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Cri-du-Chat Syndrome: A Case Report

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ABSTRACT

This study presents a case report of 11 month old female exhibits Cri-du-Chat syndrome (CdCs). Karyotyping shows partial deletion of chromosome 5p [46, XX, del (5) (p13, p15.3)].Children with Cri-du-Chat syndrome usually exhibit low weight, microcephaly, micrognathia, typical cat like cry, abnormal dermatoglyphics. Other associated problems described include cardiovascular, renal, gastrointestinal, neuroanatomical abnormalities. Behavioral characteristics associated with CdCs include aggressiveness and self injurious, stereotyped behavior, and hyperactivity. Speech and language evaluation revealed poor pre-linguistic, receptive as well as expressive delay. Radiological and electrophysiological findings show correlation with other diagnostic results. We focuses the rehabilitation from two perspectives i.e., medical and non medical. Medical rehabilitation, which expeditious the improvement in all aspects of developmental milestones in general. Whereas non-medical rehabilitation were recommended for motor, neurological, behavioral, speech and language problems. We used multisensory approach along with rhythmic intonation patterns to improve receptive as well as expressive vocabulary. This study highlighted multidisciplinary team approach aggravates improvement in pediatric cases. Early intervention in CdCs helps to achieve an accurate prognosis, rapid acquisition of psychomotor development, and better social adaptation.

Key words: Cri-du-Chat, multisensory, multidisciplinary, early intervention

INTRODUCTION

The Cri-du-chat Syndrome (CdCs) is a rare genetic syndrome first described by Jerome Lejeune in 1963, characterized mainly by the high pitched Cat like cry. The prevalence of CdCs was varied in between 1:15,000 to 1:50,000 in live births (Mainardi, 2006) and more common in females with a ratio of 4:3 (Chen, 2015).

Children with cri-du-chat syndrome usually exhibit low weight (mean weight 2614 g), microcephaly (mean head circumference 31.8 cm), micrognathia (96.7%), typical cry (95.9%), abnormal dermatoglyphics (transverse flexion creases) (92%), epicanthal folds (90.2%), large nasal bridge (87.2%), round face (83.5%), hypertelorism (81.4%), down-turned corners of the mouth (81.0%), downward slanting palpebral fissures (56.9%), and low-set ears (69.8%) (Mainardi, 2006). The condition may be accompanied by developmental and cognitive delays, poor spatial awareness, impaired ambulation, and poor sensorimotor skills. Other associated problems described include cardiovascular, renal, gastrointestinal, vegetative, neurological abnormalities, preauricular tags, syndactyly, hypospadias, and cryptorchidism (Mainardi et al., 2006). Chen (2006) described all clinical features manifested in CdCs which mentioned in Appendix 1. Recent literatures show that autistic behaviours are common in various genetic disorders (Firat et al, 2018). Fatigue level of children with cri du chat syndrome was associated with the expression of autistic features (Claro et. al., 2011).

CASE REPORT

An 11 month-old female came with a complaint of delay in attaining motor and speech milestones. She was born up for a non-consanguineous parentage. Paternal and

maternal age at conception was 30 years and 29 years respectively. Mother had an antenatal bleeding (first trimester) and oligohydramnios were detected. The child delivered through caesarean 17 days before Estimated Date of Confinement (EDC) and kept in Neonatal Intensive Care Unit (NICU) for four days. The birth weight was 2.1 kg). The baby had suckling problem and because of the inadequacy of breast feeding, an alternative feeding was introduced. The delay in speech and motor milestones was observed (Neck control and turn over were attained at 8 months and 9 months). She had poor speech and language milestones (cooing attained in 2-3 months, but babbling and other mono-tonic sounds were not attained. She was immunized up to the age.

On 11 months of age, Child presented with facial dismorphism, microcephaly, retrognathic mandible, depressed nasal bridge, downward-slanting palpebral fissures, bilateral low-set ears, high arched palate, and simian crease on both hands. She weighed 6.5 kg and her occipito-frontal circumference was 40 (46.5) cm at 11 months. She had difficulty in swallowing, and a distinctive cat-like cry was obvious. On detailed physical examination, gross congenital malformation (pes planus) was observed. She was hypotonic and Left hand preference was observed. She showed certain abnormal motor stereotyped behaviors, self injurious behaviors, vacant stairs, and temper-tantrums.

Speech and language evaluation revealed poor pre-linguistic skills like eye-eye contact, response to name call and less attentive to common environmental stimulus. Child has no verbal communication and her expressive language was limited to cooing, vocalization, and differential vocal turn. Language test (Receptive and Expressive Emergent Language Scale; REELS) at 11 months showed that receptive and expressive language ages were that of 4-5 months' and 2-3 months' respectively. Behavioral Observation Audiometry was within normal limits.

