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Autism Spectrum Disorder in the Emergency Department: Looking Beyond Behavior

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Autism spectrum disorder (ASD) is a complex neurodevelopmental condition that is behaviorally defined by its well-recognized impairments in verbal and non-verbal communication and social interactions in addition to distinctive restrictive and repetitive behaviors (APA, 1994). Over the past decades the incidence of this disorder has dramatically increased. Although the reason or reasons for this increase is still up for debate, the fact remains that ASD is now estimated to affect 1 in 68 children in the United States (Developmental Disabilities Monitoring Network Surveillance Year Principal, Centers for Disease, & Prevention, 2014). ASD is defined by behavioral manifestations, yet children with ASD have a high prevalence of many medical conditions including recurrent infections (Doshi-Velez, Ge, & Kohane, 2014), gastrointestinal (GI) disturbances (Chaidez, Hansen, & Hertz-Picciotto, 2013), seizures and epilepsy (Frye et al., 2013), anxiety (Sukhodolsky, Bloch, Panza, & Reichow, 2013), allergies (Angelidou et al., 2011) and metabolic disorders (Frye & James, 2014; Frye & Rossignol, 2012) including mitochondrial disease (Frye & Rossignol, 2011; Rossignol & Frye, 2012). With the increase in prevalence and the significant co-morbidity of medical problems, it is likely that medical professionals in the emergency and urgent care facilities will have increasing exposure to individuals with ASD for urgent medical management, particularly acute behavioral dysregulation. When this occurs it will be important to consider their special needs and understand the unique manner in which common medical problem may present in individuals with ASD. Indeed, children without typical communication skills, aberrant behaviors may be the manner in which the child is communicating the need for medical attention (Buie et al., 2010).

ASD is associated with a wide spectrum of behavioral manifestations. Some of the most disruptive behaviors, referred to as aberrant behaviors, can cause significant disability and distress to the patient and caregiver (Baghdadli, Pry, Michelon, & Rattaz, 2014). Aberrant behavior is divided into subcategories by the Aberrant Behavior Checklist (Slosson Educational Publications Inc, East Aurora, NY). These categories include Irritability, Social Withdrawal, Stereotypy, Hyperactivity and Inappropriate Speech. Irritability, which includes severe tantrums, aggression, and self-injury, is one of the major and most disruptive aberrant behaviors (Stigler, 2014). Irritability is commonly treated with antipsychotic medication with or without behavior therapy (Aman et al., 2009). Treating with a medication to suppression symptoms rather than understanding if there is an underlying medical cause for such behaviors can be problematic for several reasons. First, treating symptoms instead of identifying a cause can lead to increased morbidity and mortality from an undiagnosed disorder. Second, antipsychotic medications can detrimentally affect glucose, cholesterol and lipids and weight, even in the short-term (Correll et al., 2009; Wink et al., 2014) and long-term anti-psychotic use increases the risk for type II diabetes (Bobo et al., 2013) and can result in tardive dyskinesia, a potentially permanent movement disorder (Correll & Kane, 2007). Thus, it may be best to look beyond the obvious of controlling behavior and understanding what the behavior means in order to solve potentially important medical conditions to improve the long-term health of a child with ASD. Several examples are given below of the medical condition that can present as behavioral dysregulation in children with ASD.

GI disturbances have been reported to occur in 9% to 70% of children with ASD, with high quality studies suggesting that GI symptoms are very prevalent. GI symptoms commonly manifest as behavioral manifestations in children with ASD (Buie et al., 2010). For example, abdominal pain, gastroesophageal reflux disease and/or constipation can manifest as vocal symptoms such as frequent repetitive throat clearing or swallowing and/or screaming, crying, whining or sobbing for no reason; motor behaviors such as facial grimacing, teeth grinding, chewing on clothes or other objects, applying pressure to the abdomen or aggressive or self-injurious behavior; and/or general behaviors such sleep disturbance or irritability (Buie et al., 2010). Thus, it is important to obtain a GI history, including symptoms of gastroesophageal reflux, stool frequency and consistency, and perform a careful GI examination to look for abdominal distention and/or impaction.

Many of the GI symptoms may drive aberrant behavior through causing pain. When a child cannot communicate verbally, aberrant and unusual behaviors may be the only manner in which the child can communicate that pain exists. Thus, the clinician needs to have a high index of suspicion for obvious and non-obvious sources of pain. For example, head banging is sometimes associated with headache. Other sources of pain not uncommon in childhood such as pharyngitis, sinusitis, otitis media and dental caries, just to name a few, must also be considered. A trial of analgesics might be appropriate if pain is believed to be driving the behavior. Interestingly celecoxib has been shown to be an effective adjunctive treatment to risperidone for irritability in a double-blind placebo-controlled trial (Asadabadi et al., 2013).

