Growing Up with Autism: Incorporating Behavioral Management and Medication to Manage Self-Injurious Behavior

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Case

Khaled is a ninteteen-year-old young man with autism spectrum disorder who first presented for evaluation and psychiatric management at age twelve. His history of ASD is complicated by multi-domain developmental delays, ADHD, epilepsy, aggression, and self-injurious behavior. His treatment had included many medication trials that were minimally efficacious. At the time of presentation, Khaled was attending a full-time, specialized school for autistic children where he received a variety of services including speech therapy, occupational therapy, and behavioral therapy as well as developmentally appropriate academic services and art classes. He was being treated with escitalopram 15 mg daily, naltrexone 25 mg twice a day and olanzapine 5 mg daily. However, he continued to experience symptom breakthrough that put his and others' safety at risk.

Khaled was born at 28 weeks gestation by uncomplicated spontaneous vaginal delivery without prenatal trauma or exposures. His birth weight was 1.5 kg, and he was hospitalized for 27 days due to initial breathing and feeding difficulties. His early development was within normal limits, and his parents described him as playful, smiling, and very socially responsive. He started to walk and speak in single words at about thirteen months.

When Khaled was eighteen months old, however, his parents observed behaviors that concerned them. In particular, they remark that he had stopped responding when called by name and had become less responsive during play. His parents and primary care physician suspected a hearing problem due to decreased

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responsiveness, but an audiology evaluation showed results within normal limits. He was evaluated at 26 months by a speech pathologist who concurred that there were significant language delays. Speech and language therapy was initiated.

A full psychological evaluation, including formal autism assessment and Vineland adaptive skills scale, was done which indicated autism spectrum disorder. The psychologist also noted the presence of hyperactivity, which met the criteria for comorbid attention-deficit/hyperactivity disorder, combined type. His neurological evaluation was grossly normal at that time, and all ancillary tests, including brain MRI, EEG, urine amino acids, and chromosomal analysis, were normal. Additional tests at age four including karyotype, fragile X testing, and infectious, metabolic, and autoimmune panels all were normal as was a repeat brain MRI.

When Khaled was 4, his parents noted that he had shown some developmental progress: He was using single words to express his needs, such as "water" when he wanted a drink. He would use idiosyncratic words to represent specific terms, such as "dodo" for sleep, "naughty" when he was upset with his sister, or "wawa" when he was about to hit himself. Additionally, he was developing socially and behaviorally; the family commented that he was more responsive to play, would cuddle, and frequently sought his mother's affection and expressed affection for her. These gestures would include hugging and placing his head over her shoulder. He enjoyed going out with the family to the shopping mall. He also started routinely visiting a nearby public park every evening. Despite these improvements, Khaled continued to demonstrate dysregulated and hyperactive symptoms that were treated initially with methylphenidate 10 mg to allow him to attend to his speech and behavioral therapy sessions. His neurologist also treated him with haloperidol 1 mg daily, which was later increased to 3 mg. His therapist observed that he was better engaged, more responsive, and making stronger gains in learning activities. Methylphenidate was increased over time to 10 mg twice daily to address worsening behavioral and attentional problems.

When Khaled was 4.5, his parents had become concerned that his medication might be negatively affecting his behavior and eventually worked with his neurologist to discontinue them gradually. Irritability and hyperactivity subsequently increased. IVIG infusion treatment was done over the course of a 3-day hospitalization without apparent benefit. A course of risperidone 0.5 mg daily was started to address worsening behavioral difficulties. Trials of clonidine 37.5 μg were added, and fluoxetine was started and soon titrated up to 7 mg per day. Brief improvement was noted. However, fluoxetine was soon discontinued due to apparent inefficacy.

