Deletion of 8p: A report of a child with normal intelligence

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Abstract
The case is presented of a female infant with a distal deletion of 8p (8p23.1 --> pter) whose development was monitored over a 5-year period from 12 months of age. Although previous literature has suggested that 8p deletion is associated with mild to moderate intellectual disability, the child reported here has normal intelligence. Despite initial delays in gross motor and language skills, cognitive development (assessed with the Bayley Scales of Infant Development) and intellectual ability (measured on the Stanford-Binet Intelligence Scale) were within average range. It is argued that the small number of previous case reports may have created a misleading impression of intellectual development in individuals with distal deletions of 8p.

This paper reviews the literature on developmental consequences associated with distal deletions of chromosome 8p (8p-), and presents the case of a child with 8p- with normal intelligence whose development has been monitored over a 5-year period. With only two exceptions (Pettenati et al. 1992, Reddy 1999) there are no reported cases of normal intelligence associated with this chromosome deletion and, indeed, there are few such reports about children with deletions on other chromosomes.

Among the case descriptions of 8p- there are reports of both interstitial and terminal deletions (most frequently with breaks in bands p21 to p23), as well as deletions occurring in combination with duplications. Individuals with 8p- are reported to share a distinctive pattern of clinical features which include low birthweight, growth retardation, intellectual disability, congenital heart defects, and physical abnormalities such as microcephaly and mild facial anomalies. This has led several authors to propose a distinct 8p- syndrome phenotype (Dobyns et al. 1985, Ostergaard and Tommerup 1989, Pecile et al. 1990, Claeyts et al. 1997). It has been suggested that the critical region for producing this phenotype may lie between 8p21.3 and 8p23 because individuals with deletions in this region show the most severe consequences (Ostergaard and Tommerup 1989) while those with very distal deletions (e.g. 8p23-8pter) show fewer or milder features (Fryns et al. 1989, Digilio et al. 1998).

Intellectual disability is the most frequently reported developmental outcome. In a recently published review of terminal deletions (Digilio et al. 1998), intellectual disability was claimed to occur in all 38 individuals. We would argue, however, that there is insufficient evidence to suggest that intellectual disability is inevitably associated with 8p-.

There does, however, seem to be a relation between the size of the deleted region on chromosome 8 and the degree of intellectual disability (Digilio et al. 1998), with more distal terminal deletions at 23.1 being associated with higher functioning (Hutchinson et al. 1992). This review focuses on developmental outcomes for those with terminal deletions at p23.1. As shown in Table I, among 18 previously reported individuals with this deletion, only two were more than mildly intellectually impaired (Fagan et al. 1988, Blennow and Brondum-Nielsen 1990). Data about other aspects of atypical development were reported for some of these individuals, including slow or impaired motor skills in eight children and delayed speech for seven children. Ten children with this deletion reportedly displayed behaviour problems including hyperactivity, inattention, and aggression.

Several authors have suggested that 8p- may be more frequent than the relatively small number of case reports would suggest (Hutchinson et al. 1992, Wu et al. 1996, Claeyts et al. 1997, Digilio et al. 1998).

It is possible that only children with apparent delays or anomalies are being referred for cytogenetic analysis, while those with few or more subtle effects remain undiagnosed and unreported in the literature. Consequently, the current literature may not be portraying the range of developmental consequences associated with 8p-.

Even among reported cases, the influence of 8p- on intellectual, behavioural, and social development has not been clearly established. The result is that families and professionals do not have access to information that is crucial for making decisions about the lives of individuals with 8p-.
The present report describes a child whose cognitive development has proceeded typically. The study is unique because it documents consistent psychometric evidence of normal intelligence across the early childhood years.

Case report

EARLY DEVELOPMENTAL HISTORY

Our patient was born at term following a relatively normal pregnancy and delivery. A miscarriage was suspected at 6 weeks when bleeding occurred, but the pregnancy proceeded without any further problems. Birthweight (3218 g, 47th Gentile) and length (50.2 cm, 56th Gentile) were within the normal range. Moderately severe jaundice due to ABO blood group incompatibility responded well to phototherapy.

The child's mother described her as a very placid baby who appeared less responsive than her older sibling had been. She sat without assistance at 6 months and rolled halfway over at 10 months. At 12 months of age the child was taken to a paediatrician because of parental concerns about her lack of responsiveness and slow gross motor development. At the time she was neither weight-bearing nor crawling. An occupational therapy assessment confirmed the presence of significant delays in gross motor development and moderate delays in language and social skills. Fine motor skills appeared to be progressing normally.

Chromosome analysis at 14 months of age revealed a deletion on the short arm of chromosome 8 (8p23. 1-pter). It is not certain that the deletion arose as a de novo event because the parents decided not to have their chromosomes studied at that time. The child has no cardiac defects or other medical conditions and her facial features display no obvious dysmorphic characteristics. Due to the fact that some milestones were significantly delayed, she received intensive blocks of physiotherapy, occupational therapy, and speech therapy at various times during early childhood. She stood unassisted at 22 months, walked independently on her second birthday, and spoke her first single words at 18 months. By 21 months, she had a vocabulary of 20 spoken words and seven sign words. She began combining words consistently at 23 months. Toilet training was reliably achieved in the daytime at 2 years six months with night control gained at 5 years. The child has experienced no significant illnesses and her physical growth has progressed normally For instance, her weight at 6 months, 2 years, and 5 years were at the 32nd, 46th, and 53rd Gentiles, respectively. Across these ages, height followed the 25th Gentile.

FORMAL ASSESSMENT RESULTS

Assessments of intellectual functioning were conducted over a 5-year period and are presented in Table II. All results indicated that the child's cognitive development was within the normal range for her chronological age. Language assessments are also presented in Table H. Both receptive and expressive language skills were within the normal range. Specific motor assessments at 35, 50, and 72 months showed that most motor skills were within the normal range, although muscle tone was low. Some difficulties were observed in balance (at 35 and 72 months) and fine motor skills (at 50 and 72 months).

OBSERVATIONAL REPORTS

Although our patient tends to be reserved in new situations, she is usually very confident and competent in her social interactions. During the assessment sessions she was always very cooperative, attentive, and highly persistent with tasks. She is now in her second year of formal schooling and her parents and teachers report no difficulties with learning. Apart from reading, which she particularly enjoys, her interests include swimming, music, and drawing. She spends a lot of time engrossed in imaginative play, has many friends, and displays a great deal of empathy towards others.

Discussion

Despite some initial delays in language development, our patient's intellectual ability is within the average range. Across all assessments, the results were very consistent. This finding contrasts with most previous 8p- case reports, which have described individuals with mild to moderate intellectual disability.

The main areas of impairment for the child have been motor skills and early expressive language, aspects of development that have been associated previously with 8p-. Her initial language delays appear to have been overcome, and she is experiencing no difficulty in learning to read. She displays none of the developmental problems with behaviour, social skills, and hyperactivity, which are often reported in the literature.
This case report suggests that intellectual disability and behaviour problems are not inevitable consequences of deletions on chromosome 8. Although it is possible that our patient represents an exceptional case, it is also possible that there are numerous other children with 8p- who are developing typically in many respects but who have not been reported in the literature. Given the relatively small number of published case reports and the range of developmental outcomes that appear to be possible, we would argue that prognoses for children with 8p- should be tentatively optimistic. We hope to see an increasing number of published studies, which report data about intellectual ability, social skills, language, and behaviour so that early interventions can be based on accurate information and realistic expectations. Our patient demonstrates that positive developmental outcomes are achievable for at least some children with 8p-.

References


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