Sleep disruption is estimated to affect from 44% to 83% of individuals with ASD, with delayed sleep onset and nighttime wakening being the most predominant symptoms (Krakowiak et al., 2008). Several studies have demonstrated that disruption in sleep patterns is associated with problem behaviors during the day, particularly in low-functioning ASD individuals (Cohen et al., 2014), and lower overall functioning in several measures of development including greater problems with language and communication (Taylor, Schreck, & Mulick, 2012). Melatonin is a safe and effective treatment sleep duration and sleep onset latency but is less effective for night time wakening (Rossignol & Frye, 2011) and has been shown to improve daytime behavior and parenting stress (Malow et al., 2012). In addition, a case series reported that the selective melatonin receptor agonist ramelteon can also be effective for improving sleep and daytime behavior (Kawabe, Horiuchi, Oka, & Ueno, 2014). Thus, a careful focused sleep history may provide important information which can lead to appropriate evaluation and treatment.

Anxiety is very common in ASD (Vasa & Mazurek, 2015), particularly in high-functioning ASD children (Chandler et al., 2015). Anxiety is related to aggressive behavior (Pugliese, White, White, &

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Ollendick, 2013), more severe repetitive behaviors and lower overall development (Magiati et al., 2015) and sleep disruption (Mazurek & Petroski, 2015). A wide variety of treatments for anxiety have been studied in individuals with ASD. The best studied treatments for anxiety in ASD include intranasal oxytocin (Hofmann, Fang, & Brager, 2015) and cognitive-behavioral therapy (Ung, Selles, Small, & Storch, 2015). Although selective serotonin reuptake inhibitors were previously considered useful in the ASD population, such medications may increase the risk of behavioral activation (Vasa & Mazurek, 2015) and may be best suited for treating repetitive behavior (Hollander et al., 2012). Thus, it is important to screen for symptoms of anxiety as such a significant psychiatric comorbidity could be driving disruptive behavior.

There appears to be a wide range of behavioral manifestations that are related to immune dysregulation, although the treatments for these disorders are not well studied. Pediatric Autoimmune Neuropsychiatric Disorders Associated With Streptococcal Infections (PANDAS), a disorder which can result in sudden onset obsessive compulsive behavior, tics and Tourette like behavior (Martino, Defazio, & Giovannoni, 2009), is associated with ASD (Libbey & Fujinami, 2010). Recently PANDAS has been brought in under the umbrella of Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS) and recommendation for diagnostic workup have been outlined in a consensus conference (Chang et al., 2015). The recent recognition of the association of PANDAS/PANS with specific antibodies titers to basal ganglia has provided a medical test to help with diagnosis of these patients (Cox et al., 2015). Other immune abnormalities, which are less well-studied, have been reported. These include the associated between depressed plasma immunoglobulin concentrations with aberrant behavior (Heuer et al., 2008) and the recognition of a subset of children with ASD with behavioral dysregulation following episodes of immune activation (Jyonouchi, Geng, Streck, & Toruner, 2012). Although treatments for immune abnormalities are not well studied, identifying immune abnormalities can result in appropriate referral and treatment.

A disorder related to depressed folate concentration in the brain appears to be rather common is ASD and may be related to behavioral dysregulation. The folate receptor alpha autoantibody is prevalent in ASD with up to 75% of ASD patients being positive for the blocking or binding autoantibody (Frye et al., 2013). Autoantibody titers are directly correlated with increased aggressive behavior (Ramaekers et al., 2007). Titers are increased by the ingestion of milk and behavior can be improved with the treatment of a milk free diet (Ramaekers, Sequeira, Blau, & Quadros, 2008). Since this autoantibody blocks the ability of folate from crossing the blood-brain barrier, an alternative form of folate, high-dose folinic acid, can improve behavior in ASD patient with folate receptor alpha autoantibodies (Frye et al., 2013; Moretti et al., 2005).

These medical conditions which are associated with behavioral dysregulation are under recognized across many medical settings, but it is of the upmost importance for medical professional in the emergency and urgent care departments to recognize these potential medical conditions since many children with ASD will arrive in the emergency department when behavior suddenly escalates. Unfortunately, the evaluation of children with ASD and behavioral dysregulation has not been standardized and many of the medical abnormalities associated with behavioral dysregulation have not been well studied, especially in regards to treatment. Recognition of these conditions can lead to appropriate management and referrals. With the rising number of children with ASD it is important for front line medical professional to be comfortable with evaluating children with ASD and to consider the medical complexities associated with ASD.

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