

CASE REPORT

A Tale of Two Boys: Case Report on Non-Consanguineous Siblings with Cerebral Palsy

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ABSTRAK

Palsi serebrum (CP) adalah penyebab biasa kecacatan kanak-kanak. Ia mempunyai kesan yang besar kepada ibu bapa dan penjaga, terutama apabila ianya melibatkan lebih daripada satu ahli keluarga yang sama. Walaupun CP kekeluargaan (familial CP) sangat jarang berlaku, kes-kes yang dilaporkan di kalangan kanak-kanak dari perkahwinan yang mempunyai pertalian darah atau sebaliknya, dan kehamilan kembar telah mencadangkan kemungkinan ianya melibatkan masalah keturunan genetik yang kompleks. Pakar perubatan perlu sedar tentang CP kekeluargaan untuk pengesanan dan kaunseling awal. Kami melaporkan kes CP yang jarang berlaku pada dua adik-beradik lelaki daripada perkahwinan yang tiada mempunyai pertalian kekeluargaan.

Kata kunci: palsi serebrum, kekeluargaan, genetik, keturunan, pertalian darah

ABSTRACT

Cerebral palsy is a common cause of childhood disability. It has a great impact on parents and caregivers, especially when it reoccurs in the same family. Although familial cerebral palsy is relatively uncommon, cases have been reported among children from consanguineous, non-consanguineous marriages and multiple pregnancies suggesting a possible complex genetic mode of inheritance. Physicians need to be aware of the possibility of familial cerebral palsy for early detection and counseling. We describe a rare case of two male siblings from a non-consanguineous marriage affected by cerebral palsy.

Keywords: cerebral palsy, familial, palsy, recurrent, siblings

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INTRODUCTION

Cerebral palsy (CP) is a group of permanent non-progressive disorder of movement and posture causing limitation of activities. It is attributed to the non progressive disturbances of the fetal or infant developing brain. Motor disturbances occur in combination with disturbances of sensation, perception, cognition, communication and behavior. Epilepsy and secondary musculoskeletal problems may co-exist (Rosenbaum et al. 2007). Microcephaly, drooling and varying degree of mental retardation are other manifestations (National Institute of Neurological Disorders and Stroke 2013). Symptoms are usually detected in infancy when a child presents with delayed milestones of development.

The prevalence of CP differs from country to country ranging from 2.0 to 2.5 per 1000 live birth (Reddihough & Collins 2003). Many causes have been implicated for CP such as congenital and environmental factors. These include malformation of the brain, intrauterine infections, low birth weight and birth asphyxia. Some studies have hypothesized genetic factors or a combination of genetic and environmental factors as the underlying cause for CP (Gibson et al. 2008; Djukic et al. 2009).

Familial CP or recurrent CP among siblings has been described in the literature (Rajab et al. 2006; Mukherjee et al. 1973). However recurrent CP among non-consanguineous siblings is rare. We describe an unusual case of two male siblings from a non-consanguineous marriage affected by familial CP. It is hoped that this

case study increases the awareness on familial CP so that early detection, genetic counseling, appropriated health education, and care can be provided for the affected families.

Informed consent for the publication of patient's information and images used in this article was obtained from the parents.

CASE REPORT

Two male siblings of Indian ethnicity, aged 22 (sibling A) and 20 years (sibling B) were identified to be affected by CP. Patient A, the eldest son was diagnosed to have CP at the age of three while his younger brother, sibling B, was diagnosed to have CP at the age of two years. The third and youngest male sibling, currently 11 years old is physically and mentally normal. All three children were delivered at term without any significant antenatal, intra-partum and post-partum events or complications. Maternal age at first, second and third delivery was 26, 28 and 37 years, respectively.

Sibling A is the eldest of the three. He was delivered at term through spontaneous vaginal delivery with a birth weight of 2.8kg. The antenatal and birth history was uneventful except for congenital talipes equinovarus (CTEV) which was diagnosed at birth. Parents noted a delay in milestones of developments compared to his peers, however they postponed professional advice until he was three years of age, hoping for spontaneous improvement. He could barely walk at the age of three years. He was diagnosed as CP based on global developmental delay

of milestones and presence of spastic motor features. At the age of four years, he developed seizures and was started on anti-epileptics. He is currently 22 years of age, has dysmorphic features such as microcephaly, microngathia, drooling of saliva and dysarthria. He also has surgical scars over both ankle and calves from the corrective CTEV surgery. He can walk short distances with an ataxic gait, able to scribble and feed himself with minimal help. He can indicate his toilet needs however, requires assistance from his mother who is his main caregiver. His speech is slurred and limited to single words and incomprehensible sounds. Physically, his lower limbs appear smaller and underdeveloped compared to his upper limbs. Neurological examination of the lower limb shows increase tone with a power of 4/5 bilaterally. All reflexes are brisk. Babinski's sign is up-going bilaterally. Upper limbs demonstrate occasional clumsy and non purposive movements.