At age five, Khaled started to exhibit new behaviors. He would become angry when his demands were not met and would become dysregulated when told "no." He would throw temper tantrums with episodes of screaming and throwing himself on the floor. He began to become uncharacteristically oppositional and stubborn. Despite this, he did show improvements in hyperactivity and was able to sit alone at a table and attend to the task of completing a jigsaw puzzle for over 45 min with little adult involvement. He loved to sit alone and play with toys. These periods of calm, on the other hand, were punctuated by episodes of self-stimulating behaviors including spinning around and repeatedly clenching his fist.

Khaled's self-injurious behavior began at age ten. These include punching himself in the head and face repeatedly and banging his head against the wall to the point of causing severe contusions. These self-injurious episodes would occur

several times throughout the day and would be preceded by arm flapping and verbal and physical agitation which would gradually escalate into more violent self-directed aggression. At first, these behaviors were mild and were presented only during periods of transition or interruption of rituals or schedules. They occurred before meals, shower time, or before his daily walks with the family to the nearby mall or public park. They would especially occur if there was any delay by his family members, his nanny, or behavioral therapist in starting the activity on time. He also would engage in self-injurious behavior in response to feeling cold, yet he refused at times to wear warm clothes.

With time, episodes of self-injury evolved to take place when family members or caregivers would refuse to give in to his demands such as leaving the house for a walk at unscheduled times. There was a degree of situational selectivity to the behavior at times. For instance, he would be observed to be punching himself harder and more repeatedly if his mother was watching. The behaviors would abate when his demands were met.

Initially, the self-injurious behavior could be managed through minor behavioral intervention; however, over time, they became worse and uncontrollable to the point where he would have to wear a helmet and gloves to prevent serious injury. A sponge ball was also used at times to distract him from those behaviors and could sometimes occupy him for short periods. By this time, he would no longer respond to verbal prompts or redirection. Several dietary interventions were attempted by his family including introducing casein-free and gluten-free diets which were discontinued due to a lack of efficacy.

Over time, the behaviors became more frequent and difficult to control and, as Khaled grew in age and size, he became physically harder to manage. Family members and caregivers frequently gave in to his demands to prevent him from hurting himself. Additionally, at age 12, Khaled was admitted to the hospital emergency room after having an unprovoked generalized tonic-clonic seizure with loss of consciousness and loss of bladder and bowel control. He had an extensive workup in the emergency room including non-contrast head CT, chest X-ray, EKG, CBC, electrolyte panel, liver functions, CRP, PT/INR, and random serum glucose. All results were within normal limits apart from slightly low serum sodium, chloride, and phosphorus that were resolved with repletion. He was diagnosed with a seizure disorder and was discharged with a referral to pediatric neurology. The neurologist who saw him for outpatient follow-up started topiramate which was gradually increased to 50 mg twice a day. Over the course of the following three months, he had two other episodes of generalized tonic-clonic seizures. Behavioral dysregulation was noted to markedly worsen around the times of his seizures.

Neuropsychiatric Reevaluation

Khaled and his family presented for reevaluation and further pharmacotherapeutic management at a point of crisis at age twelve. His medication at that time included escitalopram 15 mg daily, naltrexone 25 mg twice a day, topiramate 50 mg BID, and olanzapine 5 mg daily. His parents reported that they had continued the

current medication regimen because they feared that his behavior would regress even further.

In the context of his intake evaluation, the role of behavioral reinforcement as an escalating factor worsening Khaled's behaviors became particularly salient. Focusing on behavioral intervention was determined to be a priority at this stage in addition to the medication regimen, which had previously been the focus of treatment. The behavioral goals were to decrease self-injurious behaviors while minimizing necessity for restraint and protective gear while simultaneously increasing positive behaviors and tolerance of schedule changes and transitions. Effective use of verbal prompts and directions was emphasized. Full Applied Behavioral analysis (ABA) services were not initiated, but a system was put into place that utilized behavioral principles. For instance, both antecedent and extinction-based strategies were put into place at home and at school.

