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Patau syndrome

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Genetic syndromes caused by chromosomal aberrations involve a recognizable pattern of multiple congenital anomalies with increased neonatal and infant mortality, making care challenging for the family, primary care practitioners, and specialists. About 28% of children born with trisomy 13 die during the first week of life. The median life expectancy is about 2.5 days. We present a 12-year-old girl, the longest living patient with Patau syndrome in Croatia, followed-up from the birth until the age of 12 years. The conventional nonintervention approach has been revised and we suggest changing the traditional view of the condition.

Keywords: Patau syndrome; life expectancy; chromosomal anomalies

INTRODUCTION

Patau syndrome (trisomy 13) is one of the most common chromosomal anomalies clinically characterized by the presence of numerous malformations with a limited survival rate for most cases. It is the third most frequent chromosomal trisomy with estimated incidence of about 1/8000-12,000 births. Spontaneous abortions, after 12 weeks of gestation, are 100 times more often caused by trisomy 13 than by any other condition. Between 12 weeks of gestation and term, 49% (95% CI: 29-73%) of pregnancies diagnosed with trisomy 13 are estimated to end with miscarriage or stillbirth (1, 2).

Compared to the general neonatal mortality rate, the estimated mortality rate for trisomy 13 is about 50 times higher (1). Trisomy 13 is cytogenetically classified as a full trisomy (47,XY,+13) due to the nondisjunction at meiosis I or II, or at mitosis (mosaicism) and partial trisomy due to translocations. Patau syndrome due to translocations can be inherited if one of the parents carries a balanced rearrangement of genetic material between chromosome 13 and another chromosome. Robertsonian translocations may involve two chromosome 13 /46,XX,t(13;13)/, or chromosome 13 and another acrocentric (14,15,21,22). Robertsonian translocation 13:14 is the most common translocation of this type in the population. Robertsonian translocation 13;14 in about 60% of cases occurs *de novo,* in 25% is maternally and in 15% paternally inherited. In most cases, translocation 13;13 arises *de novo* because one of the parents carries a 100% risk of Patau syndrome in the offspring. The mean maternal age is increased for free trisomy 13 (1, 2). Twenty-eight percent of newborns with Patau syndrome die within the first week of life, 44% in the first month, and 86% by one year of age. The median survival age is 2.5 days, and only a small number of cases experience puberty age. Most infants with Patau syndrome have a high mortality: 69% from cardiopulmonary failure, 13% from congenital heart defects, and 4% from pneumonia (1, 2). Newborns with Patau syndrome present at birth with low birth weight and often with intrauterine growth retardation, one umbilical artery, prolonged persistence of fetal hemoglobin, doubled organs, microcephaly, microphthalmia, arrhinencephalia, bilateral cleft lip and palate, postaxial hexadactyly, and a wide spectrum of anomalies of the heart and great vessels. About 4/5 of cases reveal renal anomalies and a variety of muscular and skeletal anomalies. Most of these patients are blind and deaf, with epilepsy and severe developmental delays (1).

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CASE REPORT

We present a 12-year-old girl, the longest living patient with Patau syndrome in Croatia. She is the second child of healthy young parents who had a child with Edwards syndrome (full trisomy 18 with karyotype: 47,XY+18) from previous pregnancy. The child died a few days after birth. The parents have normal karyotypes; after genetic counseling, they refused prenatal diagnosis for the second pregnancy.

Our patient with Patau syndrome has a full trisomy, a tandem translocation 13;13 *de novo* 46,XX,der(13;13)(p11.2;p11.2). The diagnosis was confirmed by fluorescent *in situ* hybridization (FISH) from peripheral blood and skin culture: ish psu idic(13;13)(13pter→13cen→13p11.2::13p11.2→13p su cen→13qter)(D13Z1++). FISH was performed on metaphase chromosomes using alphoid 13 and 21 specific centromeric DNA probe (D13Z1/D21Z1, Kreatech). Hybridization showed one centromeric signal on normal chromosome 13, and two signals on der(13;13) chromosome. The Robertsonian translocation (13;13) was dicentric.

Upon delivery, the newborn manifested right-sided cleft lip and palate, coloboma of iris on both eyes, heart defect (atrial septal defect II), and right double urinary channels. She also developed acute respiratory failure, was intubated and mechanically ventilated in the Pediatric Intensive Care Unit (PICU), and tracheotomy was done. She was successfully weaned from the respirator some months later and surgical correction of the cleft lip and palate was performed. At the age of 3 years, decannulation was finally performed.

