VELOCARDIOFACIAL SYNDROME - PHENOTYPIC VARIABILITY AND MANAGEMENT

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Velocardiofacial syndrome (VCFS):

- highly variable phenotype;
- congenital heart disease (74%), particularly conotruncal malformations;
- palatal abnormalities (69%);
- characteristic facial features;
- learning difficulties (70-90%);
- additional findings : hypocalcemia (50%), significant feeding problems (30%), renal anomalies (37%), hearing loss, autoimmune disorders, seizures (without hypocalcemia).
- prevalence 1: 4.000 live births .

Genetics:

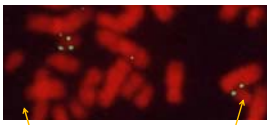
- microdeletion 22q11.2 detected by fluorescence in situ hybridization (FISH) (95%; in a small number of patients microdeletion 10p13-14);
- a contiguous genes syndrome inherited in an autosomal dominant transmission;
- 93% of probands – *de novo* and 7% have inherited the microdeletion from a parent;
- *TBX*1 - candidat gene;
- variable expressivity;
- no anticipation;
- penetrance is complete.

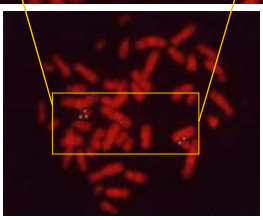
Case report
Case 1

- 18 years old female;
- the third child of an young, unrelated, apparently healthy couple;
- pregnancy and natural birth, uneventful;
- diagnosed with *patent ductus arteriosus* (after birth) and diabetes mellitus type I (15 y old);
- physical examination (15 y old): dysmorphic face (ocular hypertelorism, prominent nasal root, bulbous nasal tip, auricular abnormalities), submucosal cleft palate, nasal speech;

Investigations

- psychological examination: mild mental retardation;
- radiological examination: C2-C3 vertebral block;
- normal karyotype;
- FISH analysis: 22q11.2 deletion; probes BAC CTA-201C11 and BAC CTA-799F10 for 22q11.2 and 22q13.33



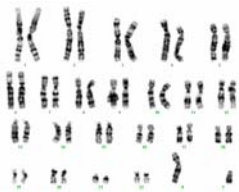


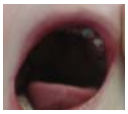
Case report
Case 2

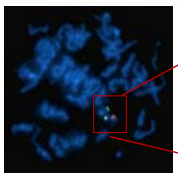
- 2 years old male;
- the second child of an young, unrelated, apparently healthy couple;
- fetal ultrasound scan: ventricular septal defect;
- natural uneventful birth;
- physical examination: dysmorphic face (long face, bulbous nasal tip, microretrognathism), hypernasal speech, hypermobile joints (especially fingers), balanic hypospadias, mild developmental delay;

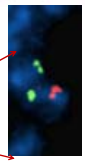
Investigations

- psychological examination: mild mental retardation;
- abdominal ultrasound: left renal agenesis;
- normal karyotype;
- FISH analysis: 46,XY.ish del (22q11.2) (TUPLE 1-); probes 22q11.2 LSI N25/ Tuple 1 Spectrum Orange and 22q13(control probe, LSI ARSA) Spectrum Green









Management

- multidisciplinary team approach, with specialists in medical genetics, cardiology, diabetes, speech pathology, otolaryngology, dentistry, child psychology and general pediatrics;
- speech therapy and special educational programs;
- periodic evaluation: cardiology, glycemia (case 1), psychology;
- karyotype and FISH of the parents.

Genetic counseling

- offspring of the probands are a 50% risk of inheriting the mutation;
- because of the significant variable expressivity, the phenotype of affected offspring cannot be accurately predicted .

Prenatal testing

- high-resolution ultrasound examination;
- amniocentesis and FISH;
- preimplantation genetic diagnosis.

Conclusions

• we present two case of VCFS in order to illustrate this genetic disorder but also to discuss the variable expression, the management and the genetic counseling;

• FISH confirmed the microdeletion on chromosome 22;

• SVCF is suspected in children with a combination of: congenital heart defects, characteristic dysmorfic face, nasal speech and learning difficulties.