

## Morphological and ultrasonographic study of fetuses with cervical hygroma. A cases series

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### Abstract

Cystic cervical hygroma or cervical cystic lymphangioma is a congenital benign disease of the lymphatic system that is characterized by the accumulation of lymph in the jugular lymphatic sacs of the nuchal region. The factor that causes this pathology is not clarified yet but the physiopathological mechanism seems to be multifactorial. The incidence and prevalence of cervical hygroma are increased in patients with Turner syndrome, Down syndrome, Klinefelter syndrome, Edwards syndrome, Patau syndrome, Noonan syndrome, pterygium syndrome, Cantrell pentalogy, Fryns syndrome, Apert syndrome, Pena–Shokeir syndrome and achondroplasia. The gold standard method in establishing the antenatal diagnosis is ultrasonography, a non-invasive and low-cost procedure. We report four cases of fetuses who were diagnosed antepartum with cervical hygroma in the Department of Obstetrics and Gynecology of the University Emergency Hospital in Bucharest, Romania. Two products of conception were sent to the Department of Anatomy of the "Carol Davila" University of Medicine and Pharmacy, Bucharest, for an extensive morphological analysis. Cervical cystic hygroma is a congenital condition of variable expression in terms of both morphology and chronology. A complete ultrasound examination, performed by an experimented specialist in maternal-fetal medicine is essential in establishing the diagnosis of cervical hygroma. Screening for aneuploidies, between the 11<sup>th</sup> and 14<sup>th</sup> weeks of pregnancy is also mandatory due to the frequent association between cervical hygroma and congenital anomalies.

**Keywords:** cervical hygroma, ultrasonography, management, congenital disease.

### Introduction

Cystic cervical hygroma or cervical cystic lymphangioma is a congenital benign disease of the lymphatic system that is characterized by enlarged lymphatic ducts determined by the accumulation of lymph in the jugular lymphatic sacs of the nuchal region [1, 2]. It occurs due to the lack of communication between the lymphatic and venous pathways, caused by obstruction [2, 3]. These macrocystic lymphatic anomalies appear in the 6<sup>th</sup> week of gestation [1].

At the end of the 5<sup>th</sup> week of gestation, the lymphatic system begins to develop [2, 4, 5]. The lymphatic channels and lymph sacs (two jugular, two iliac and one retroperitoneal) are formed by the early lymph capillaries [2, 5]. The left and right thoracic ducts connect the jugular lymph sac with the other systems [2, 5]. The lymphatic nodules appear during the 9<sup>th</sup> week of pregnancy when the conjunctive tissue merges with segments of the lymphatic sacs [5, 6]. If there is a miscommunication between the lymphatic and venous system, the jugular lymph sacs start to enlarge due to fluid accumulation at that level [2, 4, 5]. Therefore, in cystic cervical hygroma the typical large masses located in the cervical region are sequestered segments of the primitive lymphatic sacs [7].

The factor that causes this pathology is not clarified yet but the physiopathological mechanism seems to be

multifactorial. Some authors state that segments of the primitive lymphatic sacs remain sequestered due to aberrant lymphatic growth that determines a miscommunication with the venous vessels or lymphatic nodules; anomalies of endothelial vascular growth factor C and its receptor seem to play a determinant role in this pathology [2, 6, 8, 9]. Other specialists discuss the importance of viral infection that determines alterations of the extracellular matrix causing alterations in lymphangiogenesis or even trauma [2, 6, 10].

The incidence of cervical hygroma varies from 1:850 to 1:1000 pregnancies according to different studies, but the majority are interrupted, this is why the incidence reaches 1:17 000 births [5–7, 11]. 65–75% of them are found at birth, while 80–90% can be diagnosed in the first three years [6]. Also, this pathology is frequently associated with fetal aneuploidies and structural malformations (especially vascular anomalies such as left hypoplastic heart and aortic coarctation) [7, 12]. The incidence and prevalence of cervical hygroma are increased in patients with Turner syndrome, Down syndrome, Klinefelter syndrome, Edwards syndrome, Patau syndrome, Noonan syndrome, pterygium syndrome, Cantrell pentalogy, Fryns syndrome, Apert syndrome, Pena–Shokeir syndrome and achondroplasia [6, 7, 12–17].