The patient was recommended for detail genetic evaluation and the test results revealed that partial deletion of chromosome 5p [46, XX, del (5) (p13, p15.3)]. Parents had a normal karyotype. The child was diagnosed with CdCs with global developmental delay.

Electroencephalogram (EEG) at 11 months revealed epileptiform discharges. Magnetic Resonance Imaging (MRI) revealed pontine hypoplasia, thinning of corpus callosum, and reduced myelination in both the anterior limbs of internal capsule. Mild diffuse atrophy of the deep white matter of bilateral cerebral hemispheres. There was normal myelination of white matter in the cerebellar hemispheres. Routine hematological examination including blood sugar, serum - urea creatinine, liver function, renal function and thyroid function also showed normal results.

DISCUSSION

Karyotyping is considered as a gold standard for every genetic disorders including CdCs. Distal of p15.3 region was implicated by abnormal gene expression in anomalous cerebral lateralization which implicate that it is a separate region for the speech delay. Such individuals used to exhibit overall developmental delay with complete absence of speech (Tesner et al., 2018). Collins & Cornish (2002) postulated that subjects with deletion in 5p15.3 had a milder degree of cognitive impairment and behavioral problems than those with deletion in p15.2. Behavioral characteristics associated with CdCs include hyperactivity and self injurious, aggressive, and stereotyped behavior (Cochran et al., 2015). The case which we dealt with also exhibited autistic features (stereotyped behaviours, self injurious behaviors, vacant stairs, aggressiveness) and CARS score got as 31.5 [mild-moderately severe] .

Majority of cases with Cri-du-Chat syndrome shows radiological findings as

brain stem hypoplasia, mainly involving the pons (Ninchoji et al 2010, Uzunhan et al 2014, Hong et al 2013, Tamraz et al 1993, De Michele et al 2009). The present study mentioned similar findings like pontine hypoplasia as in the case previous studies, which shows clinical correlations such as affected vegetative & sensory skills, visual deficits(squint & poor visual tracking), respiratory/ breathing difficulties, disturbed sleep cycles, central auditory processing deficits(delayed responses to auditory stimuli suspecting a processing delay), & Equilibrium problems(while standing, walking, occasionally sitting).

The previous imaging studies showed structural abnormalities in brain such as atrophic middle cerebellar peduncles, atrophic cerebellar white matter, vermian (or cerebellar) hypoplasia, thinning (or dysgenesis) of the corpus callosum, reduced myelination in anterior limbs of the internal capsule, and mega cisterna magna (Ninchoji Tet al 2010, Uzunhan TA et al 2014, Hong JH et al 2013). In this present case, MRI at 11 months showed thinning of the corpus callosum (Hyo Jin Lee, et al 2015, Ninchoji et al 2010, Uzunhan TA et al 2014, Hong JH et al 2013). Our current study shows similar clinical correlation with respect to radiological (thinned corpus callosum) finding such as spastic paraplegia by birth, poor bladder control, sensory deficit in general(both upper & lower extremities, facial, etc.), occasional seizure episodes, pyramidal and extra-pyramidal signs along with distal(upper) amyotrophic changes) (Lossos et al, 2006; Halevy et al, 2014; Stevanin & Boukhris, 2008). Similar to the previous research studies, the present case exhibited the signs of lesions in the extrapyramidal system i.e., simple dyskinesias (dysstonia/myoclonus) & complex tics (jumping, lip smacking, repeated/rapid movements)(Nguyen et al 2015).

The radiological findings in Cri-du-Chat syndrome includes, reduced myelination in both anterior limbs of the internal capsule as mentioned in previous studies (Hyo Jin Lee, et al 2015, Hong H J et al, 2013). Hyo Jin Lee, et al (2015) hypothesize that cases with cri-du-chat syndrome exhibited decreased myelination in the anterior limbs of the internal capsule plays a role in the developmental delay. Similarly, the present case has developmental delay, language and cognitive impairment with respect to the results from Receptive and Expressive Emergent Language Scale (REELS). The diffused atrophy of the white matter in the bilateral cerebral hemispheres also leads to impairment in cognitive & linguistic skills. The radiological findings has major role in diagnosing cri-du-chat syndrome (Hyo Jin Lee, et al 2015), especially later (adolescence or adult) stage in life. However, there needed to be further more studies to explain the clinical correlation with radiological findings.

EEG at 12months of age showed moderate asymmetry between the activities in the fronto-central regions with no any definite paroxysmal features. Client was under medication on the basis of these detailed clinical evaluations after neurological consultation.

Client was recommended for physical therapy due to delayed motor milestones & hypotonicity. She is able to sit without support after attended almost one year physical training. Crawling and sitting were reported after 1year of old. Routine physical examination showed improvements within one year. Gradually gaining weight, she was 9.2 kg at 22 months.