As part of a careful behavioral plan, Khaled's caregivers were directed to keep themselves from rushing into physically stopping him from hurting himself and to utilize judicious "active ignoring." With time and careful behavioral technique instruction with his caregivers, Khaled was able to tolerate a relative decrease in restraint and an increase in verbal redirection. Soft hand restraints were applied for short periods during repeated and prolonged episodes of self-injurious behavior.

Multiple medication trials were utilized concurrently, including risperidone, which was ineffective. Clonidine was titrated to 75 μg three times a day, and naltrexone was increased to 75 mg daily. Khaled's parents soon stopped clonidine due to excessive sedation. Chlorpromazine was added up to 50 mg twice a day when necessary for periods of more severe increased agitation. With behavioral interventions, administration of chlorpromazine could be reduced from daily to almost once a month. Khaled would still experience periods of increased agitation primarily because of summer vacation and a change in his daily routine. During these periods he would have increased occurrences of wetting himself at night with interrupted sleep. Additional behavioral interventions were successfully introduced at these times to address any novel behavioral issues.

The next few years were better but still included periods of marked behavioral fluctuations. Lorazepam 1 mg twice a day was introduced as needed in addition to other behavioral interventions including soft hand restraint. Chlorpromazine was gradually also titrated to 500 mg at nighttime but was changed to quetiapine XR due to inefficacy, and naltrexone was increased to 50 mg twice a day to target self-injury. Memantine 10 mg daily was introduced to target some of the core symptoms of autism, but was discontinued a month later because of escalating behavioral problems. Interrupted sleep was addressed over time as necessary with lorazepam but could eventually be discontinued. Ultimately, he stabilized on the following regimen: quetiapine XR 200 mg in the morning and 400 mg at night, naltrexone 50 mg twice a day, topiramate 50 mg twice a day, omega-3, and multivitamins.

Now nineteen years old, Khaled's receptive language has improved, and he is able to follow verbal commands. He continues to receive substantial ongoing therapeutic services. He has limited level of expressive language, and his parents estimated that, currently, he is consistently able to use about 30 words. When calm, he is able to utilize

three-word sentences but has limited verbal communication during periods of regression. He has acquired basic reading and writing skills including the ability to tell time on a clock, read the day and date on a calendar, and write using single letters and filling in the blanks. He is mostly independent with regard to self-care with some occasional help for activities such as showering. His schedule continues to be rigid. He generally goes to sleep at 9 pm and is able to sleep uninterrupted through the night without interruption.

He is calm and frequently participates in group activities at school, although he often chooses to sit or play alone outside the classroom. He continues to be bothered by loud noises made by others, even though he enjoys listening to music and dancing. He struggles with seasonal temperature changes and is bothered by heat in the summer time, preferring to stay indoors. He wears a baseball cap nearly all the time and becomes irritated when unable to do so. He goes out of the house for walks or to the mall at specific times in the day when the weather is not hot.

Khaled's self-injurious behavior has essentially subsided permitting medications to be weaned as tolerated. At his most recent visit, in addition to ongoing discussion of academic and educational optimization, independence in self-care, and some instrumental activities of daily living, the focus has shifted toward helping Khaled transition to adulthood which includes increased independence and development of vocational skills. His parents are working toward placement in a long-term adult residential program specializing in treatment and rehabilitation of adults with autism in another country where such resources are more readily available.

Case Reflections

Khaled's case reflects early signs of developmental disability and the evolution of symptoms to include dangerous self-injury. As is often the case in treating individuals with neurodevelopmental disabilities with behavioral challenges, many treatments were attempted, often out of a sense of desperation, with varying degrees of evidence base and efficacy. Self-injury, and tolerance of therapeutic interventions, gradually and painstakingly improved with close monitoring and the combination of behavioral psychotherapeutic techniques and pharmacotherapy. Understandably, Khaled's family and caregivers felt overwhelmed with Khaled's behaviors and, at times, unknowingly reinforced those behaviors. Many alternative therapies were tried with little report of success from the family.

