"Chiari II malformation with Trisomy 18 – A rare bird

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Abstract

Studies have revealed an association of neural disfigurement with trisomy 18. Hereby, we report a rare coalition of Trisomy 18 and Arnold Chiari malformation along with myelomeningocele in a premature neonate. Despite managing hydrocephalus, the patient' condition deteriorated over time due to underlying cardiothoracic defects.

Chiari II malformation with Trisomy 18- A rare bird

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ABSTRACT

Studies have revealed an association of neural disfigurement with trisomy 18. Hereby, we report a rare coalition of Trisomy 18 and Arnold Chiari malformation along with myelomeningocele in a premature neonate. Despite managing hydrocephalus, the patient' condition deteriorated over time due to underlying cardiothoracic defects.

KEYWORDS

Arnold Chiari II Malformation, Trisomy 18, Myelomeningocele, Hydrocephalus

KEY CLINICAL MESSAGE

Although treating hydrocephalus has proven to be a successful management option for symptomatic Chiari II disfigurement, but concurrent illnesses, particularly cardiothoracic defects call for prompt management to reduce morbidity and mortality.

INTRODUCTION

Trisomy 18 is a rare eugenic aneuploidy with an estimated incidence of 1:3500 to 1:8000 newborns. The fatality rate is massive among these patients with less than 10% survival incidence over one year[1]. The occurrence of an unwanted additional genetic material on chromosome number 18 gives rise to myriad of congenital abnormalities, growth retardation, and prominent cognitive defects[2]. Studies have revealed an association of neural disfigurement with trisomy 18. Hereby, we report a rare coalition of Trisomy 18 and Arnold Chiari malformation along with myelomeningocele.

Arnold Chiari Malformation II is the herniation of the hindbrain through the foramen magnum compressing the cervical spine. Identified based on cerebral gyration, dysmorphic corpus callosum, and hydrocephalus and manifesting with symptoms including dysphagia, motor insufficiency, and stridor, ACM II is believed to be stringently linked with myelomeningocele[3, 4]. The frequency of myelomeningocele varies 0.2 to 2 per 1000 live births that may result in diverse clinical presentations, including hydrocephalus[6].

The complications arising secondary to myelomeningocele encompass seizures, learning deficits, cognitive impairment, sensory diminution below the level of lesion, bowel dysfunction, neurogenic bladder with recurrent Infection and decreased mobility due to associated muscle weakness[6]. Early diagnosis can help in paring down the severity and subsequently the death rate, further assisting in the management of such patients.

CASE PRESENTATION

A newborn girl was delivered at 35 weeks by emergency C-section due to non-reassuring fetal heart rate tracings and intra-uterine growth restriction. The mother was 39 years old at the time of delivery and had a past obstetric history of spontaneous abortion of a fetus with Trisomy 22. Prenatal ultrasound revealed polyhydramnios, an atrial septal defect, a horseshoe kidney, and severe intrauterine growth restriction (<1st percentile). The mother had received penicillin for group B streptococcal infection and corticosteroids for lung maturation at 30 weeks of gestation.

The patient was diagnosed with Trisomy 18 via non-invasive prenatal testing (NIPT). She was born after a third pregnancy. Her APGAR scores were 5 and 8 at 1 and 5 minutes, respectively. Physical examination revealed dolichocephaly, a prominent occiput, microstomia, nasal hypoplasia, a short-webbed neck, malformed ears, pectus carinatum, and clenched fists overlapping fingers, large lumbosacral myelomeningocele, and talipes equinovarus with rocker-bottom feet. Vital signs were: weight, 1.45kg; temperature, 100.4°F; heart rate, 171 beats/ min; respiratory rate, 52 breaths/ min; blood pressure, 52/84 mmHg; and oxygen saturation, 100%. Neurological examination revealed the spontaneous movement of bilateral upper extremities, no movement and decreased bulk in the lower extremities, and 2+ reflexes at biceps, patella, and ankle, with intact cranial nerves and sensation. The rest of the systemic examination was unremarkable. The anus was patent, and she passed meconium within the first 24 hours. She was immediately intubated and placed on synchronized intermittent mandatory ventilation (SIMV). An orogastric tube (OGT) was attempted, but the tube did not pass beyond 6 centimeters.

Laboratory profiles, including complete blood picture (CBC), serum urea, creatinine and electrolytes, and coagulation profile, were routinely monitored during admission. The test results were unremarkable except for low platelet count (94x103/μL) and increased creatinine levels (0.81 mg/dl), observed on the second day of admission, which subsequently achieved normal limits. Urine output was 3.3 ml/kg/hr. TORCH panel was negative. Lumbar puncture was performed (opening pressure was not measured), and cerebrospinal fluid (CSF) appeared red due to traumatic tap (1000 RBCs to 1 WBC ratio), while the remaining indices were clinically insignificant. CSF cultures and meningitis/encephalitis panel PCR were negative. A postnatal karyotype analysis confirmed 47 XX +18, consistent with the diagnosis of Trisomy 18. On chest x-ray, OGT was seen in the upper part of the chest and air trapped in the gastrointestinal tract, which portends to

esophageal atresia with a tracheoesophageal fistula.

