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CASE REPORT

Emanuel Syndrome in Infants: Case Report

João Batista Siqueira de Albuquerque Neto[1], Marcelo José Duque Pacheco Filho[1], Ana Alves de Oliveira Melo[2], Camila Fonseca Leal de Araújo[3], Gabriela Ferraz Leal[3]

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Abstract

Introduction: Emanuel syndrome is a rare genetic disease caused by the presence of a supernumerary derivative chromosome that contains material from chromosomes 11 and 22. This imbalance usually results from a 3:1 malsegregation of a parental balanced translocation between chromosomes 11 and 22. The clinical findings include weight and height changes, persistent hypotonia and cognitive impairment. Diagnosis is confirmed by G-banding karyotype and/or CGH array/SNP array. **Case report:** This work describes the case of an 11-month-old child treated at a tertiary center for the investigation of global hypotonia and neuropsychomotor development delay, who presented pre-auricular appendages, epicanthus and cleft palate (already repaired at the time of medical consultation). A karyotype was performed, with a result of 47,XX,+mar and a Microarray was performed, which showed duplications involving chromosomes 11 and 22, characterizing Emanuel Syndrome. At the moment, he remains under the care of the multidisciplinary team, with improvements in his neurodevelopmental milestones. **Conclusion:** The clinical manifestations of Emanuel syndrome are relatively common inpediatrics, and it is in the general pediatricians interest to identify when these ?ndings may correlate with a genetic syndrome. This research was submitted to the Ethics Committee of the monitoring service and approved by number: 76760623.9.0000.5201.

[1] Faculdade Pernambucana de Saúde, Medicina - Recife - Pernambuco - Brazil.
[2] Centro Universitário Maurício de Nassau, Medicina - Recife - Pernambuco - Brazil.
[3] Instituto de Medicina Integral Professor Fernando Figueira, Departamento de Pediatria - Recife - Brasil - Brazil.

Correspondence to:
João Batista Siqueira de Albuquerque Neto.
Faculdade Pernambucana de Saúde. Av. Mal. Mascarenhas de Morais, 4861, Imbiribeira, Recife, PE, Brazil. CEP: 51150-000.
E-mail: jnetoalbuquerque@hotmail.com

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INTRODUCTION

Emanuel syndrome (ES) is a rare genetic disorder caused by the presence of a derivative supernumerary chromosome that contains material from chromosomes 11 and 22. This supernumerary chromosome usually results from the 3:1 meiotic nondisjunction of a balanced translocation between chromosomes 11 and 22, which is present in one of the parents of affected individuals. For this reason, this condition is also known as supernumerary der(22)t(11;22) syndrome.[1] The incidence and prevalence of this syndrome are not precisely known, but it is estimated that two cases occur in every 100,000 births.[2]

Patients typically present with low birth weight, generalized hypotonia, and global developmental delay. They experience difficulties with sucking and ingesting food. Gastroesophageal reflux disease is also prevalent, further hindering weight and height gain. Approximately half of the patients are born with a cleft lip and/or palate.[2] Craniofacial alterations, such as microcephaly, a prominent forehead, dysmorphic ears, preauricular appendages, and ocular abnormalities, have been reported. Congenital heart defects, including atrial septal defect (ASD) and ventricular septal defect (VSD), occur in more than half of the cases.[3] Cognitive impairment has also been noted. Those affected generally do not develop spoken language; however, they can express emotions and desires through body language, voice, and facial expressions. Brain malformations, including agenesis of the corpus callosum, and kidney abnormalities have also been documented.[2]

Primary diagnostic methods include high-resolution G-banded karyotyping, chromosome microarray analysis, and targeted duplication analysis using fluorescence in situ hybridization.[4] A high-resolution G-banded karyotype showing a marker chromosome and microarray analysis detecting duplications of segments of chromosomes 11 and 22 confirms the diagnosis.[5] Typically, one of the parents carries a balanced translocation between chromosomes 11 and 22, which is the most common non-Robertsonian translocation in humans. Individuals with this translocation are generally asymptomatic, but they may have children with an unbalanced karyotype due to defects in meiotic segregation.[1]

Given the wide variety of clinical signs and symptoms associated with Emanuel syndrome, individuals with the condition should undergo early multidisciplinary monitoring to maximize their development and quality of life.[4] Although it is a rare condition, some of the signs and symptoms of Emanuel syndrome, when observed individually or together, constitute common complaints in pediatric outpatient clinics.

