Diagnosis and Management of Opsoclonus-myoclonus Ataxia Syndrome

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Abstract-In most rural medical centers general practitioners with little or no specific postgraduate medical training in emergency medicine frequently staff emergency departments. General practitioners working in emergency departments often face unique challenges when caring for patients presenting with sign and symptoms of obscure or rare medical conditions. In this case report, I discuss specific strategies for early recognition and management of one such rare neurological condition-- Opsoclonus-myoclonus Ataxia Syndrome.

Keywords: Opsoclonus-myoclonus Ataxia Syndrome; Emergency Medicine; Pharmacology; Rare Neurological Disorders; organophosphate Ingestion; Family Medicine

Introduction

Opsoclonus-myoclonus Ataxia Syndrome (OMS) is a rare neurological condition affecting mostly children. [1] There is no specific mechanism proposed that explains the precise etiology of this disorder. However, most investigators now believe the etiology of OMS is immunological in nature. [1]. Regardless of its etiology or its rarity, OMS responds to early diagnosis and therapeutic intervention. [2] However, neurological relapse post and cognitive deficits are common post-treatment sequelae. The age of onset, although variable, is predictable and usually afflicts toddlers but it can also occur throughout childhood. But toddlers are particularly at a high risk of developing OMS [3].

The most prevalent type of OMS is found in children who also present with neural crest cell derived ganglioneuroblastoma. There is a high association between presentation of OMS and ganglioneuroblastoma in as many as 7-46% of afflicted reported cases. Although a high degree of association is established between OMS and ganglioneuroblastoma, a minority of patients presents with signs and symptoms of OMS without the accompanying neuroblastoma. It is therefore critical for the clinician to screen toddlers suspected of having OMS even in the absence of neuroblastoma.

In one study comparing the survival rate of children with combination of OMS and neuroblastoma against the survival rate of children presenting with OMS alone, Rudnick et.al found that children presenting with OMS and accompanying neuroblastoma had an excellent chances of survival but were at a greater risk of developing severe and often permanent post-treatment neurological sequelae. [4] Although a search for an antibody screen test has been underway for some time, neither unique auto-antibodies nor a cellular mechanism for pediatric paraneoplastic disease have been discovered. [5]

The only advances made to date in identifying a screening test for OMS associated paraneoplastic disease has been the discovery of B cell proliferation in the cerebrospinal fluid (CSF) of patients presenting with OMS. But CSF B cell expansion by itself is too nonspecific to be of any diagnostic value. In fact, many infectious agents affecting the central nervous system also result in increased B Cell proliferation in the CSF but those infectious agents may not be the causative culprits for OMS. [1]

In cases where patient presents with symptoms of OMS but with absence of neuroblastoma, the patient invariably reports a preceding infection or recent poisoning with OMS symptoms appearing as post-infection sequelae. [6]. The progression of OMS and its high rate of relapse have been poorly understood. The current hypothesis appear to suggest both progression of the disease and its high rate of relapse might be correlated to the increase in CD19+ B-cell and a corresponding increase in and γδ T-cell. The populations of CD4+ T-cells and the ratio of CD4/CD8 are somewhat lower in these patients. These effectors of the immune system appear to remain active even years after the onset of the disease and following treatment with conventional therapeutic agents. Based on these findings,
Pranzatelli and colleagues suggested that CSF B- and T-cell inactivation is suggestive of neurological manifestations in pediatric OMS. These immunological mediators may be responsible for the relapses and disease progression observed in children presenting with OMS. [7, 8]

Clinical Case Report

A 10 year-old female was admitted to the pediatric neurology department of a local children’s hospital. Her pediatrician referred the patient after she presented to the ER with symptoms of OMS, which were dramatic and clearly visible by the examining physician. The rapid eye movements occurred in "spells or bursts". The patient’s mother reported to the ER physician that the rapid eye movement started first and a few days later, the child developed a “jerked” like movement in her hands, feet, trunk, and face. The jerk like movements seemed to get worse by certain events like noise, light, and pinprick. Crying appeared to bring out the myoclonus and child’s myoclonus appeared to intensify during the physical examination. The child was reported to have little or no ability to walk and had lost her ability to speak. She exhibited behavioral tantrums and cried frequently. Feeding the child had become increasingly difficult and she sometimes vomited shortly after feeding. She was able to use her hand and touch her nose. Deep tendon reflexes were normal. Muscle tone and strength were also normal. A sensory test done at the ER was also unremarkable. The child came from a rural region where predominate occupation is farming. The child had a habit of going to the farm and picking fruits from the tree and eating the fruits without first washing them. The ER physician made a diagnosis of cerebellar ataxia and myoclonic seizure and prescribed anti-seizure medication. He told the parents to take the child to her regular pediatrician. After examining the child the following day, the pediatrician referred the child to a childrens’ hospital for evaluation because the pediatrician was concerned about the possibility of a central nervous system infection. Upon arrival at an urban full service pediatric hospital, a pediatric neurologist conducted a battery of tests and conducted a through physical and neurologic examination. She made a diagnosis of OMS due to organophosphate ingestion.