The cervical region is the most common site, but tumors with similar features may also be found in the head,

neck, axilla, tongue, mediastinum, retroperitoneal space or even in the pelvis [7, 13, 15, 17–20]. Cystic hygromas are dilated lymphatic vessels separated by fibrous tissue and they can be classified as microcystic (smaller than 2 cm), macrocystic (more than 2 cm) or mixed (a large mass composed of multiple cysts, which are separated by multiple septa) [1, 2, 5, 6]. The shape depends on the size of the tumor, the consistency is mild and the fluid has a pale yellow color, alkaline pH and is rich in albumins [2, 5–7]. This is why differential diagnosis should be made with thymic cysts, pericardial cysts, bronchogenic cysts, soft tissue tumors, abscess or hematoma [21].

The gold standard method in establishing the antenatal diagnosis of cervical hygroma is ultrasonography, a non-invasive and low-cost procedure [1, 3, 22]. Since the 10<sup>th</sup> week of gestation a specialist in maternal-fetal medicine can establish the diagnosis of cervical hygroma by identifying a large hypoechoic mass, with small septa inside and regular borders located in the posterior region of the neck extending laterally [1, 3, 22].

Cervical hygroma can be transient or associated with other congenital abnormalities of the brain [23]. Some ultrasonographic features can help to differentiate these malformations. Cervical hygroma does not present a bony defect in the occipital vault [23]. Also, for cervical hygroma the extension of the fetal neck and vertex can be identified [3, 22, 23]. Moreover, cervical hygroma has always a translucent aspect, this is why determining the nuchal translucence (nuchal fold) is a mandatory step in the ultrasound examination during the first trimester [22–24]. During the second trimester of gestation, specific characteristics of other congenital anomalies may be detected during the periodic ultrasound examinations [4].

Due to frequent association with aneuploidies, screening for chromosomal anomalies is also a mandatory step in evaluating a patient for cervical hygroma [7, 12–17, 25].

Postpartum diagnosis of cervical hygroma is established based on the clinical examination followed by imagistic methods. Clinical examination shows a regular, renitent, well-delimited tumor, located in the posterior region of the neck that may extend laterally [2, 5, 22]. Ultrasound examination, magnetic resonance imaging or computed tomography aid the diagnosis [2, 5, 22].

The management of an antepartum-diagnosed fetus

with cervical hygroma depends on the karyotype, the associations with other malformations, the risk of spontaneous abortion, the risk of premature birth and the probability of spontaneous resolution of the tumor [1, 4, 25, 26]. Usually, the prognosis is unfavorable if the diagnosis is established antepartum during the first trimester [27]. If the karyotype is abnormal, termination of pregnancy should also be taken into consideration [28]. However, if the karyotype is normal the pregnancy should be carefully followed-up and terminated only if there is no regression until 20 weeks of gestation [28].

When the diagnosis is established in the 3<sup>rd</sup> trimester or in full-term pregnancies, there is not a consensus regarding the modality of delivery. Some specialists recommend vaginal delivery, while others support Caesarean section [11, 19].

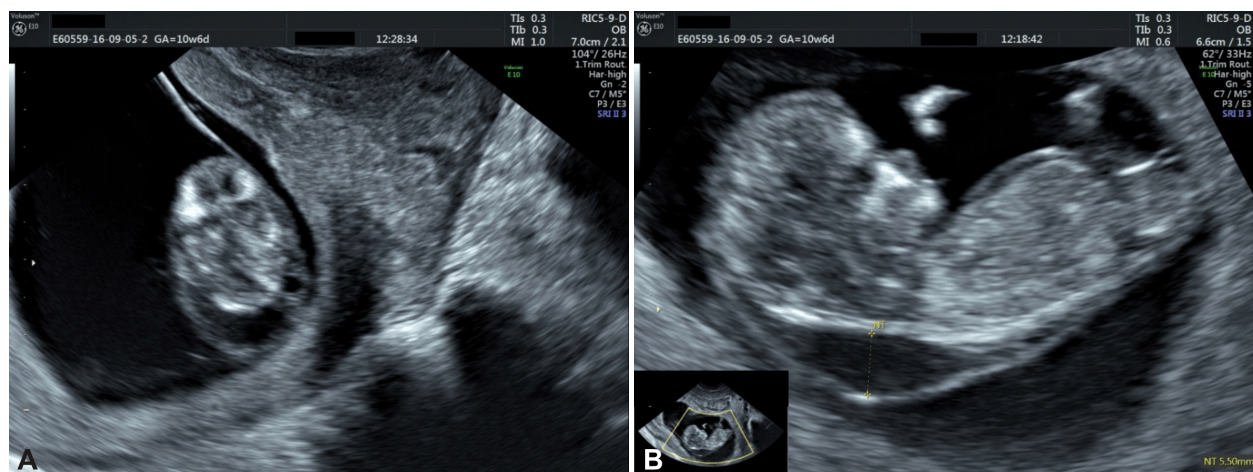
Postpartum management depends on the dimensions of the tumor and therefore the dysfunctions caused by the cervical hygroma [2, 5, 6]. If the tumor compresses vital structures (larynx, trachea, esophagus or the vascular-nervous bundle of the neck) a surgical intervention is recommended in the first days after birth [1, 2, 5–7]. In other cases, the surgical intervention can be postponed. Although surgery is the gold standard treatment for cervical hygroma, conservative methods such as sclerotherapy, drainage-aspiration, steroids, radiofrequency ablation or radiotherapy can be used [2, 5, 6, 8, 27–33].

