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# Edwards Syndrome: Family positive effects when life survival surpasses the expectation. Case report.

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**Abstract.** *Aim:* Reporting the case of a patient with Edwards syndrome of above-average survival. Edwards syndrome is a chromosomal disorder with multiple and severe congenital malformations, a profound delay in neuropsychomotor development, and an average survival of around 2.5 to 14.5 days. *Description:* Patient age of seven years and six months, female, who presented at birth, congenital heart disease, microcephaly, micrognathia, cutis marmorata, pectus escavatum and other typical alterations of Edwards Syndrome. Intensive interventions were performed, and karyotype exam confirmed full trisomy of chromosome 18. The patient currently undergoes intensive occupational and speech-language therapy, physiotherapy, and is stable. *Comments:* Edwards syndrome has a reserved prognosis, and although it is proven that aggressive interventions improve the survival of these patients, there is still no consensus in neonatal resuscitation protocols, and there are differences in perception about prognosis and therapeutic recommendations. However, parental autonomy must always be considered, and it is known that patients who survive to childhood bring positive results in the family circle. The discussion of prognosis and therapy is necessary and should aim at the homogenization of medical conduct.
**Key words:** Edwards Syndrome, Trisomy 18, Survivorship, Medical Ethics

## Introduction

Trisomy 18, also known as Edwards Syndrome, was first described in 1960 by John Edwards, who reported the case of a newborn with "peculiar facies, winged neck, congenital heart disease, neonatal hepatitis and other minor abnormalities", later associating this clinical picture with the extra copy of a small chromosome (EDWARDS, 1960). Trisomy 18 presents characteristic phenotypic changes and has a poor prognosis, since most live births cannot reach adulthood (IMATAKA, 2016).

Behind only Down Syndrome, Edwards Syndrome is the second most common aneuploidy (RASMUSSEN, 2003). Its incidence is estimated at approximately 1/6000 live births; most children die before completing 15 days, and only 5% manage to exceed the first year of life (IMATAKA, 2016) (RASMUSSEN, 2003) (CRIDER, 2008). There is a higher incidence of the syndrome in women, in which a longer survival is also observed. It is important to highlight that the syndrome has high rates of spontaneous abortions during the gestational period, so that the real incidence may be even higher (RASMUSSEN, 2003) (ROSA, 2013) (CEREDA & CAREY, 2012) (DOTTERS-KATZ, 2016).

The clinical picture of Edwards Syndrome is broad, with more than 130 anomalies described in the literature, none of these pathognomonic, although there are certain characteristic clinical signs that are highly suggestive (ROSA, 2013). Among these, we highlight the profound delay in psychomotor development (BATY, 1994b); low birth weight and slow growth (BATY, 1994a); craniofacial, trunk and extremities malformations, in addition to internal organs, especially cardiac, renal and central nervous system abnormalities (BATY, 1994a) (LIN, 2006) (CAREY, 2010) (ROSA, 2013) (ROBERTS, 2016).

Even with high clinical suspicion, the definitive diagnosis can only be made with the detection of a complete or partial trisomy of chromosome 18 through chromosomal studies (CAREY, 2010). Prenatal diagnosis is suspected when typical ultrasound alterations are seen (choroid plexus cysts, overlap of the second and fifth fingers on the third and fourth, respectively), both in the first, (WIECHEC, 2016) (CEREDA & CAREY, 2012) and second trimester (WATSON, 2008), but confirmation

only occurs with karyotype examination. Among other alterations that corroborate the suspicion are low levels of human chorionic gonadotropin, alpha-fetoprotein and non-conjugated estriol in the maternal blood, when compared to the dosage in a non-syndromic fetus pregnancy (CEREDA & CAREY, 2012).

Data in the literature describing the outcome of the development of these syndromic patients are scarce (CAREY, 2010), being restricted to a few case reports (ROSA, 2013). There are no criteria or protocols that define the indication of intensive treatments, and the parents are left with this decision, together with the medical team; although it is known that surgical interventions improve the survival of these patients (NELSON, 2016) (LORENZ,2014) (HURLEY,2014).

**Case presentation**

RVB, female, white, was born in Sinop-MT, on 04/06/2013, cesarean delivery. The mother, 29 years old, married, housewife, primiparous, diagnosed with albinism, denied history of syndromic diseases in the family or consanguinity, and reported having correctly followed up prenatal care and using folic acid since the third month of pregnancy. She reported ultrasound follow-up with increased nuchal translucency (2.6 mm. Reference value: 2.4 mm) at 12 weeks of gestation. She received guidance to proceed with amniocentesis, which was not performed by the patient's desire. On morphological ultrasound examination, there were bilateral choroid cysts, and cardiac malformations were not visualized. RVB was born premature (36 weeks), weighing 2,040kg, measuring 43 cm, head circumference of 33cm, Apgar 3-7, respiratory failure and heart murmur suggesting the presence of malformation. As RVB had a phenotype suggestive of Edwards Syndrome, it was difficult to refer her to an Intensive Care Unit (ICU). The karyotype was collected before ICU admission, along with the other examinations. RVB remained for 8 days in the ICU with a diagnosis of Transient Tachypnea and did not require mechanical ventilation. After discharge from the ICU, she remained in hospital for a period of 20 days for weight gain, until the definitive discharge. The karyotype result confirmed the diagnosis of Edwards Syndrome with complete trisomy.

