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De novo unbalanced translocation t(15;22)(q26.2;q12) with velo-cardio-facial syndrome: A case report and review of the literature

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Abstract. The present study reports the case of a 3-h old male with a *de novo* unbalanced t(15;22) translocation and velo-cardio-facial syndrome (VCFS), with other abnormalities. The manifestations of the condition observed in the patient included cleft palate with feeding difficulties, respiratory infection, dysmorphic face with almond-shaped eyes, a long and wide nose, small and low-set ears, tetralogy of Fallot, cryptorchidism and varus equinus. Standard lymphocyte cytogenetic analysis using G-banding demonstrated a 45,XY,-22,der (15),t(15;22)(q26.2;q12) karyotype. Fluorescent *in situ* hybridization with DiGeorge/VCFS TUPLE 1 confirmed 22q11 deletions. These cytogenetic aspects appear to be rare in the etiology of VCFS, as >1% of all 22q11 deletions are the result of an unbalanced translocation, which involves chromosomes 22 and another chromosome. To the best of our knowledge, this is the second reported case where the clinical features associated with VCFS are combined with an unbalanced (15;22) translocation involving the critical 22q11.2 region.

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Abbreviations: OMIM, Online Mendelian Inheritance in Man; VCFS, velo-cardio-facial syndrome; FISH, fluorescence *in situ* hybidization; PRS, Pierre Robin Sequences; DGS, DiGeorge syndrome; CATCH 22 acronym, (C=cardiac anomalies, A=abnormal faces, T=thymus hypoplasia, C=cleft palate, H=hypocalcaemia, 2=affected chromosome); IVF, *in vitro* fertilization

Key words: velo-cardio-facial syndrome, unbalanced (15;22) translocation, 22q11.2 deletion, cleft palate

Introduction

Velo-cardio-facial syndrome [VCFS; Online Mendelian Inheritance in Man (OMIM) cat. no. 192430] is a multiple malformation syndrome, which is characterized by highly variable clinical features, including cleft palate, cardiac anomalies, atypical facial development and cognitive and neuropsychological difficulties (1,2). The first case of VCFS was described in 1955 by Eva Sedlačková. DiGeorge described the association between VCFS and thymic aplasia, hypoparathyroidism and congenital heart disease in children in 1968. While in 1978 R. J. Shprintzen presented 12 cases of VCFS, including a family of one, and established it as a distinct inherited genetic disorder (3). In 90% of patients with VCFS, a *de novo* variably sized deletion at chromosome 22q11.2 is responsible for the syndrome (4).

VCFS occurs in between 1 in every 4000 and 7000 births (3). The condition has been previously described by several physicians and has been given several different names including, VCFS, Shprintzen syndrome, DiGeorge syndrome (DGS), DiGeorge sequence, CATCH 22, deletion 22q11 syndrome, Cayler syndrome and conotruncal anomaly face syndrome. VCFS is the fourth most common type of congenital anomaly worldwide. However, in Romania there is no comprehensive data on the prevalence of the disease.

The present study reports the case of a newborn male with keilopalatoschisis, dysmorphic face, heart anomalies, genital hypoplasia and varus equinus, including the clinical data and cytogenetic information. The cytogenetic evaluation revealed an unusual, unbalanced translocation involving chromosomes 22 and 15 in a karyotype with 45 chromosomes, which is a rare rearrangement.

Materials and methods

The present study complied with the Declaration of Helsinki and was approved by the institutional ethics committee of the Victor Babeș University of Medicine and Pharmacy

(Timișoara, Romania). Written informed consent was obtained from the legal guardian of the child for the use of their case details and associated images in the present study.

The present paper presents the case of a male child with VCFS. Physical examination was conducted in order to identify anatomical problems. Cardiac disorders have been identified, according to clinical and paraclinical criteria, by thoracic radiography, ECG and Ecocardiography. ECG and Echocardiography were recorded with a Schiller and ESAOTE machine, respectively. Oxygen saturation was assessed with a pulse oximeter.

