

## A case report of truncus arteriosus communis and genetic counseling

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### Case Report

#### Abstract

**BACKGROUND:** Truncus arteriosus communis (TAC) is a rare heart disorder with the prevalence of approximately 1%, mostly in male newborns. In this disease, aorta and pulmonary artery have not been separated during fetus development and both originate jointly from left ventricle. In addition, various disorders are reported like ventricular septal defect (VSD), mitral and tricuspid valves defects, aortic septal defect (ASD), reduction of lung and lung vessels' resistance, pulmonary hypertension, increase in heart rate, high perspiration, bad digestion, and tetralogy of Fallot.

**CASR REPORT:** Parents of deceased patient were referred for genetic counseling after the death of third girl due to severe cardiac disorder. Cardiologist declared the disease in deceased girl as TAC based on findings along with VSD, ASD and hypoplastic aortic arch which resulted to death in the first day of birth.

**CONCLUSION:** There was no chromosomal disorder in chromosome analysis of patient's skin. Parents were interested to have another child, so they were referred to university's Genetic Counseling Center to become aware of their next child's condition. This disorder is genetically heterogeneous and multifactorial and because all external factors are not recognized, the accurate estimation of risk is not possible and the probability of risk for the next child is about 10% to 20%.

**Keywords:** Heart Disorder, Truncus Arteriosus Communis, Genetic Counseling

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#### Introduction

Congenital cardiac disorders are one of the most common congenital disorders with the prevalence of 1-5% in every 100 newborns.<sup>1</sup> Among them, truncus arteriosus communis (TAC) is a rare cardiac disorder,<sup>2-4</sup> in which aorta and pulmonary artery were not separated completely during fetus development and both originate jointly from left ventricle. In addition, various disorders like ventricular septal defect (VSD), mitral and tricuspid valves defect, aortic septal defect (ASD), reduction of lungs and lungs' vessels resistance, pulmonary hypertension, increase in heart rate, high perspiration, and bad food digestion along with tetralogy of Fallot are some of reported disorders.<sup>5-8</sup> Prevalence of this disease is low and in males is higher than females.<sup>8,9</sup> During past 20 years, diagnostic and therapeutic methods along with immediate intervention for surgery in infancy with

complete reparation of VSD lead to evident improvement and less morbidity in newborns.

Along with genetic role including microdeletion of 22q11.2 in 30% of isolated conotruncal disorders, the effect of external factors has been considered in these disorders.<sup>2,3,10</sup> Because of diversity in disease demonstration, its causes had been classified by Collet and Edwards in 4 different types in 1949.<sup>11</sup> Because of later reported deviances,<sup>12,13</sup> another classification was introduced by van Praaghs in 1965 with modifications in 4 initial types,<sup>14</sup> but it seems that none of classifications are ideal because there are cases which does not belong to any of classifications,<sup>4,11,15-17</sup> defined as unpredictable differences.<sup>18-20</sup>

In order to diagnose before birth, procedures like ultrasound, echocardiography and measurement of alpha-fetoprotein of maternal serum (Quadric test) were used and methods like X-ray angiography,

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contrast enhanced magnetic resonance angiography (CEMR) and other imaging techniques were used after birth.<sup>9,21,22</sup>

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Parents were not relatives and were 34 years old at the birth of their first daughter. At the time of this study, this girl was 10 years old (Figure 1 IV/1), she was healthy with natural growth. The second pregnancy was a boy who was aborted before third month of pregnancy (Figure 1 IV/2). Forth pregnancy resulted in early abortion without determining the gender of fetus (Figure 1 IV/4). Proband in this study was the fifth pregnancy which died in the evening of the first birth day with TAC diagnosis (Figure 1 IV/5). Then parents were seeking consultation for sixth pregnancy. Father had natural karyotype (Figure 1 III/1). Father's younger brother had the same cardiac disorder (Figure 1 III/3), his disease was diagnosed by cardiologists of Munich University and was operated in US, now he has good physical health (Table 1). One of the father's cousin of patient (Figure 1 III/6) died after Hiatus hernia operation because of a sub-diaphragm abscess. She suffered from tetralogy Fallot (defect of ventricle septum, high discharge of right ventricle