This article describes the case of an infant who was seen at the general pediatric outpatient clinic of a tertiary hospital in Northeastern Brazil for global developmental delay and hypotonia, and was later diagnosed with Emanuel syndrome. The article was submitted to the Ethics Committee of the monitoring service, which granted certificate no. 76760623.9.0000.5201.

CASE REPORT

An 11-month-old female infant was taken to the pediatric outpatient clinic of a tertiary hospital for hypotonia and global developmental delay. The mother stated that the child had a weak neck, causing her head to lean to the left or right. She also failed to achieve the expected developmental milestones for her age: she could not sit without support; she held objects during the consultation but did not transfer them from one hand to the other; she babbled but did not form syllables. Physical examination revealed an epicanthic fold on the right eye and a preauricular appendage on the left ear. Neurological examination found global hypotonia predominantly in the axial muscles, with preserved trophism. No deficit in strength during maneuvers was observed, and she had normal, symmetrical reflexes.

The infant was born preterm after 36 weeks of gestation. Her APGAR score was 9/9, and she weighed 2655g, which was deemed appropriate for her gestational age (p50). Her head circumference measured 31.5cm (smaller than expected for her age), and she was 47cm long, which was described as adequate. The mother was 38 years old and developed gestational diabetes during prenatal care. The parents were healthy and non-consanguineous. The infant did not have siblings or a significant family history of disease.

Physical examination at birth revealed a cleft palate (which had been repaired at the consultation), microretrognathia, and overlapping frontoparietal sutures. Echocardiogram results indicated interatrial communication without hemodynamic repercussions and slight narrowing of the aortic isthmus. Head computed tomography scans showed slightly asymmetrical lateral ventricles and an enlarged retrocerebellar space.

Subsequent ultrasound examination of the lumbar spine revealed a posteriorly angulated coccyx. Ultrasound images of the kidneys and urinary tract showed no abnormalities. An investigation was initiated with the Genetics department, yielding a karyotype result of 47, XX, +mar. An SNP array was then performed, demonstrating duplications involving chromosomes 11 and 22, which characterize Emanuel Syndrome.

The patient was placed on a follow-up program with the General Pediatrics team. At 1 year and 5 months of age, she had not gained weight or grown as expected. Her parents received guidance and were asked if an underlying disease or a recent infection had caused the infant's failure to thrive. Her condition further deteriorated during the following visit, going from a Z score of 0 to close to a Z score of -2. Monitoring was intensified with the addition of a multidisciplinary care team, which included a general pediatrician, a geneticist, and a physiotherapist. The child resumed growing and reached several developmental milestones: at 2 years and 7 months, she exhibited a pincer grasp, played with objects, and walked with support. She displayed a social smile but had not developed speech and was still reduplicant.

DISCUSSION

This is a rare syndrome with few descriptions in the literature. Phenotypic findings vary; those observed in our patient have been documented in medical articles. Since no specific ultrasound markers are available in prenatal care, most individuals with Emanuel syndrome are diagnosed after birth. A retrospective analysis found that approximately 80.9% of individuals with Emanuel syndrome have central nervous system alterations on ultrasound examination.[1]

Although no alterations were detected in prenatal care, the neuroimaging findings at birth were consistent with the pattern indicated in the other tests. As described in the literature, an atrial septal defect was identified on the echocardiogram.

Other frequently described alterations include left diaphragmatic hernia, kidney defects, and fetal growth restriction, which our patient did not have.[1] The infant had trouble growing and gaining weight for reasons other than acute complications, and this was resolved after optimizing follow-up with a multidisciplinary team and introducing a proper diet.

Our patient has been monitored by a multidisciplinary team since birth, facilitating a collaborative approach to addressing her multiple signs and symptoms. Continuous care in a tertiary service has allowed for a holistic approach to both patient and family care, emphasizing the improvement of the infant's quality of life.

Once the diagnosis is confirmed, understanding the disease and its various clinical repercussions is essential for proper multidisciplinary follow-up. To date, the precise mortality rate and prognosis of Emanuel syndrome are unknown; however, many patients survive into adulthood when well monitored and provided appropriate care.[1]

CONCLUSION

Pediatricians should always consider genetic syndromes in the differential diagnosis of global developmental delay associated with facial and organ malformations. Emanuel syndrome is a rare yet possible diagnosis. Failing to identify individuals with this condition early on may postpone the introduction of treatment and multidisciplinary care. Once initiated, effective care leads to noticeable improvements in the child's growth, development, and quality of life.

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