DIVERGENCE EXCESS EXOTROPIA
IN A
POSSIBLE CASE OF CHILDHOOD
DISINTEGRATIVE DISORDER

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Abstract

This case reports a 5-year-old Hispanic female who had been diagnosed with divergence excess exotropia. She had initially experienced significant objective and subjective gains with vision therapy; however, after several months there was a sudden increase in the exotropia that coincided with significant regressions of behavior, language and bladder control. A pediatric consultation was ordered, and the possibility of a pervasive developmental disorder was raised. The various conditions subsumed under pervasive developmental disorder and the differential diagnosis of the some of the conditions of pervasive developmental disorder are discussed.

Key Words

Asperger's disorder, autism, childhood disintegrative disorder, childhood regression, divergence excess exotropia, Landau-Kleffner syndrome, pervasive developmental disorder, Rett's disorder

INTRODUCTION
Exotropia

Primary exotropia is classified as divergence excess, convergence insufficiency, basic exotropia, or simulated divergence excess. Divergence excess and convergence insufficiency are deviations greater at distance and near by at least 15 , respectively.[1-3] Basic exotropia is characterized as the same deviation at both distance and near. Simulated divergence excess is revealed as basic exotropia, after testing with prolonged occlusion and +3.00 sph decreases accommodative convergence and/or fusion, and demonstrates an increased near deviation equal to the distance deviation.[2]

The prevalence of exotropia in young children has been reported at 0.3% to 1.46%.[4-5] Treatments for exotropia include vision therapy, minus lenses, patching, prism, and surgery.[3,6-14] For divergence excess exotropes with a high AC/A, concave lenses decrease the exodeviation by stimulating accommodative convergence. Minus lenses for these patients have not been shown to cause a significant development of myopia.[14] Indicators of successful vision therapy for exotropia include good equal visual acuity, intermittency of turn, and presence of gross stereopsis.[15] Children with various types of developmental delays have a higher incidence of strabismus.[16-20]

Pervasive Developmental Disorder

Pervasive developmental disorder (PDD) is a category of conditions listed in the 4th edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV, 1994).[21] This category includes the following subgroups: autistic disorder, Rett's disorder, childhood disintegrative disorder, Asperger's disorder, and pervasive developmental disorders not otherwise specified. Scharre and Creedon found strabismus in 21% of autistic children, the majority of whom were intermittent exotropes.[16] Schulman also noted a high incidence of intermittent strabismus in her autistic patients.[18]

Childhood Disintegrative Disorder

In 1908, Theodore Heller observed six cases of children who displayed normal developmental milestones up to the ages of 3 to 4 and then experienced regression of language and behavior, as well as incontinence.[22-25] This condition became known as "dementia infantilis" or Heller's syndrome. In 1943, Kanner proposed that dementia infantilis was a separate diagnosis from autism.[24] Volkmar and Cohen reported cases of a disintegrative disorder, in which children developed an autistic-like state after a period of normal development.[26] The DSM-IV introduced the term "childhood disintegrative disorder" as a separate subgroup under PDD. DSM-IV criteria for childhood disintegrative disorder are the following:[21]

Apparently normal development for at least the first two years of life after birth as manifested by the presence of age-appropriate verbal and non-verbal communication, social relationships, and play and adaptive behavior;
Clinically significant loss of previously acquired skills (before age 10 years) in

at least two of the following five areas: expressive or receptive language, social skills or adaptive behavior, bowel or bladder control, play, or motor skills; Abnormalities of functioning in at least two of the following three areas: qualitative impairment in social interaction, qualitative impairment in communication, or restricted, repetitive, and stereotyped patterns or behaviors, interests, and activities including motor stereotypes and mannerisms; Disturbance not better accounted for by another pervasive developmental disorder or schizophrenia.