Discussion

Organophosphates (OP) are a varied chemical compound that are abundantly available and in which the precursor is alcohol. Due to its toxicity to animal and humans, organophosphates are widely used as a pesticide in variety of agricultural settings. Although highly toxic, its use in agriculture has not been outlawed in most countries. Organophosphates are extremely toxic to bees, wildlife, and humans. Published data suggest that even at small concentrations, these compounds are highly toxic to children. Organophosphates (OPs) may affect children differently. The increased susceptibility of children to these compounds has not been conclusively established. But it may involve delayed or persistent effects that may be less severe in adult populations. More work in this area is underway that may help identify the true risk potentials to Ops to children. [10]

The mechanism of action of OP pesticides is due to its ability to inactivate carboxyl ester hydrolases the most of which is acetylcholinesterase (AChE). AChE is an enzyme that breaks down the neurotransmitter acetylcholine (ACh) into choline and acetic acid. ACh is found in the human central and peripheral nervous system, neuromuscular junctions, as well as the red blood cells.

Ops inactivate AChE by phosphorylating the serine hydroxyl group located on the active site of AChE. The phosphorylation occurs by the loss of OP leaving group and creation of a covalent bond with AChE. [9] It is not entirely clear how these molecular events culminate to the development of OMS.

The general central nervous system (CNS) effects of exposure to OP are anxiety, emotional lability, restlessness, confusion, ataxia, tremors, seizures, and coma. [10] In cases of suspected OMS, it is important to know that the patient’s cerebrospinal fluid is normal in majority of cases but can present with a mild lymphocytic pleocytosis. Brain imaging is also normal in most cases. Some children may present with absence seizure but urge to diagnose a seizure disorder must be resisted. [11] Since most laboratory and imaging studies in these children appear normal, without a high index of suspicion for OMS on part of the emergency room staff, the likelihood of missing the correct diagnosis in vast majority of these cases remain fairly high. [10]

The ER physician must first deal with the symptoms of OP poisoning. This is important because those initial symptoms can be life threatening if left untreated. In the above case presentation, the child was treated for OP poisoning at one hospital and evaluated for the neurological sequelae at another facility. Both facilities were rural hospitals where the emergency room was staffed by family physicians without specialized training in emergency medicine.

It is unlikely the full scope of OMS will emerge immediately after exposure to OP. The initial presenting symptoms will be those closely associated with exposure to OP compounds. The full scope of neurological symptoms such as OMS will emerge over time. These subsequent symptoms often prompt another emergency room visit. The parents often mistakenly believe emergency room visit is warranted based on the erroneous belief that the symptoms of OMS is associated with a new episode of poisoning. In these situations, the most important diagnostic clue will emerge from a careful history, which must include specific diagnostic questions around prior poisoning as well as recent previous infection. OMS is not an emergency and need not be treated in the emergency setting. For patients who present to emergency room with symptoms of OMS,
the most important role for the emergency room physician is to rule out specific conditions in which emergency care is warranted. Children affected with OMS must be referred to a pediatric neurologist at specialized centers where long-term treatment is usually initiated.

**Conclusion**

The diagnosis of OMS requires a high degree of suspicion and a systematic approach to diagnostic testing, especially for neuroblastoma, recent poisoning or infections. Future research studies are required to determine whether early, aggressive therapy will improve the typically poor long-term neurological outcome. Should future studies present data substantiating early diagnosis and treatment for OMS, then the role of emergency physicians become even more important because they will be required to make timely referrals based on proper, evidenced based diagnosis. But for the time being, the generalists who practice emergency medicine would serve OMS patients best if they recognize the condition, take active steps to make the appropriate referral, and provide basic education to the patient’s parents and about the condition and the need for immediate assessment by a pediatric neurologist.

**References:**


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**Author Information**

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