Prenatal diagnosis of cleft lip and cleft lip palate – a case series

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Abstract

Aim: Orofacial clefts comprise cleft lip (CL) or cleft lip-palate (CLP) and are the most frequently encountered malformation of the facial region, accounting for approximately 1-2.2/1,000 live births. The aim of this study was to reveal the particularities regarding the prenatal diagnosis of orofacial clefts in a series of 11 cases diagnosed in a tertiary center. Material and methods: The study was performed in a tertiary diagnostic center for a period of 8 years (January 2010 – December 2017), on 8125 patients that were assessed for screening or suspicion of malformations. Results: During the assessed period a number of 11 fetuses (0.13%) were diagnosed by 2D and 3D ultrasound with CL (4 cases) or CLP (7 cases). The smallest gestational age at diagnosis was of 14 weeks, whereas the highest was 35 weeks. Of the 7 cases diagnosed with CLP, 4 presented also other associated anomalies that involved the central nervous system, the kidney, the skeleton and the stomach. All 4 cases of CL had identifiable associated anomalies. Termination of pregnancy was encountered in 3 cases with CLP. Conclusions: CLP can be diagnosed even at the end of the 1st trimester of pregnancy. CL is usually diagnosed during the 2nd trimester ultrasound exam and is commonly an isolated anomaly. Keywords: cleft lip; cleft lip palate; ultrasound; prenatal diagnosis

Introduction

Orofacial clefts comprise of cleft lip (CL) or cleft lip-palate (CLP) and are the most frequently encountered malformation of the facial area that develop during the 6th-8th week of the intrauterine life. They represent also the second most common birth defects [1,2]. The etiology of these malformations involves multiple factors. Genetic predisposition and fetal exposure to teratogenic factors during the 2nd and the beginning of the 3rd month are the most commonly incriminated triggers for these malformations [3,4]. The worldwide incidence of orofacial clefts varies between 1-2.2/1,000 live births, whereas the prevalence depends on the geographic area and ethnic features and ranges from 1:500 to 1:2,500 live births [5–7]. These types of clefts can be encountered isolated or as a part of other genetic syndromes. Approximately one third of these orofacial malformations are associated with other anomalies, such as the central nervous system, heart or limbs, ones that can threaten life itself [8,9]. Additionally, it is well-documented that CLP (80%) are more commonly associated with other birth defects (37%) [10,11]. Among these genetic and chromosomal anomalies associated with CLP are: trisomy 13 and 18, triploidy, and other syndromes such as Goldenhar, Treacher-Collins, Sticklers, Pierre-Robin, DiGeorge, Meckel-Gruber, Nager, Gorlin, Hydrocephalus, orofacial-digital type 1 and 2, and Van der Woude [12].

The so called primary palate is formed by the lips, the jaw, the nasal bone, while the secondary palate involves the hard (behind and horizontally of the incisive foramen) and soft palate (behind the hard palate, ends in the uvula) [13]. The clefts of the primary and secondary palates have a different embryological origin. Thus, the primary palate clefts are a result of the fusion failure of the medial nasal process and maxillary swellings [14],
while the secondary clefts are due to a failure of fusion of the two palatine shelves and are always in midline and posterior to the incisive foramen [13]. Therefore, the secondary palate defects can include or not a defect of the soft palate. During the gestational age of 10-12 weeks, the ossification of the visceral cranium is complete.

The prenatal diagnosis is usually easier in the case of CL and CLP compared to isolated cleft palate (CP) anomalies. The sonographic assessment of the palate structures, especially the soft palate ones is very hard, even for an experienced physician in prenatal ultrasonography. Therefore, orofacial clefts have been reported to be diagnosed usually during the 2nd and 3rd trimester of pregnancy based on the mid sagittal, coronal and axial views of the fetal face and head [15,16]. Even in case of combined two-dimensional (2D) and three-dimensional (3D) assessments, the detection of these malformations has been rarely described. Therefore, a screening study at 11-13 gestational weeks performed on over 45,000 pregnancies concluded that the prenatal diagnosis of isolated CLP was positive in only 5% of fetuses that were born with this anomaly [17]. Transabdominal ultrasound should always represent the first approach, but it can be improved by transvaginal examination in case of inconclusive images. A multidisciplinary team involved in the care of a patient diagnosed with orofacial clefts should involve specialists in an obstetrics, genetics, neonatology, pediatrics, radiology, oral and maxillofacial surgery and medical ethics. The prognosis of the newborn diagnosed with this malformation depends on both the accuracy of the prenatal diagnosis and the presence of other associations. CLP with the involvement of soft palate and uvula leads to deglutition and phonation disorders that are difficult to be repaired, while isolated CL presents esthetical implications. Prenatal genetic testing could be useful in predicting the recurrence rate of clefts.

