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Case Report
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CHILD WITH MILLER-DIEKER SYNDROME SURVIVING MORE THAN A DECADE: RARE INSTANCE IN LITERATURE

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Abstract:
Miller Dieker Syndrome (MDS) is characterized by abnormal brain development and lissencephaly. As a result, babies have severe intellectual disability, developmental delay, multiple seizures and hypotonia. Characteristic facial features and mental retardation is indicative of a karyotypic evaluation. Microdeletion of chromosome 17p13.3 confirms the diagnosis. Management includes genetic counselling, frequent medical check-up, palliative treatment with physiotherapy and seizure control.

Introduction

It is indeed rare to find a baby with Miller-Dieker Syndrome (MDS) survive healthy beyond a decade [1]. They succumb to death mostly due to aspiration of food or fluids, respiratory distress or status epilepticus. Till date, maximum age attained was 17 years [1]. We report a case of MDS who is presently 12 years of age and is currently bedridden. Developmental milestones are equivalent to a 6 to 9-month infant. Dedicated parental care, physiotherapy and continued medical consultations have helped her to survive more than a decade.

Case Report

A 42 year-old third gravida with previous 2 vaginal deliveries reported to a tertiary care institute hospital for antenatal booking. Her first child was 12 years old and had global mental retardation. Antenatal and intrapartum period was uneventful. Pregnancy was not adequately supervised. No aneuploidy screening and anomaly scans were done. There was spontaneous onset of labor at term and she gave birth to a live born girl of 2.3 kg with good Apgars. Baby was apparently well for the first 6 months. Parents gradually noticed that the infant was having poor neck holding reflexes. Suspicion profounded when baby was unable to sit without support even at 1 year of age. It was at this time when paediatric and genetic consultations were taken. A detailed evaluation was done. Routine blood investigations were within normal limits. There were no inborn errors of metabolism. Meanwhile, she had multiple episodes of unprovoked seizures for which MRI brain was done which showed global flattening of gyri and sulci suggestive of lissencephaly. A sedated electroencephalogram (EEG) showed disorganized background rhythm with multifocal spikes and sharp slow wave discharges. There were periods of electrodecremental responses in between bursts of generalized discharges suggestive of modified hysparrhythmia. A Fluorescent in-situ hybridization with locus specific indicator probes revealed the presence of microdeletion of chromosome 17p13.3 [Figure 1].

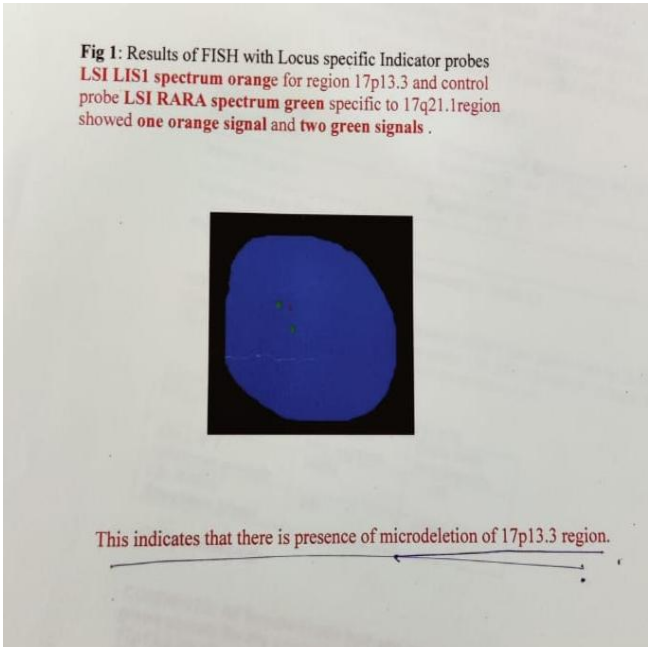

Figure 1: FISH showing microdeletion of chromosome 17p13.3

Following the diagnosis of MDS, parents were explained about the morbidity associated with this chromosomal disorder. Palliative treatment with physiotherapy was soon initiated. However, developmental milestones were poor and baby is hardly able to sit for a few minutes unsupported. Currently she is bed ridden for the past 12 years. While most children of MDS succumb to death by 10 years of age, this child luckily survived upto 12 years Figure 2.

Figure 2: Child with MDS surviving successfully upto 12 years of age.

Second pregnancy was uneventful. Amniocentesis was performed in antenatal period and as fetal karyotype was normal, so pregnancy was continued. Baby was delivered by vaginal delivery. Neonatal and childhood period were uneventful and baby has attained all developmental milestones till present age of 5 years.

In the index pregnancy, all antenatal investigations were normal. Fetal aneuploidy screen and anomaly scan were normal. Amniocentesis and fetal karyotype were also normal. Genetic consultation was taken. Parents reassured and pregnancy continued till term. She delivered vaginally a live born boy of 2.8 kg with good Apgars.

Discussion

Several deletions of chromosome 17p13.3 regions have been detected [2]. Most cases are not inherited and occur randomly. Few cases are being reported to be caused by balanced translocation from either parents. Clinical manifestations depend upon the size of the microdeletions. It is found that a larger deletion of the distal arm of chromosome 17 is primarily associated with MDS [2]. This syndrome is characterized by dysmorphic facial features, childhood growth retardation and lissencephaly. Facial features include bitemporal hollowing, prominent forehead, downslanting palpebral fissures, epicanthal folds, broad nasal root with upturned nares, low-set ears, midfacial hypoplasia, protuberant upper lip with thin vermilion border and a small jaw [3]. Clinically, infants present with psychomotor retardation, multiple seizure episodes, opisthotonus, feed intolerance resulting from swallowing difficulties and failure to thrive. Certain rarer abnormalities like renal and cardiac malformations, omphalocele, limb contractures and clinodactyly of 5th digit [3].

In a series of cases, with deletions including YWHAE, babies presented with neurocognitive impairment, childhood growth retardations, cognitive impairment, craniofacial features but no lissencephaly [4]. One patient in the group did not have any growth restriction. It was found that CRK gene was responsible for growth restriction [5]. Conversely, YWHAE gene encoding tyrosine 3-monooxygenase is believed responsible for the brain findings.

Babies present with multiple seizures. MRI studies show microcysts in the white matter and corpus callosum, ventricular dilatation, enlargement of subarachnoid spaces and Arnold-Chiari type 1 malformation [3,5,6].

Patients should undergo formal developmental evaluation. Brain MRI studies are recommended to determine the presence of neurological abnormality. Neurological evaluation with EEG and ophthalmological evaluation are also recommended.

Majority of the babies do not live more than 2 years, with only a handful of them reaching upto 10 years. Index baby is 12 years and is thus worth reporting. According to J Child Neurol, the oldest known case survived upto 17 years [5]. Life expectancy is proportional to the degree of lissencephaly, most common cause of death being aspiration pneumonia due to airway dysfunction.

Global developmental delay is almost universal [7]. The highest developmental level in affected children is equivalent to that of a 3 to 5-month old baby, even with good seizure control. In rare instances, the child may be able to sit without help. Those having poor seizure control may have developmental milestones equivalent to a neonate [7].

Conclusion

With a renaissance in medical knowledge and physiotherapy in last 2 to 3 decades, lifespan of MDS babies have increased manifold. Symptomatic management with gastrostomy, seizure prophylaxis drugs, tracheostomy and suction machines have helped in improving the quality of life. Some children may be able to sit up, crawl or say a few words. Nevertheless, respiratory distress and aspiration pneumonitis remain the commonest cause of death.

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