Khaled's seizure disorder, with his first generalized tonic-clonic seizure at age twelve, further complicated his management. Notably, his history included a strong correlation between seizure episodes and behavioral escalation which improved once seizures were adequately controlled. However, these episodes, often resulted in prolonged behavioral setbacks that required additional behavioral and psychotropic medication modification. It is important to consider the impact of uncontrolled seizures on neurocognitive development as well as the impact of antiepileptic medication on cognition. Self-injurious behaviors in individuals with limited communication and intellectual disability can often occur in the setting of medical illness, such as untreated pain, constipation, and dental or periodontal disease. This is particularly

the case when there are changes in baseline behaviors, such as new-onset or increased frequency or intensity of self-injury.

Khaled was started on psychotropic medications at a very young age to control hyperactivity behavioral dysregulation. His treatments, as they occurred outside of the United States, did not necessarily follow quite the same pattern of prescribing (e.g., initial neuroleptic trial with haloperidol, early use of chlorpromazine), though it was generally focused on the same categories of pharmacotherapeutic treatment as are often trialed in the United States. The choice of pharmacotherapy was also heavily impacted by medication availability and cost. His medication regimen evolved over time, striking eventual success with a combination of neuroleptic management, naltrexone, antiepileptic medication, and strong behavioral management protocols.

Neuroanatomy

Neuroanatomy studies suggest that individuals with autism and self-injurious behavior (SIB) may have somatosensory cortex and thalamus abnormalities along with structural and functional alterations in related white matter pathways [1]. Abnormalities in the cortico-striato-thalamo-cortical loops appear to be involved as well, with particular implication of altered striatal morphology in SIB in both idiopathic autism spectrum disorder (ASD) and fragile X [2]. Functional neurosurgical interventions have targeted this loop, specifically at the the globus pallidus internus, in Lesch-Nyhan syndrome, a developmental disorder with very high rates of SIB and intellectual disability (ID) [3, 4]. One study utilizing functional neurosurgery in ASD for intractable SIB targeted the basolateral nucleus of the amygdaloid complex. Authors argue that this was successful due to its inhibitory GABA-ergic connections to a broad range of brain regions [5].

Most major neurotransmitter systems have been implicated in SIB in ASD and ID. Alterations in serotonin and dopamine have been implicated in studies in both ASD and other neurodevelopmental conditions associated with SIB, particularly Lesch-Nyhan syndrome (dopamine), cri du chat syndrome (dopamine), Prader-Willi syndrome (serotonin), and Cornelia de Lange syndrome (serotonin). GABA and glutamate, inhibitory and excitatory neurotransmitters respectively, have also been implicated [6].

Importantly, alterations in the endogenous opioid system have been suspected in SIB in ASD and other developmental conditions. There are two primary models. In the "endorphin model," pain stimulates endogenous opioid release resulting in postsynaptic downregulation of receptors which results in a sort of "addiction" to self-injurious behaviors [6–8]. An alternative model theorizes that individuals with SIB have increased levels of endogenous opioids which result in subsequent pain insensitivity, possibly mediated by stress or anxiety. It appears that there are alterations in the opioid pathway, including proopiomelanocortin, which shows abnormal regulation in 30–70% of individuals with SIB, and downstream beta-endorphin and adrenocorticotropic hormone, all of which are involved in the hypothalamic-pituitary-adrenal axis and stress response [6, 9].

Lessons Learned About Neuropsychiatry

The data available on self-injury in ASD is limited; studies in SIB and ASD are often limited by study design, sample size, and methodology. Self-injurious behavior (SIB) and aggression are two serious concerns in autism that result in care-level escalation and hospitalization. Estimated rates of SIB in ASD range from 15% to 50% with one report as high as 74% in a cohort of hospitalized individuals [10, 11]. Aggression can be seen in as many as two-thirds of individuals with ASD and is reported as a primary reason for medical and pediatric behavioral service referrals [12, 13]. These are phenomenologically different than in self-injurious or aggressive behaviors in typically developing individuals. For the most part, self-injury occurs on a continuum of repetitive or self-stimulatory behaviors, and aggression tends to be reactive and occurs in a setting of overwhelming sensory experience and emotional dysregulation.

