

The Cri du Chat syndrome in a 6-year-old boy

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Abstract

The partial deletion of short arm of chromosome 5, which is known as Cri du Chat syndrome, although rare is a major cause of mental retardation in children. This case report describes the cognitive and behavioural profile of a six-year old boy who displayed evidences of severe mental retardation, behavioural problem and seizure disorder.

Keywords: Cri du Chat; deletion; chromosome; epilepsy.

Introduction

The Cri du Chat syndrome (Cat cry syndrome) has derived its name from the cat-like cry, which is so striking in infancy, but which becomes less pronounced with advancing age. The cry is related to the abnormal laryngeal development (hypoplastic larynx). Affected individuals have severe developmental delay (Carlin, 1990; Cornish, 1996; Cornish and Pigram, 1996; de-Michele *et al*, 1993) and a number of characteristic physical features (Fehlow & Tennstedt, 1989; de-Michele *et al*, 1993; Dykens & Clarke, 1997) including microcephaly, hypertelorism, epicanthic folds, oblique palpebral fissures, posteriorly rotated low-set ears, and a small jaw. Cardiovascular and gastrointestinal abnormalities may occur. Cognitive assessments frequently show marked discrepancies between verbal and non-verbal abilities with language development being particularly delayed (Carlin, 1990). However, recent research (Cornish and Pigram, 1996) has shown that over three-quarters of individuals can use basic signs or gestural language to communicate their needs. Also, receptive language skills are often more advanced than expressive ones (Cornish and Munir, 1998). Other commonly witnessed behaviour includes self-injury, over activity, distractibility, repetitive movements, and hyperacusis (Dykens and Clarke, 1997). Dermatographic patterns observed include a high incidence of single transverse creases, with a more distally placed axial triradius, and a tendency to have mainly arches and whorls on the fingertips. The basic chromosomal defect in affected children is a partial deletion of short arm of chromosome 5 (Malapsina *et al*, 1992; de-Michele *et al*, 1993).

As the reports on cri du chat syndrome are scarce in world's literature, we here report a case from Nepal to enrich the store of scientific knowledge.

Case Report

A 6-year-old boy from a rural community setting in eastern Nepal was referred to the mental health team of Community Mental Health Project of Department of Psychiatry, Institute of Medicine, Kathmandu, with a 5-year history of repeated generalised tonic-clonic seizures, delayed language speech and motor development, overactivity, distractibility, repetitive movements, and growth retardation. The boy also was reported to have a characteristic cry and inability to swallow solid and semi-solid foods properly since the age of 6 months. Though his treatment history revealed that the boy was on 200 mg of carbamazepine in 24 hours for the last 4 years, the seizures were not controlled.

The boy was born of non-consanguineous parents. He was the third of five siblings and none of the other siblings had any symptoms of psychiatric, neurological, or other obvious medical/surgical disorder. A local traditional birth attendant assisted his birth, which was uneventful.

An initial assessment, the boy was very restless and hyperactive. The rate of spontaneous eye movements and blinking were increased. Sporadically he produced high-pitched sounds. However, there was no rigidity, tremors or any other abnormal movements, but posture was voluntary and movements were active. Though, head circumference was normal to his given age, his physical examination revealed characteristic posteriorly rotated low-set ears, small jaw, oblique palpebral fissures, and single transverse crease. His pupils were 2 mm, equal and reacting briskly; both optic discs were clear and signs of papilloedema were not found. There were no other systemic findings. A provisional diagnosis of Mental retardation with Seizure disorder-generalised tonic-clonic was made with probable cause being Cri-du chat syndrome. As the prime cause for consultation was frequent refractory seizures, the dose of carbamazepine was increased to 400 mg per day and clonazepam 0.5 mg. in 24 hours was added for immediate control of seizures. Further investigations including blood count, electrolytes, liver function tests, creatinine kinase, blood glucose, urea, serological test for syphilis, HIV, serum thyroid hormone level, and chest radiography were within normal limits. Cerebrospinal fluid was clear with normal cell count, proteins and glucose, and tests for viral studies were negative. Urine and stool studies were normal. Electroencephalogram has shown a normal background activity, without any obvious epileptic and slow wave discharges. Similarly CT Scan of head also revealed normal findings. The possibility of cytogenetic studies including examination of