Cytogenetic analysis. Standard lymphocyte cytogenetic analysis was performed using peripheral blood followed by GTG-banding at the 550-band level (5). A number of 20 metaphases were analyzed by two independent observers using a Nikon ECLIPE 55i trinocular microscope. For karyotyping a dedicated Lucia Karyo software was used.

Fluorescence in situ hybridization (FISH) analysis. FISH was performed using the Metasystem XL Probes for Microdeletions 22q11.2 TUPLE1 DiGeorge sample (HIRA-HIR histone cell cycle regulation defective homolog A)-red (120 kb), and SHANK3 control sample 22q13-green (40 kb) (cat. no. D-6404-050-RG). The FISH analyses were performed by two independent observers using a Nikon Eclipse 600 microscope equipped with a standard fluorescence isothiocyanate filter. The photographs were captured using Kodak Ektachrome 400 film.

The results of the cytogenetic and FISH analyses are described further according to the International System for Human Cytogenomic Nomenclature 2016 (6). The control sample was obtained from a male, 7 months old patient, admitted to the Onco-Hematology department of the Louis Turcanu hospital (Timisoara, Romania; August 2013).

Results

Case presentation. The patient was born by caesarean section at 37 weeks and 5 days of gestation, after an uncomplicated pregnancy to a healthy 18-year-old woman. It was the first pregnancy for the nonconsanguineous healthy couple. At birth the child was 3,200 g [-0.57 standard deviation (SD)], 49 cm in length (-0.9 SD), had a head circumference of 30 cm (-4.72 SD) and the Apgar score was 6. After birth the patient was artificially fed and his weight gain was impaired. The mother denies taking any treatment during the pregnancy and there are no reports of consanguinity or genetic anomalies in the family history. The parents were examined in detail and were not found to have any features of the syndrome, or any history of reproductive health problems. The parents have subsequently divorced and the mother has married an African-American male and had another child (Fig. 1). An amniocentesis performed during the second pregnancy revealed that the child had a normal karyotype.

At the age of 3 h, the patient described in the manuscript, was referred to a pediatric ward for evaluation of the plurimalformative syndrome and poor neonatal adaptation. The patient was hypertonic and had peripheral cyanosis. The clinical evaluation revealed microcephaly, a long and hypotonic face with mild orbital hypertelorism, almond-shaped eyes, dark red rings under the eyes, a prominent nasal bridge, a long but wide nose with a bulbous nasal tip, flat cheekbones, down-turned corners of the mouth, an overt cleft palate with velopharyngeal insufficiency, micrognathia, small and low-set ears (Fig. 2A and B), cryptorchidism and clubfoot. Cardiac examination revealed a grade II systolic murmur in the upper left sternal border, as well as a grade II systolic murmur in the lower left sternal border, which irradiated all over the precordium. Pulmonary rales were revealed by auscultation.

Further biological investigation identified multiple systemic and peripheral infections due to the patient's condition, including anemia and hypogammaglobulinemia. Oxygen saturation was impaired (78%) and an electrocardiogram revealed sinus rhythm, right axis deviation and right atrial and ventricular hypertrophy. Cardiopulmonary X-ray revealed a 'boot shaped' heart, a cardiothoracic index of 0.67, increased prominence of the pulmonary artery and decreased vascular markings (Fig. 3) An echocardiograph revealed a ventricular septal defect, hypertrophy of the right ventricle, overriding of the aorta and pulmonary artery stenosis, which confirmed the diagnose of Tetralogy of Fallot (Fig. 3A-C).

The hypertonia, clonus and incomplete archaic reflexes revealed a perinatal hypoxic-ischemic injury. A transfontanellar ultrasound was performed when the patient was 2 days old; it identified perinatal hypoxic-ischemic injury with intraventricular hemorrhage. The patient's audiometry was normal. These results led to a diagnosis of VCFS.