pulmonary artery stenosis, and aortic defect or ductus Botalli). It was reported that 3 paternal brother had died in childhood. One of the brothers had died because of diphtheria (Figure 1 II/2). Death reasons of other brothers (Figure 1 II/5,7) were not clear. Among 9 sisters and brothers of mother, two girls had died early; one in 5 months old because of diarrhea (Figure 1 II/12) and the other because of septicemia (Figure 1 II/16).

Even mother (Figure 2 III/8) had natural karyotype in chromosome analysis. One cousin of mother had died in 3 months old due to convulsion caused by teeth fever. Other family members were healthy. The dead patient is shown with an arrow (Figure 1 IV/5).

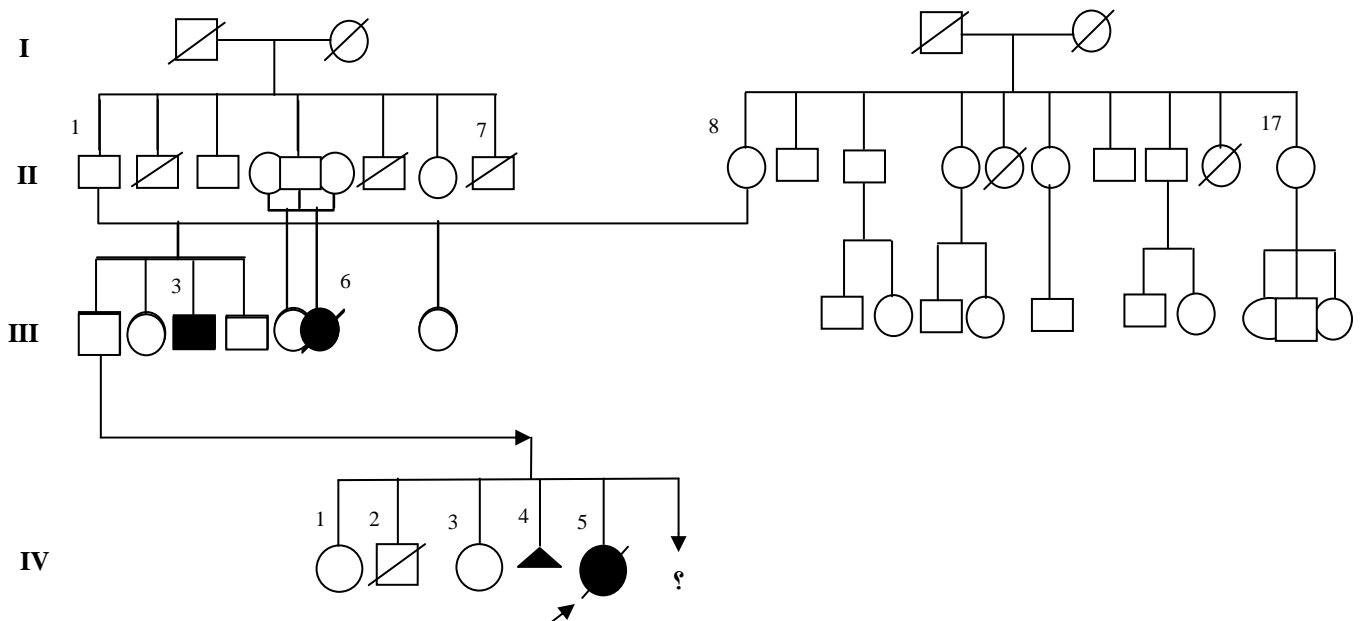
**Pregnancy, birth and newborn**

In the 9<sup>th</sup> and 10<sup>th</sup> weeks of pregnancy, patient's mother had suffered from intestinal infection and diarrhea without fever. She had been weak with pain in her abdomen and back like her second pregnancy but this time did not result in abortion. Monographic examinations had not shown cardiac or ventricle disorder. Until the moment of birth, the patient was placed in the seat position, but then turned to head position. Delivery was in 40<sup>th</sup> week of pregnancy without any problem. Amniotic fluid