The head ultrasound shows crowding of the posterior fossa, effacement of the fourth ventricle, interdigitation of the gyri along the cerebral falx, a dysmorphic corpus callosum, and mild to moderate supratentorial hydrocephalus (Fig.1). These findings were consistent with the diagnosis of Chiari type II malformation. No signs of intracranial hemorrhage were evident. An abdominal ultrasound was also performed, showing small echogenic kidneys with mild right pelvicaliectasis and a large, left lateral, diaphragmatic focal eventration. A transthoracic echocardiogram showed a significant ventricular septal defect, tricuspid valve dysplasia, large patent ductus arteriosus, and a fenestrated patent foramen ovale which was followed up by the cardiology team.

The patient was strictly NPO, and a low continuous suction tube was maintained with a Replogle tube. She was managed with palliative care and empirical antibiotic therapy (ampicillin and gentamicin) until the surgical closure of open myelomeningocele. The attending doctor discussed the patient's poor prognosis with parents who expressed understanding and were coping with their daughter's trajectories. With the parent's consent, surgical repair of myelomeningocele and right-frontal reservoir placement for hydrocephalus proceeded which was well-tolerated. The neurosurgery team continued to follow up. The head circumference was measured, and CSF analysis via the reservoir was evaluated daily for six days post-operatively.

The pediatric surgeon was consulted for transesophageal repair, gastrotomy, and bronchoscopy. Orthopedic surgery consultation was sought about rocker-bottom feet. The patient was under observation for two months, but her condition has deteriorated over time due to cardiothoracic defects.

DISCUSSION

Trisomy 18, often known as Edward syndrome, is an unusual genetic disease, manifesting as multi-system anomalies. Recognized since 1960, Trisomy 18 was initially delineated by Edwards and associate as trisomy 17, and concomitantly by Smith and colleagues as trisomy 18. The appearance of an extra autosome disrupts the stability of the gene resulting in several developmental oddities[7].

Literature reveals that females have a higher probability of embracing this syndrome with a male to female ratio of 1:3. Moreover, an average maternal age, typically more than 34.3 years is frequently associated. In addition, intrauterine growth retardation is an idiosyncratic trait for this syndrome that follows fetal discomfort leading to high rates of emergency cesarean section in such conditions. All these elements were present in our case with maternal age of 39 years and a female baby with severe IUGR, delivered through an emergency C-Section; hence corroborating with the findings from past studies[8].

Classic associations including acyanotic heart defects, diaphragmatic eventration, tracheoesophageal fistula, horseshoe-shaped kidney, spina bifida with myelomeningocele, dolichocephaly, pectus carinatum, clenched fists with overlapping fingers, and talipes equinovarus with rocker bottom feet were established as in the past literature[2, 9]. However, Arnold Chiari Malformation type II was the most striking manifestation confirmed on cranial ultrasound. Ultrasonic features like posterior fossa crowding, interdigitation of the gyri, dysmorphic corpus callosum, and effacement of the fourth ventricle along with supratentorial hydrocephalus were consistent with the findings of a previous study[4].

The association of trisomy 18 with Arnold Chiari Malformation is a rarity with only two published case reports to the best of our knowledge so far[4, 8]. Although growth and evolutionary inadequacy of CNS can be due to various etiologies, but the threshold for acquiring several defects is decreased with increasing dysraphism in trisomy 13. Subsequently, it is also suggested that certain subsidiary genes causing neural tube defects are located on chromosome 18, therefore, providing a possible rationale for this association[10].

Chiari II malformation mostly occurs with myelomeningocele, a spinal rachischisis occurring as a consequence of neural tube defect. Myelomengiocele is associated with Arnold Chiari malformation and hydrocephalus in 80-95% of the cases[11]. Even though a small number of studies have promulgated hydrocephalus with trisomy 18, the rationale was non-significant and without any autopsy authentication. Mild to moderate supratentorial hydrocephalus was possibly present in our case secondary to Arnold Chiari malformation as

suggested by ME Case[4]. Earlier, direct hindbrain decompression was the mainstay treatment but after recent advancements, treating hydrocephalus has proven to be a successful management option and an epitome for curing symptomatic Chiari II disfigurement as done in our study[3].

CONCLUSION

Babies born with trisomy 18 present with a wide array of malformations including, craniofacial, limb, kidney, cardiac, and neurological defects. Such complex medical problems can be life-threatening. Albeit, current technological advancements have enabled prompt diagnosis of trisomy 18, but management has always been a conundrum due to several ailments. Arnold Chiari II malformation with concomitant myelomeningocele is usually associated with trisomy 18. Surgical repair of myelomeningocele and right-frontal reservoir placement for hydrocephalus can improve the patient's condition and extend survival. However, cardiothoracic defects may lead to early mortality.

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CONFLICT OF INTEREST

None declared by any of the authors.

AUTHOR CONTRIBUTIONS

Sadia Yaqoob: Involved in data analysis, interpretation, literature review, drafting and revision of the manuscript.

Amna Saleem: Involved in data analysis, interpretation and drafting of the manuscript.

Vikash Jaiswal: Involved in data collection and drafting of the manuscript.

Samir Ruxmohan: Involved in data collection and interpretation, and final revision of the manuscript.

Christine Zakhary: Involved in data collection and revision of the manuscript.

ETHICAL STATEMENT

We confirm that the manuscript has been read and approved by all the authors. Informed consent was obtained from parents of the patient regarding the publication of case.

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FIGURES

Figure 1: Cranial ultrasound of neonate showing supratentorial hydrocephalus and dysmorphic corpus callosum.