The patient had multiple subsequent hospital admissions due to recurrent pulmonary infection, secondary to aspiration syndrome and their Tet spells were reported as severe. Cardiac and oral surgery were not performed as consent was not obtained from the parents. The patient was followed up until the age of 1.5 years when they succumbed to the disease.

Cytogenetic analysis. Revealed a translocation involving chromosomes 15 and 22 in a 45 chromosome karyotype; additional material was observed in the long arm of chromosome 15, and one chromosome 22 was missing (Fig. 4). The karyotype of the patient was given as 45,XY,-22,der(15),t(15;22)(q26.2;q11.2)dn. The derivate der(15) replaced a normal chromosome 15 and the homologous chromosome 22 was lost. The karyotype confirmed the etiology of the case; 22 monosomy with unbalanced translocation of the genetic material from the 22 chromosome (22q12-ter band), to the 15 chromosome. The translocation took place with a 22q11.2 deletion. The parental karyotypes were observed to be normal.

Fluorescence in situ hybridization (FISH) analysis. Due to the clinical findings, FISH was performed on metaphase chromosomes using a probe specific for the DGS critical region (TUPLE). A single red signal from the 22q11.2 probe was observed on the normal chromosome 22 (Fig. 5A). Whereas, 2 green signals from the 22q13.33 probe were observed on the subtelomere of the normal chromosome 22 and the translocated chromosome. As the 22q11.2 red probe has a size of 120 kb (4440 kDa), it is known that the deletion has a minimum of 120 kb. The results of the FISH analysis indicated 45,XY,-22,der(15),t(15;22).ishdel(22)(q11.2q11.2)(D22S451-) for the patient and 46,XY.ish q22.11.2(D22S451x2) for the control probe.

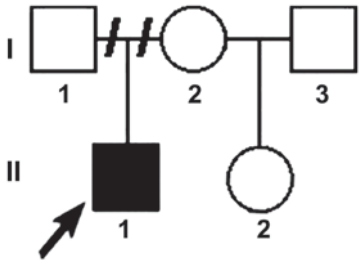

Figure 1. Family pedigree. Males and females were indicated by squares and circles, respectively. The generations investigated in this family are marked with Roman numerals (I and II) and members of each generation with Arabic numerals (1-3). The affected subject is indicated by the arrow (the index patient is II.1).

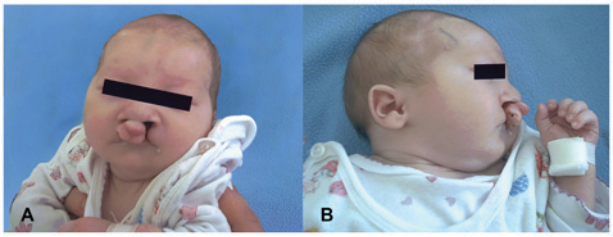

Figure 2. The patient at one month. (A) Frontal and (B) lateral profile view of the face of the patient. Typical facial findings of velo-cardio-facial syndrome may be observed, including microcephaly, a long and hypotonic face, mild orbital hypertelorism, almond-shaped eyes, a prominent nasal bridge, a long but wide nose with a bulbous nasal tip, down-turned corners of the mouth, overt cleft, micrognathia and small and low-set ears.

Differential diagnosis. A differential diagnosis was performed to consider several diseases, as the phenotypic manifestations of VCFS are pleiotropic. Kabuki syndrome (OMIM cat. no. 147920) was considered due to the observation of cleft palate, cardiac anomaly and hypotonia, however it was excluded due to the facial appearance and small ears. Other conditions were excluded due to an incorrect phenotype, including fetal alcohol syndrome (due to the heart anomaly and cleft palate), Smith-Lemli-Opitz syndrome (OMIM cat. no. 270400; due to the cleft palate), Alagille syndrome (OMIM cat. no. 118450; due to the congenital heart disease), VATER syndrome (OMIM cat. no. 192350) and Goldehar syndrome (OMIM cat. no. %164210). Recent medical advancements regarding VCFS suggest that patients previously diagnosed with Pierre Robin Sequences (PRS; OMIM cat. no. %261800) and CHARGE association (OMIM cat. no. 214800) should undergo further clinical and cytogenetic evaluation. The present case did not have CHARGE association (no coloboma in the eyes, no choanal atresia and no deafness), or PRS (no glossoptosis). VCFS, as multisystemic syndrome, is difficult to identify as a minimum of 30 different symptoms have been associated with the 22q11 deletion. Case by case evaluation is even more difficult, as the majority of symptoms are not present in all individuals who have VCFS (https://www.genome.gov/25521139/learning-about-velocardiofacial-syndrome/).