The aim of this study was to reveal the particularities regarding the prenatal diagnosis of orofacial clefts (the gestational age at diagnosis, the type and the presence of other associations) in a series of 11 cases diagnosed in a tertiary center.

Material and method

The study was performed in a tertiary diagnostic center for a period of 8 years (January 2010 – December 2017), on 8125 fetuses that were assessed for screening of malformations or suspicion of orofacial malformations. The inclusion criteria comprised all the pregnancies that were referred to our center for screening or for the suspicion of a malformation, while the exclusion criteria consisted of the refusal of the ultrasound exam. The ultrasound exams were performed with Acuson S 2000, or Voluson E8 or Voluson E10 machines. The exams were done by 2D ultrasound with sagittal, coronal and axial planes for the face and additional 3D with multiplanar reconstruction and surface rendering.

The informed consent was obtained from the mothers for the publication of these cases.

Results

During the assessed period of 8 years, of all 8125 pregnancies included in our study, a number of 11 fetuses (0.13%) were diagnosed by 2D and 3D ultrasound with CL (4 cases) or CLP (7 cases). Establishment of the cleft type through ultrasound, gestational age at the time of the diagnosis and associated malformations are described in table I. The ultrasound images of CLP are illustrated in figures 1 and 2 while the ultrasound images of CL are exemplified in figures 3 and 4.

Table I. The types of cleft syndrome in our series

<table>
<thead>
<tr>
<th>Case number</th>
<th>Cleft malformation type</th>
<th>Gestational age at diagnosis (weeks)</th>
<th>Associate anomalies or TOP</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Large CLP that involves palate and uvula</td>
<td>14</td>
<td>TOP, QF PCR of the aborted fetus ruled out trisomy 13, 18, 21</td>
</tr>
<tr>
<td>2</td>
<td>CLP with soft palate involvement</td>
<td>19</td>
<td>Fetal, symmetrical hypotrophy, absence of the stomach, bilateral pelvicavalve dilations, TOP</td>
</tr>
<tr>
<td>3</td>
<td>Medial, unilateral CL</td>
<td>19</td>
<td>–</td>
</tr>
<tr>
<td>4</td>
<td>CLP with a normal uvula</td>
<td>20</td>
<td>–</td>
</tr>
<tr>
<td>5</td>
<td>CLP with the involvement of soft palate and uvula</td>
<td>21</td>
<td>Hydrocefaly, absence of cerebellum, TOP</td>
</tr>
<tr>
<td>6</td>
<td>CLP with soft palate involvement</td>
<td>23</td>
<td>–</td>
</tr>
<tr>
<td>7</td>
<td>Medial, unilateral CL</td>
<td>23</td>
<td>–</td>
</tr>
<tr>
<td>8</td>
<td>CLP without the involvement of uvula</td>
<td>25</td>
<td>Bordeline cerebral ventriculomagaly</td>
</tr>
<tr>
<td>9</td>
<td>Medial, unilateral CL</td>
<td>31</td>
<td>–</td>
</tr>
<tr>
<td>10</td>
<td>Medial, unilateral CL</td>
<td>32</td>
<td>–</td>
</tr>
<tr>
<td>11</td>
<td>CLP without the involvement of uvula</td>
<td>35</td>
<td>Polycystic kidney</td>
</tr>
</tbody>
</table>

CL – cleft lip; CLP – cleft lip and palate; TOP – termination of pregnancy; QF PCR – quantitative fluorescence polymerase chain reaction
Discussions

Fetal malformations present multidisciplinary involvements regarding the diagnosis, the therapeutic approach and the prognosis [18–28]. Therefore, prenatal diagnosis is the cornerstone factor that can influence the prognosis of these fetuses. Orofacial clefts, the most common congenital malformations of all orofacial malformations, can be diagnosed during the intrauterine life due to the routine ultrasound scanning at different gestational ages. Even though, the prenatal diagnosis is usually established during the 2nd an 3rd trimester of pregnancy [15,16], a more recent study has shown that different ultrasound signs can predict orofacial clefts even earlier, between 11 and 13 gestational weeks [17].