Childhood disintegrative disorder (CDD) is a rare condition, with about 126 cases reported thus far.[23-24,27] Fombone determined a prevalence rate of 1.1 to 6.4 per 100,000.[28] He acknowledged, however, that this rate may have been influenced by unfamiliarity with CDD or clinician misdiagnosis. The disorder is more common in males than females, with reported 4:1 to 5:1 ratios.[22,29-30] Prognosis for CDD is considered poorer than autism.[23-25,30] Some children do have limited improvements, but others have continued deterioration.[26,31] CDD patients are more likely to be placed into residential care than autistic patients.[26,30] Results of a DSM-IV field trial showed 25% of children with autism had an IQ less than 40, compared to 60% for those with CDD.[24,32]

Age of onset of 2 years is considered the distinguishing feature between autism and CDD.[21] Children with CDD have a period of normal development for at least the first two years of life, and then experience a developmental regression, which can be gradual or abrupt, with a loss of previously-acquired skills in socialization, communication, and functioning. Language regression can be from muteness to the use of single words and phrases.[26,30] In autism, there are progressive developmental difficulties without a regression period or loss of previously-acquired skills. Some researchers complicate the issue, however, by using the term "autistic regression" to refer to regression that occurs before 2 years of age.[33] As children with CDD have behavioral features similar to autism, except for age of onset, some researchers debate whether CDD is actually a separate diagnosis from autism. However, there does appear to be a group of children who develop normally for the first few years of life, and then experience a clear regression period in language, behavior, and play.

Case Report
History

A 5 year, 2-month-old female Hispanic patient was first examined at the University Optometric Center of the State University of New York, State College of Optometry on September 20, 2002. The mother's concern was an intermittent exotropia, first noted at 3 years of age. The family history was negative for strabismus. The child was the product of a full-term birth, weighing an even 6 pounds, with normal prenatal and perinatal histories except for maternal chicken pox at 3 months gestation. Walking occurred at 13 months without any subsequent difficulties with gait, and the use of single words and phrases occurred about 2½ years of age. The child was bilingual, with Spanish at home and English at school. At our first evaluation, she spoke full sentences in both English and Spanish. Medical history was positive for obesity, asthma, high cholesterol, and ear infections. The pediatrician was also concerned about the child's intelligence. The child did have a history of a single uncomplicated febrile seizure, but had not experienced any seizures since that incident.

Optometric Evaluation

Distance and near visual acuities were 20/20 OD and OS with HOTV matching. Refraction revealed +1.00 sph OU. There were no limitations in the direction or extent of the extraocular muscles. Pupillary responses were present, with no afferent defect. External and internal ocular health examinations were unremarkable. Distance cover test revealed 65 intermittent exotropia (straight 30% of the time), and near cover test was 25 intermittent exotropia (straight 80% of the time), with a preference for OS fixation. Testing with +3.00 sph OU then revealed an increased near deviation, but not enough to be classified as simulated divergence excess. The near point of convergence was 2 inches with the OS out and to-the-nose (TTN) with verbal reinforcement. Randot Stereogram and Wirt Circle testing results were 250 and 200 sec/arc, respectively. Worth 4 Dot testing indicated flat fusion at near and intermediate distances, but suppression of the right eye at distance. We made the diagnosis as divergence excess exotropia.

Patient Management

The options of vision therapy (VT) and strabismus surgery were discussed with the mother. We recommended a trial period of vision therapy to improve binocularity but, because of the large magnitude of exotropia, stressed the probability of later surgical intervention. Good equal visual acuities, the presence of gross stereopsis, and the intermittence of the eye turn indicated a fair prognosis for VT. Goals included improvements in ocular motility, fixation, and accommodation, followed by monocular fixation in binocular field (MFBF) therapy with sensory and motor fusion training at different distances. Activities during the initial sessions included eye-hand coordination activities at near, binocular accommodative rock and ball catching, working towards increased distances and decreased ball sizes. Techniques using anaglyphic glasses, and techniques to enhance the near point of convergence were given for daily homework. Minus lenses (-1.50 sph OU) were prescribed for full-time wear to stimulate her accommodative convergence and to minimize her exotropia.