The echocardiogram detected perimembranous interventricular communication of 4.7 mm; oval fossa type interatrial communication, with 2.5 mm and persistence of the arterial canal. At one year and eight months, the patient underwent cardiac surgery for correction, after much insistence from the family. Surgical recovery progressed uneventfully. Patient has other features compatible with the phenotype of the syndrome, such as prominent occiput; narrow eyelid fissures; micrognathia; narrow palate arch; bilateral deep sensorineural hearing loss; narrowing of the external auditory canal; small nails; nail hypoplasia; closed hands with tendency to overlap the index finger on the 3rd chirodactyl and 5th over the 4th; small hallux; short sternum; pectus escavatum; hirsutism; cutis marmorata; small nipples. Currently RVB is 7 years and 6 months old, 24.4 kg, 130 cm, cephalic perimeter 39 cm. Weight gain was much lower than expected for age before when she was still fed orally. Since the age of six she has a gastrostomy. Also needs bladder catheterism 6 times a day and uses nitrofurantoine for prophilaxis of recurrent urinary tract infection. She presents delay in psychomotor development with hypotonia, absence of cervical control, involuntary limb movements, strabismus and astigmatism, irritability episodes and alteration of sleep pattern, with insomnia. In the last year and a half, she began to present convulsive seizures and started receiving levetiracetam, oxcarbazepine and phenobarbital. She receives intensive treatment for stimulation by Pediasuit ® protocol (which includes motor physiotherapy, speech therapy and occupational therapy).

**Discussion**

The prognosis of Edwards syndrome is reserved, ranging from 2.5 to 14.5 days, and hardly exceeds the first 15 days of life (ROSA, 2013) (IMATAKA, 2016) (RASMUSSEN, 2003) (CRIDER, 2008). Therefore, the survival of the patient in question is relevant and raises discussions about the medical, family, and psychological support that enabled this above-average survival. Patients with chromosomal constitution in mosaicism generally achieve longer survival and have lighter clinical manifestations (ROSA, 2013). RVB has complete trisomy and is already 4 years old. There are, in medical literature, reports of some other cases of increased survival in Edwards syndrome with complete trisomy and such patients usually present cognitive deficits and delay in neuropsychomotor development (ROSA, 2013). In this sense, it is important to state that, despite the cognitive delay, the patient developed forms of interaction with the parents, as Lorenz mentions in the literature, that patients with these deficits find an alternative behavior to establish communication (2014).

A challenge in the management of patients with Edwards syndrome is the non-standardization of available medical interventions and the absence of a care-protocol of the syndromic patient. There is no legislation in Brazil that regulates cardiovascular resuscitation for such patients. In the case of congenital malformations, the Neonatal Program of the Brazilian Society of Pediatrics states that antenatal diagnosis is necessary, considering the will of parents and the therapeutic support available to decide the conduct in the delivery room (ROSA, 2013). The American Heart Association (AHA) also does not have clear protocols of care and considers Edwards syndrome a condition with a poor prognosis and, therefore, states that physicians should not hesitate in withdrawing support from these patients. Eastern European neo-natal resuscitation protocols are aligned with the AHA recommendations (HURLEY, 2014). On the other hand, studies prove that an aggressive intervention, both clinically and

surgically, increases the survival of these syndromic patients and confers, to some extent, life quality for the patient and their families (LORENZ, 2014) (HURLEY, 2014) (ROSA, 2013) (CEREDA & CAREY, 2012). There is also divergence from the perspective of physicians who conduct such patients because studies prove that pediatric pulmonologists recommend greater clinical and surgical intervention than neonatologists, and those are more optimistic about prognosis (HURLEY, 2014). The discourse for non-treatment is based on the possibility that such interventions are too aggressive, and may cause some harm and generate risks (for example, a greater chance of evolution to sepsis after a surgical procedure of cardiac correction) and, in view of the principle of non-maleficence, physicians should not offer support. Ethical incentives for treatment are related to the fact that the therapeutic investment is of parental autonomy and positive results, if such patients survive until childhood, generate benefits to the family group (LORENZ, 2014) (JANVIER, 2012). Researches analyzing family experience reports that 88% of parents of children with Edwards syndrome say that they generate a positive experience for the family; 68% of the parents reported not having regretted having offered support to their child and 31% regret not having offered greater interventions. 82% reported that the syndromic child had a positive effect on the siblings and 68% reported a positive effect on the marriage (LORENZ, 2014) (JANVIER, 2012).

Cardiac malformations are frequent in patients with Edwards syndrome and surgical correction of these anomalies feeds the discussion, again, about the support offered. To date, there are no fixed and clear criteria for indication of corrective cardiac surgery for these patients, but it is known that this intensive management increases survival, facilitates hospital discharge and confers better quality of life for patients and family members (CEREDA & CALEY, 2012)(ROSA, 2013)(LORENZ, 2014).

Parents, given the need for decision-making and difficulties, are quite psychologically shaken and need fostering. The medical team should offer support and help in making decisions aiming at the life quality of the patient and family members, respecting the autonomy of the parents. In the United States, parents are endowed with authority, because they are the most interested in their child's health; however, the limits of this autonomy are poorly defined and it is judicially denied when parents make decisions that are clearly contrary to the child's well-being (LORENZ, 2014). In the therapeutic management construction of RVB, parents and staff were cohesive to offer the best available support to enhance survival. In addition, the parents in question had the support, through social networks, of several other families who live similar situations. The internet has become an alternative to fostering the parents of syndromic patients, as it brings together caregiver parents from around the world to exchange experiences on the management of patients with Edwards syndrome. This is a strong instrument that gives parents greater security and knowledge to make their choices (JANVIER, 2012).

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