Discussion

VCFS is caused by a microdeletion at chromosome 22q11.2 and is the most common type of contiguous gene syndrome in humans (4). Many healthcare professionals now refer to patients with VCFS as having a 22q11.2 deletion. The deleted region of the chromosome contains information for the development of organs from the third and fourth pharyngeal pouches, during the 12th week of gestation (7).

No correlations have been found between the position of the deleted fragment and the genes located at 22q11.2, which are included in Table I (6). The first large study on VCFS evaluated 156 cases with deletions localized at 22q11, and no correlations were observed between the size of the deletion and the phenotype (4). In the present case, the deletion was a minimum of 120 kb in size, as this is the size of the TUPLE1 22q11.2 orange probe used for the FISH analysis. VCFS is a complex disorder with a variable phenotype and penetrance; it is thought that several genes in the commonly deleted region contribute to the phenotype. VCFS transmission has a pattern of autosomal dominant inheritance (8). When one parent has VCFS, the probability of their children having the syndrome is about 50% for each birth. However, previous research has shown that VCFS is only inherited in 10 to 15% of cases. In the present case the parents were clinically healthy, with normal karyotypes and no signs of VCFS. It is most probable that a *de novo* translocation occurred, with a consecutive 22q11.2 deletion (9).

There are many different translocations between chromosome 22q11.2 and certain other chromosomes. This is due to the presence of a region that contains 8 chromosome-specific low-copy repeats within 22q11.2, which is a highly conserved DNA sequence (>96%), which mediates non-allelic homologous recombination, resulting in chromosome 22 rearrangements (10).

The etiology of the present case (unbalanced translocation from chromosome 22 to chromosome 15 with 22 monosomy) is very rare. However, a previous study described one case with the karyotype 46,XX,der(15),t(15;22)(p11.2;q11.2),-22 and a clinical appearance suggestive of DGS/VCFS, without a cleft palate (11). Chromosome 22 monosomy was observed, as in the present case, but with a different breaking point; the terminal fragment of chromosome 22 was translocated onto the short arm of chromosome 15.

In another case with the karyotype 46,XY,-15,+der(22), t(15;22)(q13;q11), the patient presented typical manifestations of a deletion of 15pter-q13 (severe hypotonia and lethargy) and also typical signs of a 22q11-ter duplication (hypertelorism, down-slanting small palpebral fissures, preauricular tags and long philtrum) (12). That case had chromosome 15 monosomy, and the unbalanced translocation was inherited from the father who had a reciprocal translocation with a different point of rupture on chromosome 15. One case of a reciprocal translocation t(15;22)(q22;q13) without either monosomy 15 or 22 with fronto-nasal malformation was also previously reported (13). To the best of our knowledge, only 7 live-born infants with mosaicism for monosomy of chromosome 22 associated with a unique facial appearance, similar to those with DGS, have been previously described (14).

There have been some special cases of DGS/VCFS occurring *de novo* in a patient conceived via *in vitro* fertilization (IVF), in which translocation t(3;22)(p25;q11) (15) and translocation t(6;22)(p25.3;q11.21) (10) have been identified. In patients with these translocations, the loss of the proximal 22q

