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Autism Spectrum Disorder (An Update)

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ABSTRACT

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder that typically manifests in early childhood as impaired social communication and restricted, repetitive behaviors which falls as a spectrum from mild to severe. In the past 5 decades, ASD has gone from a narrowly defined, rare disorder of childhood onset to a well-researched, life-long condition which is relatively common and heterogeneous .The prevalence of ASD has been increasing in the United States over the last two decades, which is most likely related to change in diagnostic criteria, increased public awareness , and improved screening. The prognosis of ASD today is much brighter than it was in the past and more people with the condition are able to speak, read and live independently in the community. Early diagnosis is very important as early intensive behavioral interventions have shown to improve functional outcomes and quality of life. Comprehensive, multidisciplinary evaluation is needed for the diagnosis of ASD which should include the use of standardized measures as the Autism Diagnostic Interview-Revised and the Autism Diagnostic Observation Schedule-second edition. High rate of medical and psychiatric comorbidity have seen in individuals with ASD including epilepsy, depression, anxiety, and sleep difficulties. Early and intensive behavior interventions have shown to be beneficial in improving social communication, language and play. Pharmacological treatment is indicated for psychiatric comorbidity such as attention-deficit hyperactivity disorder, emotional dysregulation, irritability and aggression.

Introduction

"Autism" derived from the Greek word "autos, or "self", refers to someone who lives in a world of his own. Leo Kanner [1], first introduced the term autism as a diagnostic label to define a specific syndrome in young children characterized by early onset of impaired social and emotional relationship. Since then, autism is now recognized as Autism Spectrum Disorder (ASD) which is a neurodevelopmental disorder defined by social communication impairments and restricted, repetitive behaviors [2,3]. Early diagnosis is important because early diagnosis and early intensive behavioral intervention programs have been shown to improve functional outcomes and quality of life [4,5]. Unfortunately, early diagnosis of ASD can be challenging and despite much earlier concerns by caregivers for possible ASD, it is often diagnosed after the age of three [6,7]. The challenges in early diagnosis might be related to complexity and heterogeneity of ASD, leading to different presentations of individuals with ASD. ASD is also associated with significant psychiatric and medical comorbidity including language disorder, intellectual disability, sleep problems, anxiety, depression, obsessive compulsive disorder, attention deficit hyperactivity disorder and epilepsy [8-10]. The exact etiology of ASD is unknown but it is thought to have strong and complex genetic underpinnings with environmental factors modulating the phenotypic expression [11,12].

Epidemiology

Among eight years old in the U.S., the prevalence is 2.3% in 2018 compared to 1.8% in 2008 with male to female ratio of 4:1 [13]. Black children with ASD tend to present at older ages than white children and often present with intellectual disability [14]. Several factors have likely contributed to the increased prevalence rate which includes change in the diagnostic criteria, increased awareness and increased access to services [15-19]. Children who often receive a late diagnosis include: females, ethnic minorities, low socioeconomic status, those from families who do not English, and those without language delay [20]. There is a concern that females are under-diagnosed and diag-

nosed at later age because of the belief that ASD occurs primarily in males [21]. There is also a possibility that the current diagnostic procedures are less sensitive to the presence of ASD among females or that females are more able to minimize ASD symptoms including social communication impairment (via camouflaging) [22,23]. Camouflaging can, for example, include suppression of repetitive movement, forcibly sustained eye contact or the use of learnt formulaic phrases [24].

Clinical Presentation

The key diagnostic features of ASD include deficit in social communication and restricted, repetitive pattern of behavior, interest, or activities. The presenting symptoms of ASD depend on age, language level, and cognitive functions. Some signs and symptoms of ASD may present between 6 and 12 months of age but reliable diagnosis, in many cases, can be made around 24 months of age [25,26]. Spoken language delay and social deficit are the most prominent features in children with ASD who are younger than three years old. Language delay without compensatory pointing or gesturing might help to differentiate ASD from expressive language delay [27,28]. The inability to coordinate one's own attention between another person and distant object to share attention (joint attention) by 15 months of age should indicate the need for ASD evaluation [27,28]. Repetitive behavior and restricted range of interest may be less apparent in younger children. Many children with ASD have several coexisting conditions that impact the presentation and the level of impairment. The prevalence of ASD is higher in individuals with special health needs including people with visual impairment, hearing impairment, intellectual disability, and Fragile-X Syndrome [29-31]. Furthermore, psychiatric and medical comorbidity are very common in ASD population, particularly attention deficit hyperactivity disorder, anxiety, depression, aggression, self-injury, sleep difficulties, feeding problem and epilepsy [32-36]. Additionally, almost 30% of people with ASD present with special skills that exceed what seems humanly possible (savant skills) most commonly manifesting in mental arithmetic, art, and memory skills [37,38].