Behavioral management for SIB in intellectually disabled individuals with ASD can take several forms. Commonly, behavioral management techniques follow Skinner's operant conditioning model, where behavior constitutes the physical behavior itself, the environmental events preceding it, and the subsequent outcomes [14]. The aim of treatment is to utilize the theory of operant conditioning, wherein the immediate consequences around a behavior will strengthen or weaken that behavior over time [15]. According to this, SIB, regardless of its precise neurochemical mechanism, can be thought of as a learned behavior that can be reinforced or extinguished based on environmental reinforcement [6].

Several steps involved in the process of behavioral management are outside of the scope of this chapter. However, a few points are necessary to mention, namely, use of intervention strategies targeting antecedents, reinforcements, and extinction. Preemptive management of antecedent factors can involve environmental enrichment, provision of alternative sensory experiences that are less dangerous or inappropriate, use of visual schedules and other techniques to facilitate ease of transitions, and careful management of demands to minimize the escape-avoidance function of SIB. Much can be said about reinforcing behaviors; however, in the case of Khaled, the reinforcing role of parental attention as well as the way SIB provided a form of control over his environment and possible escape from unwanted activities are of particular importance. Noncontingent reinforcement, such as parental attention given frequently and not in response to SIB, can decrease the need to engage in SIB. Expressions of distress, such as verbalizing frustration, can help substitute the dangerous behavior for one that is safer. This can be coupled with the use of extinction, where "planned" or "active" ignoring is done in the face of the unwanted behavior so as to decrease the social reward that may be associated with that behavior [6].

In many circumstances, behavioral management is sufficient; however, at times, particularly with more dangerous and dysregulated behaviors, medication may be necessary as well. No medication is specifically approved for treatment of self-injurious behavior in autism, and there are no treatments for the diagnostic core symptoms of autism. At present, only two psychotropic medications have regulatory indications for the treatment of irritability associated with ASD, risperidone

and aripiprazole. Significant efficacy and overall tolerability have been demonstrated after the administration of risperidone and aripiprazole for serious behavioral problems in ASD [16–19]. Risk of tardive dyskinesia, as well as metabolic, hormonal, cardiovascular and other side effects and risks, must be taken into consideration with this class of medication. First-generation antipsychotics have a long history in the treatment of hospitalized individuals with ASD or ID and SIB [20]. A small number of trials exist that show equivocal and inconsistent findings with haloperidol, chlorpromazine, and thioridazine [6]. They continue to often be used, though generally less frequently due to the burden of extrapyramidal and tardive dyskinesia risks [21]. Better benefit has been reported in second-generation neuroleptics including small trials of clozapine and olanzapine [22–25]. One of two studies on risperidone showed separation from placebo for SIB in ASD [26, 27]. Aripiprazole has been explored for agitation and a range of behavioral disturbances in autism, but not SIB specifically [6]. Ziprasidone has also been explored with some benefit in a few, small trials for severe disruptive behavior in ASD [28].

Alpha-2 agonists have shown some efficacy in irritability, attentional symptoms, sleep, impulsivity, hyperactivity, and overall severity of symptomatology in ASD [29]. Beta blockers, such as propranolol, have also been explored for treating disruptive behaviors including hypersexuality, self-injury, and aggression. While the results may appear promising, data is limited [30].