Regarding the gestational age at diagnosis in our cases ranged between 14 and 35 gestational weeks, but generally below the gestational age of 25 weeks. Thus, only 3 cases of all 11 were diagnosed after this gestational age. Also, it was reported in the literature that the half left side in medial part is more frequently encountered to be affected by orofacial clefts [29,30]. All our 11 cases presented a medial involvement. The prenatal diagnosis is much easier for orofacial clefts that involve the lip and the palate. When the lips are normal and the cleft involve just the palate, the diagnosis is more difficult [31]. Our series involved 4 cases of CL and 7 cases of CLP. Among the 7 cases of CLP, 4 associated the involvement of soft palate and uvula, worsening significantly the prognosis of these cases and augmenting the importance of an accurate prenatal diagnosis. Additionally, the earliest gestational age at diagnosis was also noticed in a case with CLP. It is also true that 4 of the 7 cases of CLP identified in our series presented other associated malformations, a fact that might have enhanced the accuracy of the diagnosis. On the other hand, all cases of CL diagnosed in our study presented no associated anomalies being classified as isolated CL. Our results are similarly to those reported in the literature underlining a more frequent association between CLP and a higher number of minor defects and syndromes [32]. The most common associated anomalies with CL and/or palate involve those of skeleton and neural tube defects [1,8,9]. Of our 4 CLP cases that presented associated anomalies, we also encountered 2 cases with central nervous system involvement, 2 cases with kidney impairment, 1 case with skeleton defects, but we also found a case with the absence of a stomach.

Regarding the prenatal ultrasound, multiple techniques were proved to improve the diagnosis. Therefore, a three-point multiplanar technique during a routine ul-
tusound screening can result in a diagnosis rate of 65% or even more of facial clefts at the 2nd trimester scan [12]. In addition, in the case of CL and/or alveolar ridge detection, 2D ultrasound improved by 3D can lead to a diagnosis of a cleft of the hard palate in more than 90% of the cases [12]. Moreover, very recent data suggest that during the 11-13 gestational weeks a scan, in the mid-sagittal view of the fetal head, face and brain, certain measurable abnormalities, such as a smaller palatino-maxillary diameter can raise the suspicion of an underlying CLP [33]. Nevertheless, the diagnosis of orofacial clefts during the 1st trimester of pregnancy has been rarely reported until now [34-36], but it was recently proved that sagittal color Doppler ultrasonography can also be useful especially in the detection of fetal hard palate clefts [37]. Regarding the soft palate, the absence of ‘the equals sign’ at 2D ultrasound was proved to be associated with CLP and is an indication for supplementary examination of this part of the palate in a median sagittal section [16].

The finding of an orofacial malformation during the prenatal ultrasound presents also a major emotional impact on the parents, being a burden for them regarding both a possible termination of pregnancy (TOP) and their child’s prognosis after birth [38,39]. Therefore, the benefits of prenatal diagnosis consist also of an adequate parental counselling involving proper communication skills [40,41] in order to improve their understanding regarding the post-natal therapeutic plan and increase their compliance. Even though the prenatal diagnosis of orofacial clefts was thought to increase the likelihood of TOP [42], a recent study performed on subjects from Netherlands proved that most parents did not agree the TOP [39]. It is also true that health-care providers, especially the obstetrician and plastic surgeon, were proved to have a great impact on parents’ decision [39]. TOP was the option in 3 cases in our series, all CLP with soft palate involvement (2 cases with associated anomalies). However, a multidisciplinary team is always required in cases of orofacial malformation in order to obtain the best outcome.

Conclusions

Prenatal diagnosis of orofacial defects is improving continuously. CLP, especially the large defects, can be diagnosed even at the end of the 1st trimester of pregnancy. CL is usually diagnosed during the 2nd trimester routine ultrasound and is commonly an isolated anomaly.

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References