Screening

Many public health systems have attempted to identify very young children with ASD in the general population. However, screening tools have not been sensitive enough to effectively identify most of children with ASD in the general population in whom parents have not been already recognized a delay [39]. When parent have expressed concern, screening instruments become effective for predicting ASD in children as young as 18 months of age [40]. The American Academy of Pediatrics recommends that all children be screened for ASD at 18 and 24 months of age [41]. The modified-checklist for autism in toddlers, revised (M-CHAT-R), a 20 item screening questionnaire, is one of the frequently used ASD screening tools in primary care settings. It is designed to identify children 16 to 30 months who are at risk for ASD [42]. Children who have a positive screening test for ASD should undergo a comprehensive evaluation and referral for developmental services. Children who receive consistent pediatric care, are in frequent contact with grandmothers, and who have older siblings receive earlier diagnoses than those who do not [43,44].

Diagnosis

For definitive diagnosis of ASD, a comprehensive assessment by a multidisciplinary team using standardized diagnostic tools to exclude other conditions, identifying any comorbid conditions and to assess the child's overall level of function [45-47]. The most widely used diagnostic tools for ASD are the Autism Diagnostic Observation Schedule, second edition (ADOS-2) and the Autism Diagnostic Interview, Revised (ADI-R) [48]. The American Academy of Pediatrics and The American College of Medical Genetics and Genomics recommend genetic testing for individuals diagnosed with ASD [49]. In particular, chromosomal microarray is recommended to scan the genome for copy number variants. Adults seeking first diagnosis of ASD are typically have comorbid psychiatric disorders but are not intellectually disabled [50]. While brief self-reports do not have adequate specificity, versions of ADOS, and Social Responsiveness Scale (SRS) are appropriate for verbally fluent adults [51,52].

Risk Factors

74-93% of ASD risk is heritable [53]. Models for genetic risk in ASD propose that complex inheritance with additive contributions from common variants that individually make small contributions to risk as well as rare variants that have larger effect sizes [54]. Several environmental risk factors have also been identified including advanced maternal or paternal age, prenatal valproic acid exposure, preterm birth, low birth weight, small for gestational age status, and large for gestational age status [55-58].

Behavioral Treatment

Early behavioral intervention for at least 25 hours per week is recommended for young children with ASD [59]. Applied Behavioral Analysis is the cornerstone for early intensive behavioral interventions, which utilize applied behavior analytic principles of learning to teach children the appropriate skills in natural settings, have been shown to improve children's language, play, and social communications [60,61]. Cognitive behavioral therapy can be very effective in reducing anxiety and depressive symptoms in individuals with ASD [62]. In school-age children without intellectual disabilities, social skills training can be useful in improving social skills and emotional dysfunctions [63]. Providing behavioral, speech, occupational and physical therapy in the school setting together with parent training resulted in improved language skills and decreased disruptive behavior in children with ASD [64].

Pharmacological Treatment

No medication is available to target core symptoms of ASD, but medications can be useful to target specific maladaptive behaviors which did not respond to intensive behavioral therapy. In addition medications can be useful to target comorbid psychiatric conditions [27]. Risperidone and aripiprazole have shown to improve symptoms of irritability and agitation in children and adolescents with ASD and are the only medications approved by the U.S. Food and Drug Administration for the treatment of ASD-Associated Irritability [65,66]. Psychostimulants (methylphenidate) and non-stimulants (atomoxetine and guanfacine) have shown to be effective in the management of ADHD symptoms in individuals with ASD [67]. Melatonin may also be useful for sleep disturbances [68]. The current evidence does not support the use of any supplement for the treatment of core ASD symptoms but N-acetylcysteine and sulforaphane have demonstrated some efficacy for behavioral and emotional symptoms associated with ASD [69].

Prognosis

Current studies show that there has been a significant improvement in outcomes of individuals with ASD in the current studies compared to the old data [70]. However, adults with ASD continue to be less likely to live independently or be employed and more likely to use mental health services compared to individuals without ASD diagnosis [71]. Better outcomes are reported in individuals with ASD with higher cognitive abilities, had earlier referrals, more intensive early behavioral interventions and fewer pharmacological interventions [72,73]. Mortality rates are approximately 2-fold higher for individuals with ASD compared to general populations and suicide rates are much higher in this population compared to the general population [74,75].

Conclusion

Life for many children and adults with ASD have improved compared to when autism was first described by Leo Kanner. More individuals with ASD can talk, read, graduate from school and live independently. ASD affect over 2% of children and adults in the U.S. The evidence continues to support early intensive behavioral interventions delivered by a multidisciplinary team as a first-line therapy, while comorbid mental health conditions such as ADHD, anxiety and aggression may be treated by specific behavioral therapy or medicine.

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