



**THE BENEFITS OF PRENATAL TESTING ASSOCIATED WITH ORAL AND  
MAXILLOFACIAL PATHOLOGY: NEW CASE REPORT**

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**ABSTRACT**

We report a case of a 39 year old Caucasian female, pregnant for the first time. Ultrasound examination showed a singleton pregnancy with multiple congenital cranio-maxillo-facial malformations: unilateral cleft lip and cleft palate, hypoplastic nasal bone, and agenesis of corpus callosum. Amniocentesis was done, and the fetal chromosomal analysis revealed a fetus with normal female karyotype: 46,XX. Serological tests for Toxoplasmosis, Rubella, CMV and Herpes were also normal. After a personalized and multidisciplinary genetic counselling the parents opted, to terminate the pregnancy. The autopsy confirm the prenatal ultrasound diagnosis.

**KEYWORDS:** cranio-maxillo-facial malformations, orofacial clefts, corpus callosum, ultrasound diagnosis, prenatal testing.

**INTRODUCTION**

Orofacial clefts and tooth agenesis represent the most common developmental anomalies and their co-occurrence is often reported in patients as well in animal models<sup>[1]</sup>.

Cleft palate with or without cleft lip can occur isolated (70% of cases), or as part of developmental syndromes that are the result of chromosomal abnormalities or teratogenic conditions<sup>[2, 3, 4]</sup>.

The current literature (PubMed, EMBASE) identify 9 genomic loci and 26 gene candidates underlying the co-occurrence of the orofacial clefts and tooth agenesis: MSX1, PAX9, IRF6, TP63, KMT2D, KDM6A, SATB2, TBX22, TGF $\alpha$ , TGF $\beta$ 3, TGF $\beta$ R1, TGF $\beta$ R2, FGF8, FGFR1, KISS1R, WNT3, WNT5A, CDH1, CHD7, AXIN2, TWIST1, BCOR, OFD1, PTCH1, PITX2, and PVRL1<sup>[1]</sup>.

Children with orofacial clefts and/or tooth agenesis can face problems during feeding, show speech and hearing difficulties, and to varying degrees suffer from disturbances in the normal facial and dental development<sup>[5, 6]</sup>.

Identification of the molecular genetic pathways that dictate palatogenesis and lip formation could offer new and exciting possibilities for the prevention and therapy of orofacial clefts<sup>[2, 7]</sup>.

Currently, craniofacial abnormalities such as oral clefts, can be detected by prenatal modern ultrasound examination<sup>[8, 9, 10]</sup>.

**CASE REPORT**

A 39-year-old pregnant woman was referred at 19 weeks' gestation for a routine prenatal ultrasound scan investigation.

Ultrasound examination revealed a singleton pregnancy with multiple congenital cranio-maxillo-facial malformations. The unilateral cleft lip and cleft palate (Figure 1 - 3), was associated with others anomalies as: hypoplastic nasal bone: 3,5 mm, height of neurocranium 31 mm, height of viscerocranium 21 mm with D1/D2 1.41 (Figure 4 and Figure 5) and agenesis of corpus callosum with hydrocephalia (Figure 6 - 8).



**Figure 1 – Unilateral cleft lip and cleft palate. 4D Real Time, Voluson E8 Ultrasound examination.**



Figure 2 - Unilateral cleft lip and cleft palate. 4D Real Time, Voluson E8 Ultrasound examination.



Figure 5 – Height of neurocranium and height of viscerocranium. 3D Static, Voluson E10 Ultrasound examination.



Figure 3 – Unilateral cleft lip. 4D Real Time, Voluson E8 Ultrasound examination.

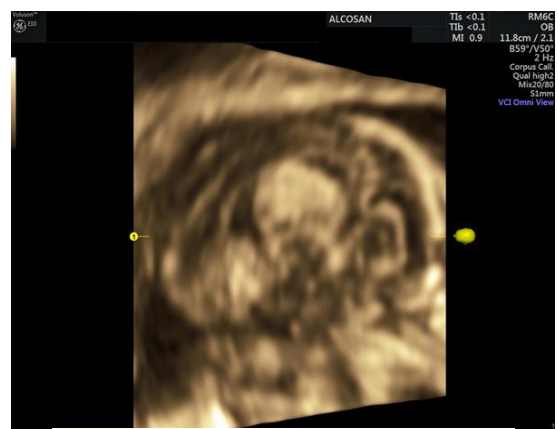


Figure 6 – Agenesis of corpus callosum. VCI Omni VIEW, Voluson E10 Ultrasound examination.



Figure 4 – Height of neurocranium and height of viscerocranium. 3D Static, Voluson E10 Ultrasound examination.



Figure 7 – Agenesis of corpus callosum. 2D, Voluson E10, Ultrasound examination.



**Figure 8 – Agenesis of corpus callosum. 2D, Voluson E10, Ultrasound examination.**

## MATERIALS AND METHODS

Ultrasound examination at 19 weeks of pregnancy, selective ultrasonography for detection of fetal abnormalities, 3D and 4D scan with General Electric Echograph Voluson E 8 and Voluson E10, amniocentesis and the fetal chromosomal analysis, serological tests for Toxoplasmosis, Rubella, CMV and Herpes and genetic counselling was done.

## RESULTS

After the prenatal ultrasound and genetic testing the following diagnosis was established: Pregnancy 19 weeks in evolution. Unilateral cleft lip and cleft palate, Hypoplastic nasal bone, Agenesis of corpus callosum. Ventriculomegaly. Estimated weight: 260 g. After a personalized and multidisciplinary genetic counselling the parents opted to terminate the pregnancy. The prenatal diagnosis was confirmed by autopsy. At the moment, the mother are feeling well.

## DISCUSSION

The development of new research tools to assess quality of life since 2000 will permit further study of the impact of oral and craniofacial conditions on children and families and the effect of treatment on quality of life<sup>[11, 12]</sup>.

Orofacial clefts have functional and aesthetic implications requiring intensive multidisciplinary follow-up to optimise development<sup>[13]</sup>.

Knowledge of the genetic mutations that cause orofacial clefts allows the genetic examination and counselling of future parents with traits of oral cleft in the family<sup>[2]</sup>.

In oral clefts, which are particularly relevant to clinical dentistry, the only therapy available for the closure of the clefts is surgical intervention. However, cleft repair rarely produces ideal facial aesthetics<sup>[14]</sup>.

The impact of the orofacial clefts on the life of the individual and the need for high cost care by a team of several different professionals, including plastic or paediatric surgeons, maxillofacial surgeons, dentists and

orthodontists have triggered intense research into the genetic causes of this condition<sup>[2, 15]</sup>.

Prenatal detection and diagnosis of clefts and craniofacial conditions have advanced dramatically, and the roles of craniofacial professionals and teams have been affected. New understandings of prenatal diagnosis and genomic sciences are redefining genetic counseling, therapy, and future preventive initiatives<sup>[11, 16, 17, 18]</sup>.

## CONCLUSION

The prenatal ultrasound and genetic testing is necessary for the early detection of fetal abnormalities associated with cranio-maxillo-facial pathology.

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