**Table 1.** Patients' status

Patient III/3	TAC with VSD	Had surgery
Patient III/6	VSD	Died after hiatus hernia surgery
Patient IV/5	Suspected to TAC with VSD and ASD	Died

TAC: Truncus arteriosus communis; VSD: Ventricular septal defect; ASD: Aortic septal defect



**Figure 1.** Paternal pedigree

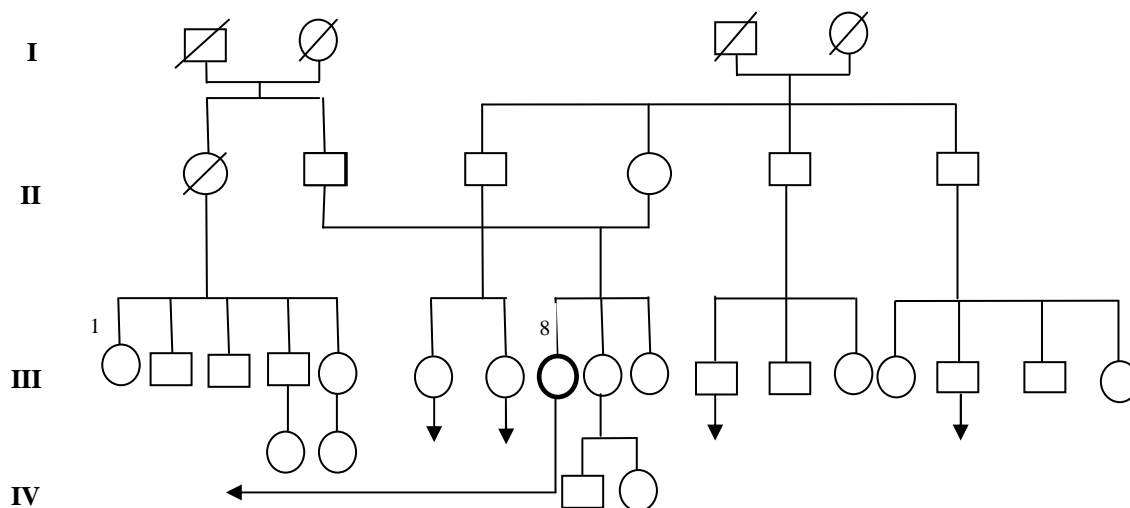


Figure 2. Maternal pedigree

was green. Length of body was 52 cm at birth which was up normal (< p90) for birth week. Apgar scores (10/10/90), birth weight (3150 g), and head diameter (33.5 cm) were normal. The patient had no apparent difference with her sisters. According to reports of her parents, she shortly cried after birth. She smiled in first 15 minutes of her life, moved her eyes and mouth, even she was curious in physical examinations. Cardiac sound was diagnosed in initial examinations. Infusion was conducted because of cyanosis and reduction in saturated oxygen pressure. Then she was transmitted to pediatric clinic and was not seen alive by her parents again. Echocardiography results in pediatric ward showed TAC with VSD, ASD, and hypoplastic aortic arch. Therefore, patient was transmitted to cardiac center by giving prostaglandin and artificial respiration to continue treatment. After establishing relatively stable condition in pediatric clinic, patient's condition was serious during echocardiography. The patient died in the evening of her first birth day. There was no chromosomal disorder or microdeletion of 22q11 in skin sampling. Despite interpretation of echocardiography, the reason of death was not clear.