Sibling B is the second born in the family and he is two years younger than sibling A. He was diagnosed to have CP at the age of two years based on global developmental delay and seizures. Currently, he has features similar to his elder brother which include dysmorphism, microcephally, microngathia, drooling of saliva and dysarthria. However, his gait is more stable as he does not have CTEV. He is able to feed himself with minimal assistance. His speech is slurred and consists of incomprehensible sounds. Neurological examination of the lower limb demonstrates increase tone, normal power and brisk



Sibling A

Sibling B

Figure 1: Images of siblings affected by CP

reflexes. His hands show sudden, non purposive movements but to a lesser extent compared to his elder brother. In summary, both affected siblings have microcephaly, spastic diplegia, dysarthria, seizure and mental retardation. Their social skills are equivalent to a three year old child. Figure 1 shows microcephaly and the dysmorphic features of these two boys.

Their father who is now 53 years old, works with the local municipal council. His mother, aged 48 years is a homemaker and cares for her two disabled children. Both parents are physically and mentally normal. Both have type II diabetes, diagnosed five years ago and maintain good glycaemic control with medications. There is a strong family history of epilepsy among the paternal cousins. Two male siblings are affected by epilepsy while another cousin is mentally challenged. However, it could not be confirmed if any of them had features CP. Figure 2 depicts their family genogram.

DISCUSSION

Although rare, familial CP has been reported as early as the 1960s among Jewish population where

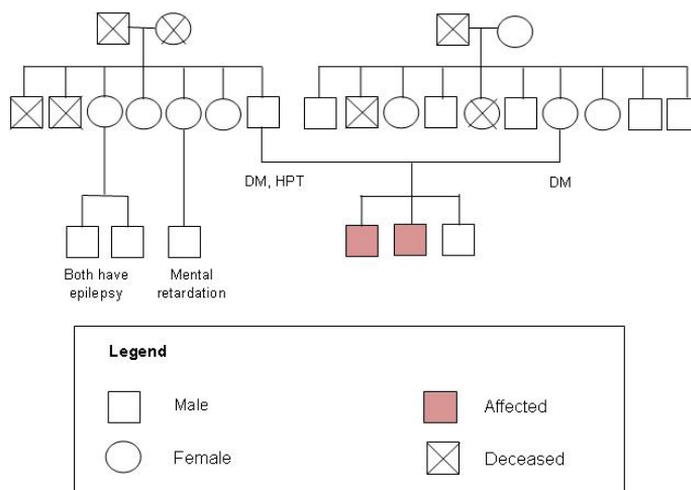


Figure 2: Family genogram

consanguineous marriages are a norm, suggesting a possible genetic inheritance (Adler 1961). Familial CP has also been reported in Asian regions where consanguineous marriages are a common practice. A case report from Oman documented 10 out of 44 members from a large family of consanguineous marriage to be affected by CP suggesting a genetic form of inheritance for CP (Rajab et al. 2006). The familial CP described by Rajab had common features such as spastic diplegia, microcephaly and mental retardation suggesting a possible recessive mode of genetic inheritance for CP.

Familial CP arising from a non-consanguineous union is rare. In Sweden where consanguinity is uncommon, familial CP accounts for about 1.6% of all cerebral palsy cases. A study by Hemminki et al. (2007) found that parents who had had one affected child with CP were at risk of recurrence. They identified a 4.8 fold risk of having a second child with

CP when the first was affected and increases to 29 folds if the siblings were twins (Hemminki et al. 2007). CP was also found to occur more frequently in multiple pregnancies compared to singleton pregnancies (Pharoah 2005). In another observation, Richer et al. (2011) suggest that recurrent CP among siblings from non-consanguineous parents could be due to a complex combination of maternal and genetic factors (Richer et al. 2011).

Recent data from a large Norwegian cohort study also suggests the possibility of a strong genetic influence. The interaction between multiple genes and the environment is postulated as the underlying cause for CP (Tollånes et al. 2014). McHale et al. (2000) identified a possible genetic link among Asian siblings affected by a similar type of ataxic CP to the involvement of chromosome 9p12–q12 (McHale et al. 2000).

In summary, this case report depicts two male siblings who are products of a non-consanguineous

marriage affected by CP. Both parents were healthy at time of conception and mother was well throughout both pregnancies. Intrapartum and postpartum events were unremarkable. These siblings share common features of CP such as ataxia, microcephaly, spastic diplegia, epilepsy and mental retardation. Family history of mental retardation and epilepsy in the paternal lineage suggests that paternal genetic factors may have a contributory role in determining familial CP. Current evidence from the literature suggests a recessive or a more complex mode of inheritance for familial CP which may only be unraveled by further research in this area. The paucity of investigations such as early MRI of the brain to study the neuronal formation and genetic studies, at the time of diagnosis of CP are some setbacks of this case. Genetic studies were not performed due to the lack of facilities and high cost involved in performing such tests. The diagnosis of CP necessitates family counseling to discuss the risk of recurrences. Early rehabilitation should also be initiated as familial CP predicts poor prognosis and low rehabilitation success rates (Adler 1961).

CONCLUSION

The recurrence of CP among siblings from non-consanguineous parents and single births such as this case, illustrates a possible complex genetic mode of inheritance. Although this form of CP is uncommon, the consequence of having multiple siblings affected by CP would have a major impact to the family and community in general. Physicians

should be aware of the familial type of CP and refer to pediatricians for genetic screening. Counseling should be provided to parents with one child affected by CP of the possible risk of recurrence. Consanguineous unions in general, should be discouraged to reduce the risk of recurrent CP and other autosomal recessive conditions. Since a definite genetic mode of inheritance is yet to be established for CP, it is a potential area for future research which may bridge the gaps in knowledge pertaining this complex condition.

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