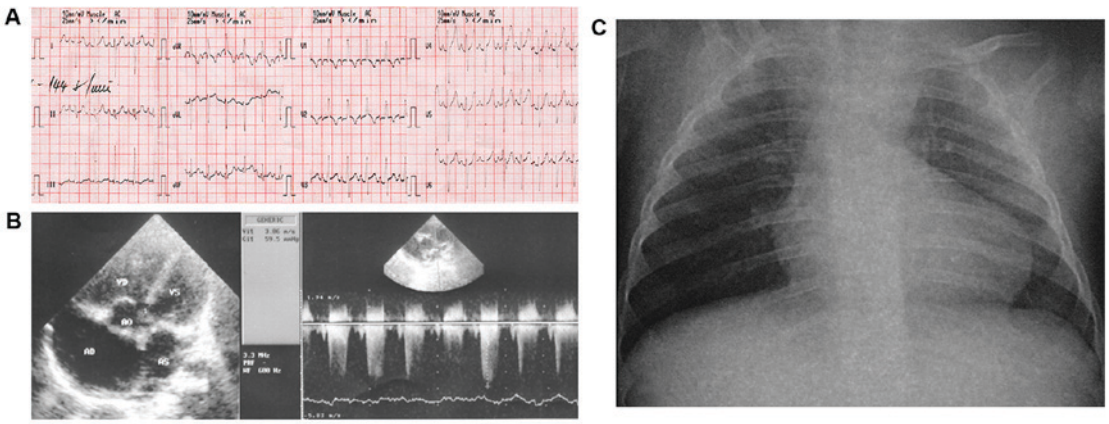

Figure 3. (A) Electrocardiogram showing right axis deviation and right ventricular hypertrophy. (B) Cardiac ultrasound demonstrating Fallot tetralogy (left) and pulmonary artery stenosis (right). (C) A chest X-ray showing 'boot shaped heart' and reduced vascular markings.

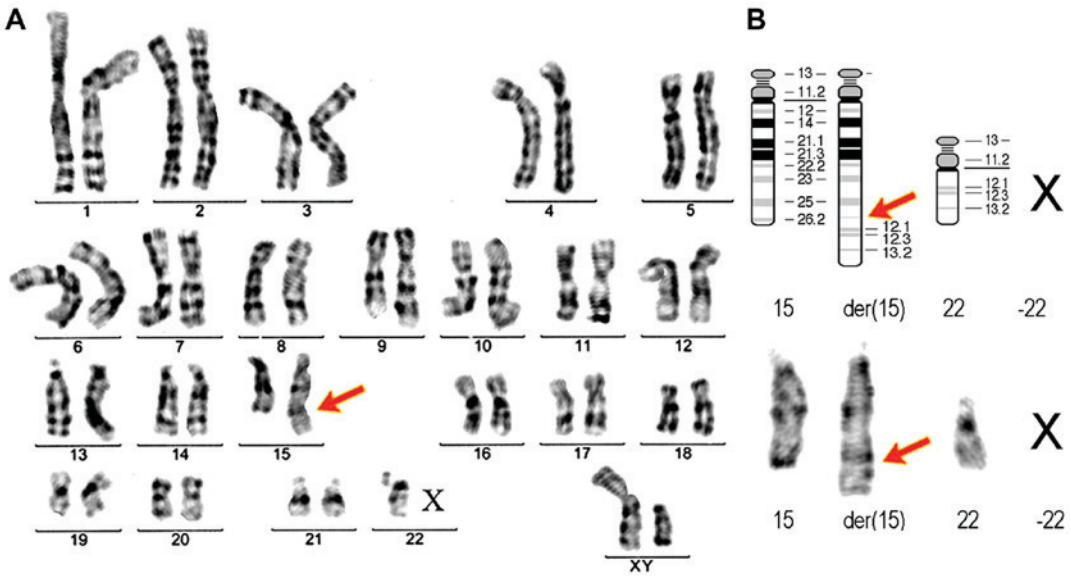

Figure 4. (A) G-banding karyotype of the patient with t(15;22). Chromosome 22 monosomy with an unbalanced translocation may be observed. The red arrows indicate the abnormal chromosome. Original magnification, x110. (B) Ideogram and partial G-banding karyotype of the patient with an unbalanced translocation (15;22). X, total monosomy.