We introduced thematic presentation through visual and auditory mode ie., multisensory approach along with rhythmic intonation patterns to improve receptive as well as expressive vocabulary. Intelligibility over receptive and expressive language vocabulary increased when visual and auditory input was used together (Erlenkamp and Kristoffersen , 2010). They proclaimed that the interaction between word and sign narrows down the range of possible targets of reference as motor development can impair sign and/or speech.

Campbell (2010) proposed that children have a natural propensity to move, clap, dance, and sing out loud when a rhythm or melody appeals to them. Winters and Griffin (2014) assumed that music has the power to enhance children's lexical acquisition at various levels of development. Musical intervention was also used in an effort to develop verbal and non-verbal communication. In recent studies, researchers believed that music will create a relaxed atmosphere and would enhance language learning (Zoghi and Shoari, 2015; Heidari and Araghi 2015). Cırık & Efe (2018) stated that music therapy is an effective method to improve learning.

We tried to reinforce this innateness and make the child engaged in hum music with meaningful bodily movements (clap, tap, move) in order to fadeout the unwanted motor stereotypes. Follow-ups after 4-5months revels improvements in the behavioral issues, during post therapeutical assessment with CARS ratings scores i.e., 26 [non autistic].

Client underwent intensive speech and language training along with music therapy, made her capable of saying single words consistently at 18months. Successively her vocabulary improved and attained seven words (consistent). She also started using some words with meaningful actions. She is able to hum music with rhythmic body movements. REELS administration at 23 months reported that receptive and expressive language ages were of 18-20 months' and 14-16 months respectively. 3Dimensional Language Acquisition Test (3DLAT) revealed that 12-14 months of age for reception and expression and 9-11 months of age for cognition.

CONCLUSION

In conclusion, the rehabilitation procedure focused on two perspectives i.e., medical and non medical. Medical rehabilitation, expeditious the improvement in all aspects of developmental milestones in general. Whereas non-medical (physical therapy, speech therapy, music therapy) rehabilitation were recommended for motor, neurological, behavioral, speech and language problems. Multidisciplinary approach is necessary in both diagnosis and treatment (Firat et al, 2018) which has to, have a positive impact on improvement in pediatric cases.

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APPENDIX I

Clinical Features [Chen H. (2006)]	
During infancy	A. Low birth weight B. Cat like cry C. Hypotonia D. Microcephaly E. Poor in vegetative skills F. Need for incubator care G. Respiratory distress H. Jaundice I. Pneumonia J. Dehydration K. Growth retardation L. Early ear infections M. Severe cognitive, speech and motor delays N. Facial features i. Hypertelorism ii. Epicanthal folds iii. Down-slanding palpebral fissures iv. Strabismus v. Flat nasal bridge vi. Down-turned mouth vii. Low set ears O. Cardiac defects i. VSD

	ii. ASD iii. PDA iv. Tetralogy of fallot P. Short fingers Q. Single palmar creases R. Less frequent features i. Cleft lip and palate ii. Preauricular tags and fistulas iii. Thymic dysplasia iv. Gut malrotation v. Megacolon vi. Inguinal hernia vii. Dislocated hips viii. Cryptorchidism ix. Hypospadias x. Rare renal malformations a. Horseshoe kidneys b. Renal ectopia or agenesis c. Hydronephrosis xi. Clinodactyly of the fifth fingers xii. Talipes equinovarus xiii. Pes planus xiv. Syndactyly of the second and third fingers and toes xv. Oligosyndactyly xvi. Hyperextensible joints
In childhood	A. Severe mental retardation B. Developmental delay C. Microcephaly D. Hypertonicity E. Premature graying of the hair F. Small, narrow and often asymmetric face G. Drooped jaw H. Open-mouth expression secondary to facial laxity I. Short philtrum J. Malocclusion of the teeth K. Scoliosis L. Short third-fifth metacarpals M. Chronic medical problems i. Upper respiratory tract infections ii. Otitis media iii. Severe constipation
In late childhood and adolescence	A. Coarsening of facial features B. Prominent supraorbital ridges C. Deep-set eyes D. Hypoplastic nasl bridge E. Affected females reaching puberty and developing secondary sex characterstics and menstruste at the usual time F. Small testis and normal spermatogenesis in male
Dermatoglyphics	A. Transverse flexion creases B. Distal axial triradius C. Increased whorls and arches on digits
Behavioral profile	A. Hyperactivity B. Aggression C. Tantrums D. Stereotypes E. Self injurious behavior F. Repetitive movements G. Hypersensitivity to sound H. Clumsiness I. Obsessive attachments to objects J. Social communication

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