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Neurocognitive functioning of a child with partial trisomy 6 and monosomy 21

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Abstract

This case study describes the neurocognitive presentation of a child with identified genetic abnormalities of trisomy 6 and monosomy 21 who was evaluated as part of a standard medical protocol for cochlear implantation following diagnosis of profound sensorineural hearing loss. This child received neurocognitive testing prior to cochlear implantation and approximately 12 months post-activation of his cochlear implant. While he has not fully developed oral language, his presentation suggested improvement in overall skills since the activation of the cochlear implant; however, less than would be expected for a typically developing child.

Keywords

Child; Neurocognitive functioning; Cochlear implant; Genetics

CASE STUDY

To date, the medical literature does not include a clinical description of the presentation of the unbalanced chromosome disorder partial trisomy 6p and monosomy 21q. Full monosomy 21 is very rare and has been described as failure to thrive, frequent vomiting, and death at age 3 weeks (Dziuba, Dziekanowska, & Hubner, 1976), as well as cleft palate, broad nose, and muscle hypertonia (Fryns, D'Hondt, Goddeeris, & van der Berghe, 1977). A more recent study described dysmorphic features including hypertelorism, downslanting palpebral fissures, low-set folded ears, and death at 8 days of life (Pellisier, Philip, Voelckel-Baeteman, Mattei, & Mattei, 1987). Similarly, full trisomy 6 is rare and often associated with hematologic malignancies, leukemia, myelodysplasia (Moormeier et al., 1991), basal cell carcinomas (Nangia, Sait, Block, & Zhang, 2001), and bone marrow aplasia (LaStraza et al., 1998). As little is known of the combination of these chromosomal abnormalities, the following case study provides a description of the clinical presentation and neurocognitive functioning of a 29-month-old boy who was referred for developmental evaluation prior to implantation.

The boy was the second offspring born to non-consanguineous parents at 37 3/7 weeks following induced vaginal delivery for gestational diabetes at a weight of 2380 g to a 30-

year-old mother gravida 2, para 2. The pregnancy was unremarkable. Amniocentesis revealed the genetic abnormalities outlined above. His APGAR scores were 8 at 1 min and 9 at 5 min. Immediately after birth, he was placed in the NICU where he received 30% Oxy-Hood and a feeding tube. By 13 days of age, he underwent exploratory laparotomy and colostomy under general anesthesia for an imperforate anus. He also was found to have an adrenal tumor, submucous cleft palate, and grade 3 vesicoureteral reflux on the left side. He received anesthesia for surgical procedures. He remained in the hospital for 20 days. He was identified 46XY with a derivative chromosome 21 and a translocation between chromosomes 6 and 21, with trisomic region of chromosome 6p from 6p22.3 to the terminus and monosomic for chromosome 21q from 21q22.3 to the terminus (46XY, t(6,21) (6pter -> 6p 22.32 :: 21qter -> 21q22.3). No family history of congenital abnormalities was reported and the karyotype of his parents was unknown. MRI of the brain at 5 months identified a reduction in white matter from normal levels, large sulci, and asymmetry in the lateral ventricles, with the right being slightly larger than the left.

Routine newborn hearing screening by ABR revealed bilateral profound sensorineural hearing loss. CT of the temporal bones demonstrated bilateral incomplete partition (Mondini) cochlear malformations. Because of recurrent otitis media, pressure equalization tubes were placed at 6 months of age. Cochlear implantation with a Med-El Pulsar device was performed in his right ear at 14 months. When the cochlea was opened during surgery to place the implant, the child experienced a cerebral spinal fluid (CSF) leak, as is commonly found in patients with cochlear malformations. This was repaired primarily and although it resulted in a temporary reduction in CSF and transient reduced intracranial pressure, it is not expected to have cognitive sequelae. The implant worked well until age 27 months when the cochlear implant failed, and he required revision surgery to replace the device. This second surgery was unremarkable.

The boy presented initially at 10 months of age with very little hair growth, slanted eyes, long forehead, small mouth, delayed eruption of his upper teeth, dysplastic lower teeth, and he was not walking independently. At that time, his mother reported that while he could produce some babbling and consonant sounds; he communicated mainly through gestures and used approximately 10 ASL signs. When he returned for re-evaluation at 29 months, the child's physical presentation was consistent with his 10-month evaluation, and he continued to have little hair growth. However, he was beginning to walk independently and was producing both vowel and consonant babbling sounds, as well as one oral word ("mama"). The mother did not report any concerns related to his social, behavioral, or emotional functioning and indicated that he received speech and language therapy, occupational therapy, and physical therapy biweekly as well as educational therapy from a hearing-impaired teacher of the deaf weekly. These therapies were initiated at 5 months of age and were continued regularly through the second evaluation.

Cognitive abilities

Prior to initial cochlear implantation, at 10 months of age, a speech and language evaluation revealed impaired auditory comprehension (1st percentile; age equivalent = 2 months) and impaired expressive communication (9th percentile; age equivalent = 9 months), as measured by the Preschool Language Scale – Second Edition. He presented for initial developmental evaluation (also at age 10 months) and was administered the Mullen Scales of Early Learning (MSEL; Mullen, 1995), a measure designed for young children to estimate functioning across areas thought to predict later intellectual development. On this test of early developmental skills, he demonstrated impaired cognitive abilities overall (Early Learning Composite = 63, 1st percentile) and his scores across all developmental domains assessed fell well below expectation. His Visual Reception skills (subtest measuring visual discrimination, organization, and sequencing, as well as visual spatial

awareness) fell in the borderline range (4th percentile). The child's Fine Motor skills (subtest measuring visual directed motoric planning) fell at the 1st percentile. Gross Motor skills (subtest measuring central motor control and mobility in the supine, prone, sitting, and standing positions) were determined to fall at the 1st percentile, suggesting significant delays. As would be expected, Expressive Language skills (subtest measuring language productivity) fell well below age-expectation (<1st percentile), as did his Receptive Language skills (subtest measuring auditory comprehension), which fell in the impaired range (<1st percentile). See Figure 1 for a comparison of age equivalents among individual subtests at pre- and post-cochlear implantation.

