michelle now lives a rewarding life as a mom with her family and dogs. She completed a doctorate degree and has maintained part-time work in the physiology research field. She also enjoys rock climbing and skiing with her family.

OMS in the Real World

LESSONS FROM THE OMS NATURAL HISTORY STUDY

To better understand the natural history and experience of patients with OMS, the OMSLife Foundation, together with NORD, created a registry for the ongoing collection of patient- and caregiver-provided information. Launched in February 2017, the purpose of the registry was to understand the population of those affected with OMS and the hurdles faced in diagnosis, effective treatment, and obtaining quality of life.

Two years later, the OMSLife Foundation is working with roughly 1,000 patients in 57 countries. As of January 2019, 305 patients or caregivers had registered and 198 had contributed data to the registry. Patients in the registry* were predominantly born in the United States (86%, 145/169), female (53%, 90/170), white (74%, 146/196), with commercial insurance coverage (62%, 98/159), and a family income >$50,000 (72%, 99/137). The registry showed that 77% (127/164) of patient households had one or more parents who graduated from a post-secondary institution (college or post high school vocational training) with 32% (52/164) having post-graduate (beyond bachelor) education. Median age at patient diagnosis was 20 months, consistent with prior findings that OMS is a disease that typically affects individuals at the beginning of life.

Though opsoclonus and myoclonus are common symptoms, the most prevalent symptom at onset is ataxia (See Synonyms for Opsoclonus-Myoclonus Syndrome.). This is a key point in OMS diagnosis since many pediatric patients are misdiagnosed with acute cerebellar ataxia. Not surprisingly, there are clusters of symptoms that may be related: sleep disturbances and temper tantrums, sleep disturbances and tremors, and opsoclonus and myoclonus. Due to the number and variety of symptoms and the rarity of the disease, OMS is not easily diagnosed.

In the OMSLife registry, 31% of the patients went undiagnosed for at least 3 months, with 8% of patients undiagnosed for more than one year. However, the time from onset to diagnosis has been improving over the years. When diagnosis was made, 95% of the time it was by a specialist: neurologists (83%), oncologists (11%), or ophthalmologists (1%), indicating lack of knowledge and awareness by general practitioners.

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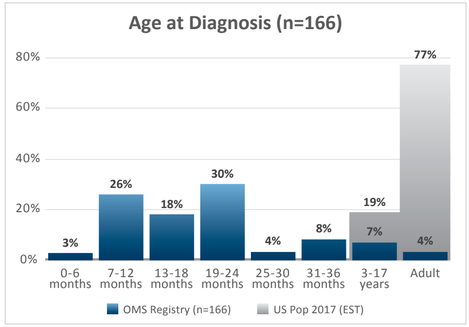
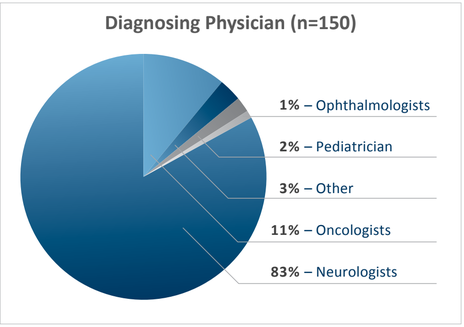


Distribution of age of OMS diagnosis (from OMS registry) compared with general US population (from US Census 2017 estimate). The distribution of age of diagnosis shows that 89% of patients in the OMS registry were diagnosed at under 3 years of age. By comparison, only 4% of the US population is below 3 years of age.



The OMS registry shows that 95% of patients with OMS were diagnosed by a specialist, either neurologists (83%), oncologists (11%), or ophthalmologists (1%).

*Please note: the denominators in the graphs may vary depending on how many responses were received for each question.

Meet OMS Warrior ZARA

Zara

Zara's fight with OMS began in May 2014 when she underwent a sudden change in her behavior, both physically and mentally. She lost her ability to sit up and maintain her balance like she had done up to around 8 months old; ataxia and opsoclonus had begun their course. With those symptoms her pediatrician thought it could be a disorder called spasmus nutans, and Zara then had a neurological appointment at Phoenix Children's Hospital (PCH) in search for a definite answer.

While waiting for her appointment at PCH, Zara contracted the flu, which made her symptoms extremely noticeable. We took her to the ER at PCH, and after numerous tests she was found to have a neuroblastoma in her pelvis area, and she was diagnosed with OMS.

Due to the rareness of OMS and lack of experience treating it, Zara's initial therapy was not as aggressive and effective as it should have been. We thought she was making progress, but in reality she was not. After 18 months of treatments her improvement reached a plateau. It was at the OMS Caregivers Conference in March 2016 in Los Angeles, California, that we first met the physician who would become her OMS specialist. Up to this this point, Zara continued to struggle to maintain her balance and she was constantly bruised due to her falls. After a visit to Florida with her OMS specialist in July 2016, and after following his aggressive treatment measures, Zara improved drastically. Five weeks after that July visit she began fully walking and turned 3 years old in August 2016.