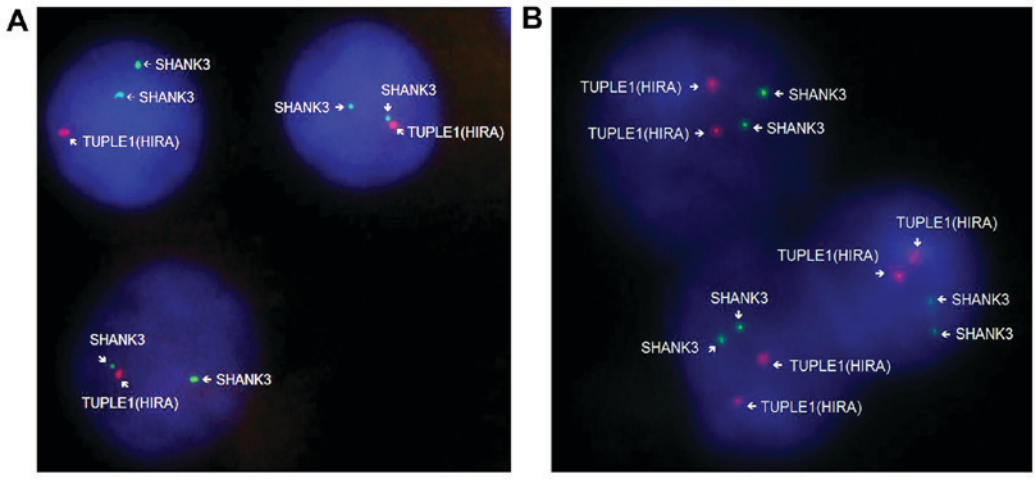

Figure 5. Fluorescence *in situ* hybridization with DiGeorge/VCFS TUPLE 1 and DAPI applied to lymphocytes obtained from the peripheral blood. Original magnification, x100. (A) The patient's probe shows one signal from the 22q11.2 probe in the normal chromosome 22 (red) and two signals from the 22q13.33 probe (green); one in chromosome 22 and the other in the der (15). (B) The control probe, obtained from a male 7-month-old patient was co-hybridized. VCFS, velo-cardio-facial syndrome.

Table I. Unbalanced translocations involving deletion 22q11.2.

Translocation	*De novo*/hereditary	Author, study	Abnormality	(Refs.)
45,XY,-22,der(15),t(15;22)(q26.2;q11.2)	*De novo*	Present case	VCFS	
45,XX,-3,-22, +der(3),t(3;22)(p25;q11)	*De novo*/IVF	Faed *et al*, 1987	DGS	(15)
46,XY,-15,+der(22),t(15;22)(q13;q11)	Paternal	Van Hove *et al*, 1992	DGS + duplication of 22q11	(12)
46,XY,t(15;22)(q22;q13)	*De novo*	Fryns, 1993	DGS	(13)
45,XX,der(4)t(4;22)(p16.3;q11.2),-22	Maternal	Reddy *et al*, 1996	DGS + Wolf-Hirschhorn deletions	(16)
46,XX,der(15),t(15;22)(p11.2;q11.2),-22	*De novo*	Jaquez *et al*, 1997	DGS + VCGS	(11)
t(9;22)(q34.3;q11.2)	Paternal	McGoey *et al*, 2009	DGS + 9q subtelomeric deletion	(19)
45,XY,der(3)t(3;22)(p25;q11),-22	*De novo*	Dundar *et al*, 2010	VCFS + 3p deletion	(17)
45,XX,der(6)t(6;22)(p25.3;q11.21),-22	*De novo*/FIV	Gollo Dantas *et al*, 2016	DGS	(10)
46,XX,r(22);	*De novo*	Kashevarova, *et al*, 2018	22q13.32-q13.33 deletion	(20)

IVF, *in vitro* fertilization; VCFS, Velo-cardio-facial syndrome; DGS, DiGeorge syndrome; t, translocation; r, ring chromosome.

region usually results in 22q11.2 deletion syndrome, associated with monosomy of chromosome 22. The rearrangements could be due to the manipulation of the embryo, or a sporadic event unrelated to IVF (10).