After six VT sessions, the mother reported greatly improved ocular alignment. MFBF and fusion techniques were now emphasized, in addition to ocular motility and fixation, to further minimize the frequency of the eye turn. Activities included physiologic diplopia awareness and motor fusion/recovery with anaglyphic glasses. Another valuable anti-suppression technique was the use of small felt red/green bears placed on a black felt background, with anaglyphic glasses. The child enjoyed matching or identifying bears of particular colors at near and distance.

The patient continued to demonstrate improvements throughout the vision training, with better maintenance of motor alignment and improved binocular performance. Nearpoint of convergence was now TTN with good reach/grasp/regrasp responses and without verbal reinforcement. Cover tests improved to 35 and 10^ of intermittent exotropia at distance and near, respectively. The mother reported that the child's eyes were straight almost all of the time.

Then at the 17th session, the mother reported strange behavior for the child during the previous two weeks; there had been a loss of speech and bladder control, along with finger waving and staring spells. The mother did not report any precipitating events associated with this deterioration. The age was now 6 years and 14 days. The child had previously enjoyed school, but no longer interacted with her classmates. She had always worn her prescription with good compliance, but now refused to wear the glasses. Her attention during subsequent vision therapy sessions rapidly decreased. Her strabismus deteriorated to an almost constant 50 exotropia at distance and a 20 intermittent exotropia at near. She no longer communicated freely with others and demonstrated extremely poor eye contact. These substantial psychosocial changes became more of a priority than VT, and the child was referred to her pediatrician for neurological and psychological evaluations. At this point of her regressions in behavior and language, the exotropia had further increased in its magnitude and frequency. The patient was also subsequently referred by the pediatrician to a special neuro-psychiatric facility for further testing and treatment, which may include pharmacological intervention.

DISCUSSION

Differential diagnoses of regression for this child included autism, CDD, Rett's disorder, and Landau-Kleffner Syndrome. The diagnosis of autism was initially considered by the pediatrician. DSM-IV criteria for CDD require normal development for at least the first two years after birth, with age-appropriate verbal and nonverbal communication, social relationships, play, and adaptive behavior.[21] In this case, age-appropriate verbal communication was not present, as speech was delayed until about 2 ½ years. In addition, as the pediatrician suspected some mental retardation before the reported regression period, the term "normal development" may not apply for this patient.

The diagnosis of CDD in this case rather than autism is strongly supported. The mother reported a clearly delineated regression period with a loss of previously-acquired skills, which is absent in autism. Although speech was delayed, the child did speak in full sentences prior to her regression. Wilson et al. reported de-layed speech before language regression in many children.[34] The patient then lost her previously-acquired language skill, with deterioration to the use of single words and phrases. Her impairments in behavior and communication, as well as her loss of expressive language, play, and bladder control, all met the criteria for CDD. The pediatrician was initially unfamiliar with CDD, but after consultation, she believed that it was a more appropriate diagnosis than autism.

Although autism usually has an onset before age 2, it can still be diagnosed later in children whose developmental difficulties do not become apparent until the ages of 2 to 3.[35] These overlapping criteria between autism and CDD raise the issue of "age of onset" versus "age of recognition."[36] True onset can often precede true recognition, as parents may not recognize the beginning of a gradual regression until it becomes more pronounced. Gradual onset, lack of parental report, and/or parental denial can all influence recognition of CDD regression. Parental ability to accurately identify the time of decline is essential, and parental perception of deterioration can change over time. As this child experienced an abrupt and rapid regression over a two-week period, the mother was instantly aware of the problem.

This case also raised the interesting possibility of an association between the onset of ocular misalignment and the onset of her regression. It appears from the history that the exotropia preceded the more general regression; However, it is possible that the onset of strabismus occurred in association with an initial subtle decline before the obvious regression period. Further decompensation of her binocular alignment was then triggered by psychogenic factors. Exotropia is often viewed as a continued process of binocular decompensation from exophoria to exotropia.[37-38] Illness and psychological stress often result in decompensation.[39] An increase in strabismus during a psychotic episode in a schizophrenia patient has been reported.[40] In the present case, it is reasonable that the child's overall condition lessened her control of the exotropia, and then the regression period further increased her binocular misalignment.