**Genetic counseling**

We talked about psychological aspects of this death in the first day of birth and newborn's severe cardiac disorder, which was known from paternal pedigree. We reflected the mental condition of parents using a model image. In consultation time, they were in emotionally difficult situations (5 weeks after newborn's death) and asked themselves why this disaster had happened for them. They remembered that they had lost 2 children and must

have coped with the fact that only two children were left for them from 5 pregnancies. Mother was more eager for third child. We talked about this issue with the father that they must end their mourning before a new pregnancy, because with remembering grief of lost child, it is impossible to improve their health. This was the first condition for health and stability of family. After mourning, parents succeed in planning for new baby. This was the first step to accept the destiny of next child.

**Probability of recurrence risk**

Paternal pedigree showed the risk of cardiac conotruncal defect in two generations and 3 family members (Figure 3 IV/5, III/6, III/3) which were relative via their healthy fathers (Figure 3 III/1, II/4, II/1).

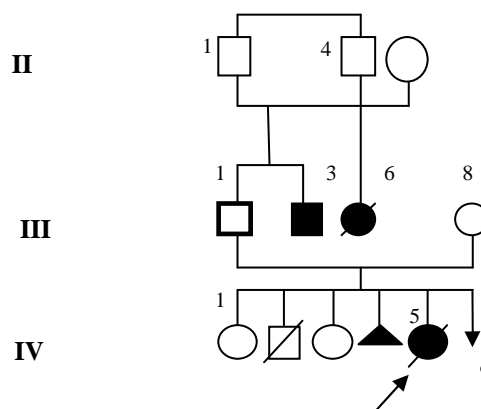


Figure 3. Pedigree of inheritance of the disease in two generations

Inherited pattern conforms with conotruncal cardiac defects reports which are not related to a

monogenic inheritance, but it is a multifactorial pathology. Accumulation inherited and various external factors' effect is shown in the figure 4. The accumulation of different external and hereditary factors is illustrated in figure 4, which explains that the different genes (polygeny) in father's family genome is responsible for conotruncal defect. However, their expression was influenced by some external factors which have not been recognized completely. Therefore, the result of this accumulation is above the fetus tolerance threshold.

Epidemiologic studies about inheritance of conotruncal cardiac disorders in scientific literature are limited.<sup>1,10,16,23-26</sup> Because all factors have not been identified, accurate statistical calculations are not possible. Probability of risk was estimated 10-20%, because the illness of brother and sister was similar. Karyotype study and microdeletion of 22q11 which is reported in 30% of TAC was rejected for deceased patient and her parents by Munich University Genetic Center and there were no other genetic examinations.<sup>10</sup>

#### Diagnosis before birth

Regarding parents age, we can consider a chromosome analysis although it imposes high costs in the absence of insurance. The probability of a new chromosome mutation for parents between 35-40 years old in the first and second pregnancies is about 1-2%. It is not possible to reject or prove conotruncal defects with these laboratory studies. Early sonography and echocardiography by experts will be promising for early diagnosis. We talked with parents about consequences of prenatal diagnosis which will result in abortion and they feared it because of their past experiences. It is important to know that there is no impulsion to receive more information about child before pregnancy, because it has no medical result for them.

## Discussion

TAC is a rare congenital cardiac disorder with the prevalence of 0.056 to 0.03 in every 1000 births.<sup>2-4,8,17,21</sup> In most reported cases there is not an even and similar picture among ill children.<sup>27-29</sup> Attempts to prepare a clear detailed pattern or classification have partially failed. In most cases, TAC has genetic origin<sup>1</sup> with the effect of teratogens (virus, metabolic imbalance, industrial and pharmaceutical factors) and caused by concurrent effect of both factors.<sup>30</sup> In more than 30-50% of cases, consistency is shown with 22q11 chromosome microdeletion and Di George syndrome; even in this case the picture of disease is not the same.<sup>8,10,16,30,31</sup>