Selective serotonin reuptake inhibitors (SSRIs) are often used in the setting of self-injury and underlying psychiatric conditions, though data in children with ASD are mixed [6]. SSRIs are often used to treat comorbid symptoms that can cluster with autism such as anxiety, depression, obsessive-compulsive disorder, and other conditions. They have also been explored for the treatment of repetitive behaviors, which can sometimes overlap with compulsions, stereotypy, and self-injury in autism. Where trials in adults with autism are generally positive, pediatric trials are somewhat less consistent, and there have been negative results in two large placebo-controlled trials [31]. Antidepressant medications broadly seem to have marginal effects on irritability in children and adolescents with ASD. The data available for the is limited, but a small number of case studies in ID, a double-blind, controlled trial in compulsive skin picking, and a trial in self-injury in Prader-Willi syndrome all showed benefits [6, 32–35]. Paroxetine and fluvoxamine have also showed benefit in small trials [36, 37]. One open trial and one small double-blinded placebo-controlled trial with clomipramine, a tricyclic antidepressant, demonstrated benefit for SIB, but the latter was limited by a significant side effect burden [38, 39].

Buspirone has been explored to a much smaller degree. A single, small, open-label trial found benefit for anxiety and irritability in ASD, and a small placebo-controlled trial showed benefit for restrictive and repetitive behaviors as an adjunctive therapy [40, 41]. Uncontrolled studies and individual case reports have suggested some benefit in SIB in ASD, and buspirone tends to be relatively well-tolerated [6].

Mood stabilizers and antiepileptic agents have demonstrated variable results in aggression, irritability, and self-injury in ASD. Valproate shows mixed results in the management of these symptoms, particularly in children [31, 42]. In a single small

randomized, controlled study with lamotrigine for individuals with ASD and severe behavioral disruption, the treatment group did not separate from placebo in any measures [43]. Studies on oxcarbazepine, carbamazepine, gabapentin, and topiramate in these populations have limited data, though positive case series and reports are present in the literature [31]. There is limited literature on the use of lithium, but benefits have been reported in symptoms associated with Phelan-McDermid disorder as well as in a thirty-person retrospective review of youth with ASD and comorbid manic-like symptoms [44, 45]. Small studies in the 1970s exploring lithium for SIB in ID found efficacy in the setting, However, they were methodologically limited [6].

There is intriguing, but limited, data on a number of medications that interact with other neurotransmitter systems. Naltrexone is increasingly being tried in individuals with self-injurious behaviors in the setting of autism and other neurodevelopmental disabilities, possibly due to its impact on the endogenous opioid system. However, studies show mixed efficacy [46, 47]. Similarly, there is small-cohort, limited research into memantine, an anti-glutamatergic NMDA receptor antagonist, to treat various symptoms associated with autism which demonstrates some possible potential benefit [48]. N-acetylcysteine (NAC), a glutamatergic modulator, has been explored for the treatment of irritability and other symptoms associated with autism and has shown some benefit in a small, randomized, placebo-controlled trial, though other studies show equivocal effects [49–51].The baclofen enantiomer, R-baclofen, a selective GABA-B agonist, has been evaluated in a small, open-label study [52]. Electroconvulsive therapy has been successfully used for individuals with severe, treatment-refractory SIB in ASD and other developmental conditions, particularly if there are overlapping catatonic features [53–55].

Clinical Pearls

1. Psychotherapeutic behavioral management is a crucial component in treating self-injurious behavior and aggression in autism spectrum disorder and intellectual disability.
2. No psychotropic medications are formally approved for treating the core symptoms of ASD; however, aripiprazole and risperidone carry indications for associated agitation and dysregulation. Many other medications are considered for off-label use when behaviors are dangerous or severe. However, such medication must be used judiciously in light of limited data and side effect profiles in individuals with ASD.
3. Behavioral challenges in ASD and ID can wax and wane based on medical events, life circumstances, or causal triggers that may not be externally obvious. Close attention and hand-in-hand collaboration between family members, other caregivers, teachers, and the treatment team, as well as the patients themselves, are crucial to providing ongoing and carefully tailored management of symptoms.

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