chromosomes was discussed with his parents and as they were willing to have this test done were referred to Delhi, which ultimately revealed the findings of partial deletion of chromosome 5. Considering all these available information a final diagnosis of "Cri du Chat Syndrome" was made. The possible prognosis was explained and was suggested to have regular follow-up at local Primary Health Centre. Till the time of reporting the seizures and behavioural problems are under control.

Discussion

This 6-year-old patient who was frequently consulted to many physicians and neurologist with a history of multiple epileptic fit even in a single day since the age of one, had a very typical phenotypic characteristics: delayed language and motor development, physical growth retardation, small jaw, oblique palpebral fissure and behavioural problems suggestive of hyperactivity and distractibility. His characteristic high pitched sounds and cat-like cry in association with the above mentioned symptoms were sufficient enough to raise the possibility of Cri du chat syndrome, a rare but one of the causes of very severe mental retardation, which was later substantiated by the reports of cytogenetic study, which revealed the finding of a partial deletion of short arm of chromosome 5.

Cri du chat syndrome is a rare condition that occurs in approximately 1 in 50,000 live birth; the majority of the affected newborn are females, however, the survival rate appears to be better for males than for females and the majority of affected infants surviving into late childhood or even early adulthood are boys (Graham *et al*, 1999). Mental retardation is an invariable feature of this syndrome (Fehlow & Tennstedt, 1989; Shoner & Mitchell, 1991; De-Michele *et al*, 1993; Cornish & Munir, 1998). However, in contrast to this, Cornish (1996) described the cognitive and behavioural profile of an 11-year-old female with cri du chat syndrome who displayed no evidence of severe learning disability as her cognitive performance indicated good verbal skills with specific strengths on those tasks that require the ability to store and retrieve verbal information vs poor non-verbal, spatial skills, and weaknesses on those tasks that require multi-step manipulation of spatial stimuli and the ability to form whole percepts from fragmentary parts. Although the majority of individuals with a partial deletion of short arm of chromosome 5 presents with features of hyperactivity and distractibility, a vast proportion of others with translocation may present with autistic-like features and social withdrawal (Dykens & Clarke, 1997). The basic chromosomal defect in affected children is a partial deletion in 15-18 per cent of the short arm of one homologue of chromosome 5 (Malaspina *et al*, 1992; de-Michele *et al*, 1993). Invariably the two distal bands 5p14 and 5p15 are missing in affected individuals. Many cases occur sporadically, but about 15 per cent of cases have been reported as due to abnormal segregation of a balanced reciprocal translocation in one or other parent (Malaspina *et al*, 1992). The identity of other participating chromosome is variable. Mosaicism for the deletion has also been described, with affected patients apparently showing all the features of the full syndrome, as do those with a ring 5 chromosome. Pericentric inversion of chromosome 5 has also been associated with the syndrome (De-Michele *et al*, 1993).

The pathogenesis of abnormal cry in people with cri du chat syndrome is still obscure and is a matter of great debate. De-Michele *et al* (1993) have found the features of hypoplasia of the vermis associated with dysgenesis of the corpus callosum in MRI Scan of a 6-year-old girl with typical phenotypic and karyotypic characteristics of cri du chat syndrome and, suggested that the cerebellar damage is involved in the pathogenesis of the abnormal cry and of the cognitive and behavioural dysfunction. This hypothesis was challenged by Shoner & Mitchell (1991) who have reported that the phonetic development is quite delayed and this could be because of the significant cognitive and/or motor delays which might have an influence on the integrity of early vocal development. The individuals with cri du chat syndrome not only present with typical dysmorphias and delayed physical and mental development but also manifest severe affective instability and irritability

(Fehlow & Tennstedt, 1989), and also symptoms of schizophrenia and refractory epilepsy (Malaspina *et al*, 1992).

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