In certain cases, translocations involving chromosome 22 and another autosom can be phenotypically associated with a combination of specific signs for DGS/VCFS and another anomaly. These other anomalies may include translocation t(4;22)(p16.3;q11.2) with Wolf-Hirschhorn deletions (16), translocation t(3;22)(p25;q11) with 3p deletion (17), translocation t(18;22)(p11.2;q11.2) with 18p deletion (18), translocation t(9;22)(q34.3;q11.2) with 9q subtelomere deletion (19) or translocation t(15;22)(q13;q11) with 22q11 duplications (12) (Table I).

There have also been previously reported cases of 22q11 deletion syndrome, due to unequal segregation of balanced parental translocations between chromosome 22 and another autosomal chromosome. These may either be a paternal balanced reciprocal translocation t(9;22)(q34.3;q11.2) (19) or maternal balanced reciprocal translocations t(4;22)(p16.3;q11.2),-22 (16) or t(18;22)(pl1.2;q11.2) (18) (Table I).

Recently (20), a case was reported with the deletion del 22q13.32-q13.33, which was associated with a ring chromosome r(22); its instability led to a monosomy for chromosome 22 in mosaic as detected by FISH.

Less than 1% of all 22q11 deletions are the result of an unbalanced translocation, in which chromosome 22 and another chromosome are involved. In the present case the translocation involved chromosomes 15 and 22. The chromosome 15 derivate had genetic material from the chromosome 22q11 band as far as the telomeres on its terminal end, in the 15q26 band. The 22-breaking point was in band 22q11, the critical region for DGS 1, and the pericentromeric region of chromosome 22 has been lost. This cytogenetic aspect correlates with the phenotypic aspect, which is suggestive of VCFS. The family underwent genetic counseling, including nature, type of transmission and clinical and social aspects of this anomaly. About 93% of all patients have a *de novo* deletion of 22q11, while 7% have inherited the 22q11 deletion from a parent (8). The risk of recurrence in a patient's siblings is relatively low as it was a *de novo* translocation. Although the precise risk of germinal mutations cannot be determined; these results have implications for genetic counseling because there is a risk of transmission by germ cells carrying the deletion, even when parents present a normal karyotype in their blood cells (21).

Most patients with VCFS have a large (>3 Mb) genomic deletion in chromosome 22q11, which includes the DiGeorge critical region; this region is deleted in 90% of DGS patients with a detectable deletion (4). In familial cases the smaller deletions were found to be predominant (22). A significant number of these patients (~10%) have no demonstrable chromosomal deletion (23). Some families have previously presented with classic features of DGS without evidence of a chromosomal deletion at 22q11, but with specific TBX1 mutations, including 2 missense mutations and a frameshift mutation (15,16,24,25). The Tbox transcription factor *(TBX1)* gene, located at 22q11.21 is considered the major candidate for 22q11.2 deletion syndrome (26), as it is associated with cardiovascular defects and craniofacial and dental features, which were also present in the patient in the current study. The T-box 1 protein acts as a transcription factor and appears to be necessary for the normal development of muscles and bones in the face and neck, large arteries that carry blood out of the heart, structures in the ear and glands such as the thymus and parathyroid (https://ghr.nlm.nih.gov/gene/TBX1). At present 2 genes (*COMT* and *TBX1)* are associated with VCFS. However, not all the genes that cause VCFS have been identified. (https://www.genome.gov/25521139/learning-about-velocardiofacial-syndrome).