Disorder in human embryo neural crest, where first neural cells of heart and aortic pulmonary are formed, is reported as a factor for the conotruncal disorders.<sup>6,7,13,30</sup> Some disorders in embryos with cardiac neural crest defect are related to growth factors [fibroblast growth factor (FGF8) and bone morphogenetic proteins (BMP)] and transcription factors (T-box, Pax, NKX2-9, ANF, GATA-C)<sup>21,24</sup> and cell membrane gap protein (connexin 40).<sup>25</sup> Cardiac-neural crest plays a role in forming smooth muscle of great vessels.<sup>30,32</sup>

In some studies, markers of cell proliferation, apoptosis, and fibronectin were significantly higher in the right ventricular myocardium of patients with hypoplastic left heart syndrome (HLHs) compared to truncus arteriosus. Type I collagen content and NKX2.5 expression were significantly lower in HLHS than the truncus group.<sup>12</sup> Regarding this and various reported mutations relating to TAC disorders including mutation in CFC1 (De George syndrome) with dysmorphic face or Velo-cardio-facial syndrome (VSFS) in 90% of cases, mutation in NKX2.6,<sup>24,25</sup> deletion in chromosome 22 (22q11)<sup>6,10,16,30,31</sup> and chromosomes 8, 16, 18, and 19,<sup>1,30</sup>

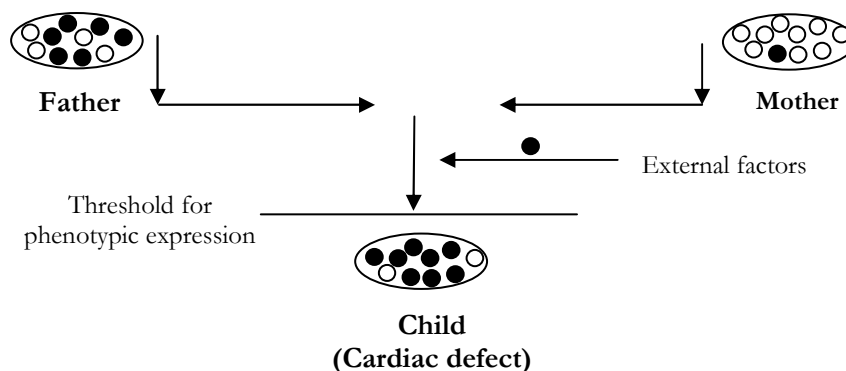


Figure 4. An illustration of external and inherited factors accumulation

mutation in cardiac homeobox containing CSX gene (5q34) which has been expressed in heart cells in fetus.<sup>33</sup> Homeobox containing Msk2 gene,<sup>23</sup> Tbx1-gene,<sup>26</sup> and even disorder in diabetic mother's child dependent on insulin,<sup>31,33</sup> which shows the polygenic and multifactorial nature of these disorders has been reported. In the absence of these various mutations, it could be imagined an autosomal dominant inheritance with reduced penetrance and variable expressivity.

In our study, there was no chromosomal disorder in infant and her parents. In terms of genetic counseling, regarding multifactorial nature of congenital TAC and its diverse epidemiologic and anatomic picture, different diagnostic tests such as ultrasound, echocardiography and quadruple test are recommended for prenatal diagnosis. Amniocentesis and chorionic villus sampling can also be used to check the relevant genes.<sup>9,21</sup> In the case of birth and diagnosis, immediate intervention with diagnostic methods for treatment, surgery and reparation of cardiac defects give an acceptable survival chance to child. Even with selecting newborn gender due to high resistance, we can increase the chance of healthy child.<sup>25</sup> Using stem cells as an alternative treatment showed that during activity of these cells, 32000 various transcripts (gene expression products) were constructed which help to improve some disorders.<sup>2,34</sup>

### Conflict of Interests

Authors have no conflict of interests.

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