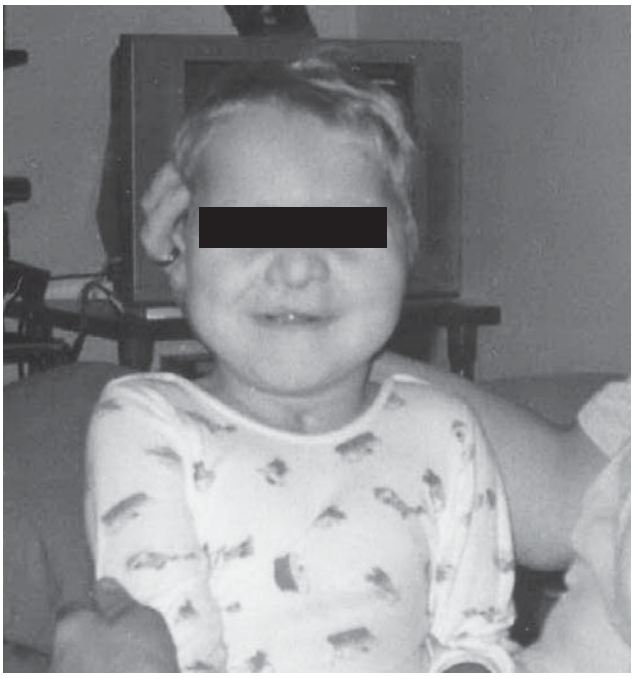

FIGURE 1. A girl suffering from Patau syndrome at the age of 7 years.

Today, she is 12-years old; she does not walk or speak, and is prone to recurrent bronchopneumonia because of which is often hospitalized (Figure 1). During her long hospitalization, her mother was educated for home care, which is primarily related to changing and hygiene of the cannula set, gauge feeding, aspiration of secretions, inhalation technique and use of oxygen through a mask. In order to achieve a satisfactory clinical condition of the girl, she was placed on home care with her family and since then has been in home conditions. After some time, she developed symptomatic epilepsy. In the process of genetic counseling, the parents were informed on the possibility of prenatal diagnosis or preimplantation diagnosis, however, they were not ready for new pregnancy.

All procedures were approved by the local Ethics Committee and carried out with full understanding and written consent of the parents.

DISCUSSION

Cases of children diagnosed with Patau syndrome or Edwards syndrome who lived longer than the average life expectancy for these conditions are rarely described in the literature (2-4). Considering the real life experience and data from medical literature, the question is how much effort, knowledge and material resources should be invested in the treatment of children with severe chromosomal abnormalities. There is a clear ethical rule that a doctor has a primary obligation of personal care for each patient (5).

Cases similar to our patient have been described in the literature from 1993, 2004, 2006, 2010, 2011 and 2014 (6-11). The intensity of delivery room care for very low birth weight infants with trisomy 13 or trisomy 18 varied depending on the timing of trisomy diagnosis. For the majority of infants, the plan for subsequent care was to withdraw care or to provide comfort care only. This practice influenced the timing of death and rates of survival to discharge (7, 8). The psychological support offered to the mother was, and has been, of great help to the development and maintenance of the mother-child relationship. This close relationship, added to the tireless maternal effort to provide the best quality of life, seems to have contributed positively to the long survival of the child (11). These reports support better prognosis of trisomies through treatment at PICU based on improved survival period. Educating parents about their child's diagnosis and developmental outcomes is important. Medical team has to make it clear to parents what can be provided, intensive or comfort management, and get informed consent from them (12).

In our case, medical decision on the intervention was supported by the choice of the parents who were eager for

their child to survive although being faced with her severe disability. Based on the experience, we think that each patient is an individual case and the final decision should be made respecting the family's choice. Considering that parents usually hope to spend some weeks, months, or maybe a few years with their child, we generally advocate intensive treatment for children with trisomies regardless of the possible complications of treatment, their disability and shorter life expectancy (12-15).

All measures and actions we take must be directed to support and care of children with chromosomal aberrations and their parents in order to benefit the lives regardless of how long they would be. The primary and tertiary care consultants who are able to provide knowledge and sensitive supportive care for children with trisomy 13 and trisomy 18 and their families, are performing a service of significant benefit. The first study which investigated the effect of intensive management including optional cardiac surgery on the survival of patients with trisomy 13 or trisomy 18 with heart defect (patent ductus arteriosus) showed significant improvement in survival through both pharmacological intervention and cardiac surgery. The patients with trisomy 13 may have a high probability of long-term survival if they survive over 60 days after birth. One of the major factors for long-term survival of patients with trisomy 13 is active resuscitation which follows immediately after birth, as well as various surgical treatments such as tracheotomy and cardiac surgery (14).

In conclusion, Patau syndrome involves a recognizable pattern of multiple congenital anomalies with increased neonatal and infant mortality and significant intellectual disability in older children, making care challenging for the family, primary care practitioners, and specialists.

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SAŽETAK

Patau sindrom

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Genetski sindromi uzrokovani kromosomnim aberacijama uključuju prepoznatljivi obrazac višestrukih prirođenih anomalija s povećanom smrtnošću novorođenčadi i dojenčadi, što skrb za njih čini teškom za obitelj, liječnike primarne zdravstvene skrbi i specijaliste. Oko 28% djece rođene s trisomijom 13 umire tijekom prvog tjedna života. Srednje očekivano trajanje života je oko 2,5 dana. Prikazujemo 12-godišnju djevojčicu, najduže živuću bolesnicu s Patauovim sindromom u Hrvatskoj, koju pratimo od rođenja do njezine sadašnje dobi od 12 godina. Konvencionalni pristup zasnovan na izostanku intervencije doživio je reviziju, a mi predlažemo promjenu tradicionalnog pogleda na ovo stanje.

Ključne riječi: Patauov sindrom; očekivano trajanje života; kromosomne anomalije