At 29 months, the MSEL was repeated during his follow-up developmental evaluation. At that time, he earned an overall Early Learning Composite of 49 (1st percentile), which again fell in the impaired range. However, he had made gains since his previous evaluation 19 months prior. Predictably, his language skills were judged to fall well below age expectation in the impaired range. His Expressive Language skills were judged to fall below the 1st percentile, which represented gains of only 1 month since his previous evaluation, as he was noted to laugh, coo, and make vowel sounds. His Receptive Language skills also fell below the 1st percentile; however, this represented a 15-month increase in skills over the previous 18 months. Specifically, he was able to understand simple verbal input, gestures, and commands. In regard to motor skills, he evidenced Fine and Gross Motor skills that fell below the 1st percentile. Overall, these results indicate an improvement of 7 and 4 months, respectively. He was able to walk with assistance and pull himself to standing, as well as imitate crayon lines and turn pages in a book. His Visual Reception abilities fell below the 1st percentile; however, he evidenced an increase of 9 months since his previous evaluation. He was able to match objects, look for a displaced toy that was covered, and make object associations. Taken together, these results indicate increases in his skills, though at a slower rate than what would be expected for a typically developing child (given the time period between evaluations, a typically developing child would be expected to evidence gains of 19 months in all domains).

Adaptive functioning

In addition, at his initial evaluation, the Vineland Adaptive Behavior Scales – Second Edition (VABS-2; Sparrow, Cicchetti, & Balla, 2005), a semi-structured interview with a caregiver, was conducted with his mother. This measure provides an indicator of how well a child is able to behave in a manner that is adaptive to his surroundings. According to his mother's responses, the child's overall adaptive functioning fell within the impaired range (Adaptive Behavior Composite score = 58, <1st percentile). As expected, she described his Communication skills (receptive and expressive language skills) to be impaired (<1st percentile; less than 1- and 2-month levels, respectively). In addition, his Motor Skills were rated to fall within the impaired range (<1st percentile; 6-month level for gross motor and 7-month level for fine motor). His mother's responses reflected borderline (3rd percentile) Daily Living Skills (personal care rated at the 6-month level); whereas his Socialization skills (spontaneously sharing toys, participating in games, interacting with others) were estimated to fall within the low average range (19th percentile; interpersonal relationships rated at 2 months, and play and leisure skills rated to fall at 16 months), suggesting an area of relative strength.

At follow-up developmental evaluation, the VABS-2 was repeated with his mother. At this time, his overall adaptive behavior again fell in the impaired range (Adaptive Behavior Composite score = 68, 2nd percentile). Again, he was rated to have impaired Communication skills, which were rated to fall at the 15-month level for both receptive and expressive language (4th percentile). His Daily Living Skills were determined to be a relative weakness, falling in the impaired range at the 7-month level for domestic and

community skills and the 10-month level for personal care (1st percentile). Another area of weakness was Motor Skills, which were rated to fall at the 10- and 18-month age range (for gross motor and fine motor skills, respectively, 1st percentile). A relative strength again was noted for Socialization skills, which were determined to fall in the low average range (12th percentile), with interpersonal relationship skills rated at the 16-month level, play and leisure skills rated at the 25-month level, and coping skills rated at the 7-month level. These ratings were consistent with observations during testing and objective test results, and again represented improvement over time.

DISCUSSION

Overall, his impaired adaptive functioning, coupled with his impaired intellectual functioning was consistent with a diagnosis of Mild to Moderate Mental Retardation. He remained neurocognitively delayed and linguistically delayed, despite his cochlear implant. However, he gained raw score points over the 2 time points and thus did not evidence cognitive decline. Instead, he showed slower than expected development over time. Although his Early Learning Composite decreased over time, this is a result of using age-adjusted norms, rather than comparisons of age equivalents. Similar gains between his expressive and receptive language skills would not be expected, given that he requires receptive input to precede expressive output. Thus, we would expect his expressive language gains to be evident in future evaluations. His gains suggest that although he was diagnosed with Mild to Moderate Mental Retardation, his cochlear implant greatly increased his quality of life and improved his functional communication (Kushalnager et al., 2007; Pierson et al., 2007).

Despite his low cognitive functioning, he made considerable gains, thus speaking to the importance of early intervention, both in terms of therapeutic intervention and medical care. Combined with his dysmorphic facial features, adrenal tumor, hearing loss, and neurocognitive profile, this description may provide evidence for phenotypic expression of the cognitive profile of his chromosomal abnormality. Taken together, this case study provides not only a description of the cognitive profile of a young child with a rare chromosomal abnormality, but also provides support for the benefits of a cochlear implant early in life.

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Figure 1.

Age equivalents for cognitive skills at both developmental evaluations, as measured by the Mullen Scales of Early Learning.