A multidisciplinary evaluation involving healthcare professionals from specialties including, genetics, plastic surgery, speech pathology, otorhinolaryngology, cardiology, cardiac surgery, child development and psychology, neurology,

orthopedics, hematology, immunology, endocrinology and pediatrics is often necessary for a successful clinical diagnosis of VCFS. Non-characteristic features are common in deletion 22q11. Many treatable conditions may be prematurely diagnosed and the pathological features may accumulate over time (27). The severity and number of problems varies from patient to patient, resulting a combination of impairments and disabilities (28). The absence of typical facial features in African-Americans patients with the 22q11.2 deletion may result in a decreased diagnosis of the syndrome within this population, and may delay the implementation of palliative care, cognitive remediation and recurrence risk counseling (8). This information could be relevant in the future as in the present study the mother's second husband was an African-American.

Aside from cleft palate, there are at least 184 other anomalies, including other abnormal facial characteristics, commonly associated with VCFS. It is considered that VCFS is the most frequent clefting syndrome, and it occurs in 8.1% of children with cleft palate (29). A rare VCFS case with cleft palate, cardiac malformation and progressive pancytopenia has also been reported (30). The patient in the current study had a complete palatal cleft, which is observed in 69% of patients with VCFS. Due to feeding difficulties and severe dysphagia the patient needed a nasogastric tube for enteric feeding; this is observed in 50% of all patients with VCFS. The patient also had tetralogy of Fallot, which is considered the most common congenital heart disease in VCFS (31). Cardiac defects are found in 84% of patients with VCFS and are the main cause of morbidity and mortality (32). The craniofacial findings were quite variable.

Although most patients have a history of hypotonia in infancy and learning disabilities (33), specific neurological manifestations are rare. Seizures were seen in some patients and were most often associated with hypocalcemia. The patient in the current study presented with neurological signs including hypertonia, clonuses and incomplete archaic reflexes.

The CATCH 22 acronym (C, cardiac anomalies; A, abnormal faces; T, thymus hypoplasia; C, cleft palate; H, hypocalcemia; 22, affected chromosome) was suggested as an alternative name for the syndrome (34). Among pathophysiological disorders, DGS is classified as an isolated T cell deficiency, due to impaired development of the thymus gland, with recurrent bacterial, viral and fungal infections (35). Both hypocalcemia, which occurs due to partial or complete absence of the parathyroid gland, and thymus hypoplasia were absent in the present case.

Genetic counseling may be very difficult and complex. Chromosome 22 at band q11.2 and chromosome 15 at band q11q13 are considered unstable regions (36). The genetic risk of the family having children with congenital anomalies exists on every future pregnancy. It was recommended that the mother should receive invasive prenatal diagnosis in all future pregnancies (37). The mother approached the authors for an amniocentesis during her next pregnancy, which revealed a normal karyotype, and a healthy child was born (Fig. 1).

In conclusion, a translocation involving chromosome 22 in a karyotype with 45 chromosomes is a rare event and, to the best of our knowledge, this has not been previously reported involving chromosomes 15q and 22q. The major malformations observed in the present case suggested the diagnosis, which was confirmed by the unbalanced t(15;22) translocation with 22q11.2 deletion revealed by standard karyotyping and FISH. Genetic diagnosis is essential to enable a successful diagnosis and genetic counseling for the family.

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Availability of data and materials

All data generated or analyzed during the study are included in this published article.

Authors' contributions

CG performed the cytogenetic analysis, the genetic counseling and wrote the first draft of the manuscript. IM, DH and MV revised and improved the first draft of the manuscript, made substantial contributions by collecting the data from the literature included in Table I and revising the manuscript critically for important intellectual content. CP and LG performed the FISH analysis. CP was also the second evaluator for cytogenetic analysis. GD performed the cardiology evaluation. RS was the pediatrician who treated the child in the clinic throughout his admissions. The mother's pregnancy was monitored by GF and CF. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The present study complied with the Declaration of Helsinki and has been approved by the institutional ethics committee of the Victor Babes University of Medicine and Pharmacy (Timisoara, Romania). Written informed consent was obtained from the legal guardian of the patient and from the parent of the child who provided the control probe for the use of their clinical data and associated images in the present study.

Patient consent for publication

The legal guardian of the child gave written consent to publish the medical information associated with the patient.

Competing interests

The authors declare that they have no competing interests.

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