Thanks to her team of specialists and our local doctors here at PCH, Zara is now 5 years old and has been symptom free and without a relapse since 2016; her last IVIg treatment was in January 2018. She is currently enjoying kindergarten and her teachers gave her the EFFORT award in November 2018. She has a joy for fashion, arts and crafts, and loves playing with her twin sister Zofia, who has been her best therapy throughout! We recommend an aggressive treatment approach against OMS, but we also know that it is Zara's will to overcome the challenges that come with OMS that make her our #1FIGHTER!

OMS in the REAL WORLD

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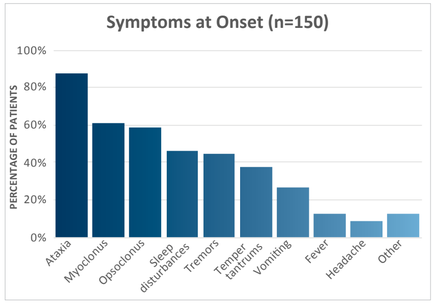
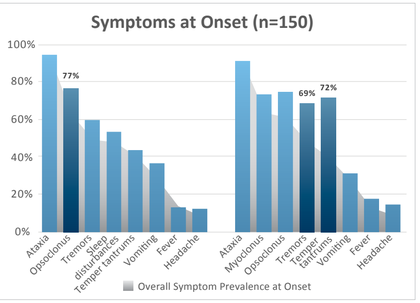


Ataxia is the most common symptom among patients with OMS, with 85% (n=150). Myoclonus ranks second at 61% and opsoclonus is third at 59% of OMS cases reported in the registry.

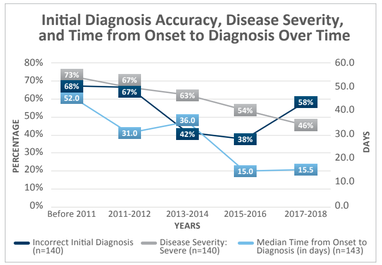
There are clusters of related symptoms that occur at higher frequencies when other symptoms are present compared with their overall prevalence.

Tremors and temper tantrums are more prevalent with issues in sleep. And opsoclonus is more frequent when myoclonus is exhibited.

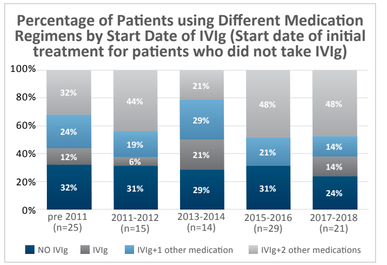


Early and accurate diagnosis is important for these young patients because of potential detrimental effects of disease on neurodevelopment. Medications for treatment of OMS include IVIg, corticosteroids/ACTH, chemotherapies, and immunotherapies, and clinical data suggest that combination therapy of corticosteroids/ACTH, IVIg, and rituximab may be useful in preventing neurodevelopmental damage. In addition to medications, non-pharmaceutical therapies are typically prescribed to address speech, physical, occupational, and behavioral challenges. In many cases, treatment of OMS with the medications and therapies will typically take from 1 to 5 years to get the patient to baseline and in remission. During treatment or in the absence of disease control, medications to treat symptoms are commonly employed (eg, sleep aids, proton pump inhibitors, mental health medications).

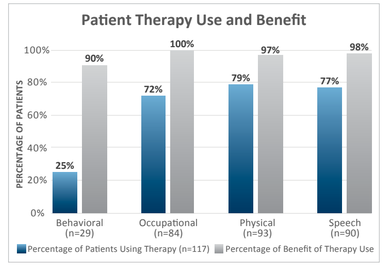
The outlook for patients with OMS is promising provided the continued trend of early diagnosis and early treatment. The main challenge to effective intervention is awareness, and the difficulty may be decreased through continued efforts of NORD, OMSLife, and publication of patient data from the OMS Natural History registry.



Trends show a decrease in incorrect initial diagnoses, disease severity, (Mitchell Pike OMS Scale) and time from onset of symptoms to diagnosis. Factors that might be contributing to these positive changes include greater awareness of the disease by medical personnel, greater collaboration mechanisms for caregivers and patients via social media and websites, and continued advocacy efforts by NORD, OMSLife, and other organizations.



Trends reported in the OMS registry show that more patients with OMS are utilizing the treatment protocol of IVIg plus two other therapies (Rituximab and either ACTH or a corticosteroid).



Ancillary forms of therapy utilized by patients with OMS: behavioral, occupational, physical, and speech therapies, respectively. These supplemental therapies are found to be beneficial by more than 90% of the patients who reported using them.