Among some researchers, there is the hypothesis that CDD is always associated with a progressive neurological disorder. It has been observed in association with diseases such as tuberous sclerosis, seizures, and neurolipidoses.[22,24] Seizures in those with CDD have been reported at about 50%.[24,41] There are also reports of associations with sibling birth, familial death, parental problems or illness, and accidental injury.[22] This significance is unclear, however, since many of these events are not uncommon in childhood. Although some cases of CDD have occurred with neurological conditions, this has only been observed in a minority of cases.[23,27] Thus far, there appears to be no consistency of an association between CDD and a neurological condition.

Recent research has suggested that genetics may play a role in causality. Russo et al. proposed that those with predisposing genetic factors experience deposition of amyloid as a result of environmental stress, and this process then results in disintegration.[42] Family history of children with CDD has usually revealed an absence of autism, schizophrenia, or organic illnesses.[24,43] Zwaigenbaum et al. reported on a case of co-occurrence of CDD and autism in half-brothers, which suggested a shared genetic mechanism between the two disorders.[44] The role of genetics in CDD requires further investigation.

Other differential diagnoses of childhood regression include Rett's disorder and Landau-Kleffner Syndrome. Rett's disorder is characterized by a developmental regression that occurs at about 5 months of age with deceleration of head growth, loss of hand skills, loss of social engagement, poorly coordinated gait, and severely impaired expressive and receptive language development with severe psychomotor retardation.[21,45] For this patient, there was neither deceleration of head growth nor ataxic gait, and her regression did not occur until 6 years of age.

While not an included condition of PDD, Landau-Kleffner Syndrome (LKS) is a childhood disorder that usually occurs between the ages of 4 and 7 and is characterized by language loss, without autistic features and cognitive decline, as well as seizures and/or EEG changes.[34,46-47] Seizures are observed either months before or after the language regression. This patient did not experience any seizures other than the one febrile seizure, although she had not undergone an EEG. As in CDD, chil-

dren with LKS have normal development and then lose language, either gradually or abruptly. As severe regressions in behavior and functioning do not occur in LKS,[34] the diagnosis of LKS was not supported in this case.

The relationship between childhood regression and seizures is still being investigated. Children with regression without seizures are often not referred for an EEG. In this case, does the absence of seizures before and after her regression mean that she should not have been referred for an EEG? Or, should EEG abnormalities have been ruled out before diagnosing autism or CDD? Rapin proposed that while epilepsy may be the aggravator in language and autistic regression, it may instead be a manifestation of an underlying process responsible for both epilepsy and language loss.[48] Many researchers maintain that all children with regression of behavior and language, regardless of the presence or absence of seizures, should have an EEG.

Others continue to debate whether regression at different ages represents different conditions, or one syndrome in which the age of the child determines whether regression is global or limited. Wilson et al.[34] and Shinnar et al.[49] concluded that language regression in children is more often associated with a global regression in behavior and cognition, rather than a limited deterioration.[34,49] Childhood regression is therefore a serious disorder with significant implications for future functioning.

CONCLUSIONS

The debate over whether CDD is a separate diagnosis from autism continues. Despite the arguments, there is a group of children who develop normally for the first few years of life, and then experience a clear regression period in language and behavior with loss of previously-acquired skills, as in this child. This case presented an association between loss of binocular alignment and onset of childhood regression. Her regression and inattention resulted in the inability to maintain fusional control of her divergence excess exotropia. There is clearly a need for continued research in the areas of childhood regression, autism, and CDD disorder. More definitive diagnoses may lie in the area of genetics, because without medical testing, diagnoses will continue to depend on behavioral manifestations subject to clinician interpretation.

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