## Case presentations

We report four cases of fetuses who were diagnosed antepartum with cervical hygroma, in three tertiary care referral centers (see authors affiliations).

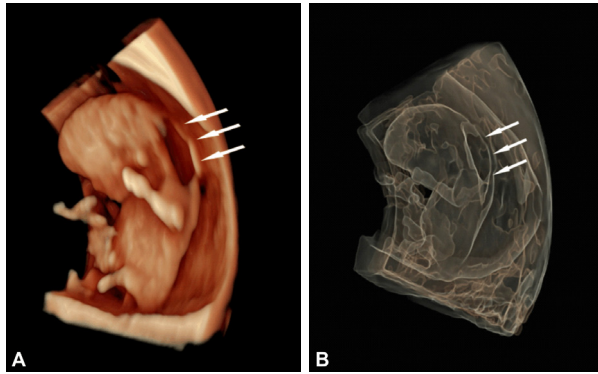
### Case No. 1

The first case is a 32-year-old woman with history of right ectopic tubal pregnancy and a spontaneous abortion during the first trimester who was referred to our Department with the suspicion of cervical hygroma. The gestational age was 10 weeks and six days. We established the diagnosis of cervical hygroma after a complete ultrasound examination (Figures 1 and 2). No other anomalies were detected. She also presented a high risk of Down syndrome during the screening test for aneuploidies and decided to terminate the pregnancy.



**Figure 1 – 2D ultrasound examination of the fetus 1: (A) In the transverse section through the cephalic extremity, note a large hypoechoic mass, with small septa inside and regular borders located in the posterior region of the neck extending laterally; (B) In the sagittal section, note the same large hypoechoic mass and a nuchal translucency of 5.5 mm.**



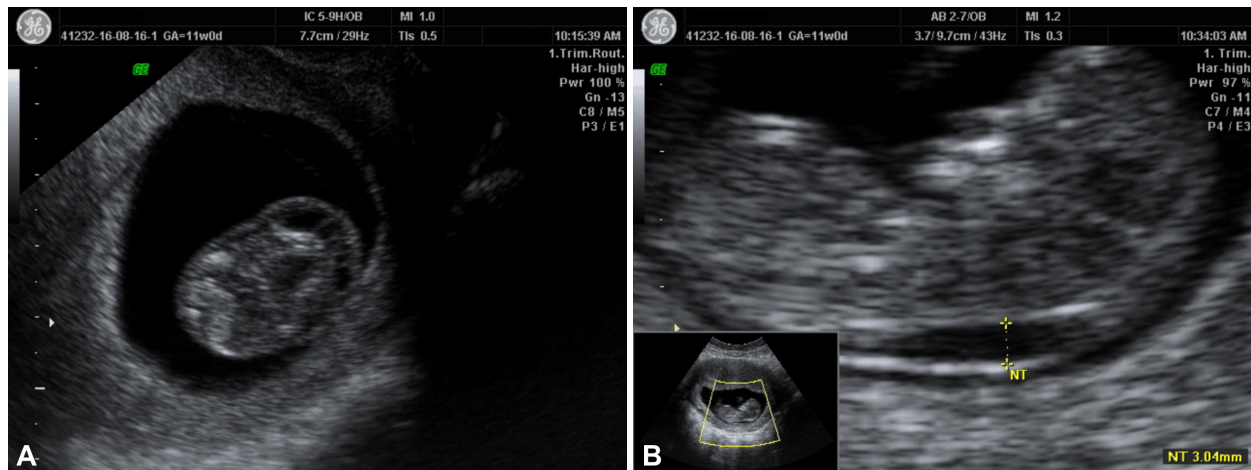


**Figure 2 – 3D ultrasound examination of fetus 1:** (A) Conventional 3D reconstruction emphasis the cervical tumor (white arrows); (B) However, the 3D reconstruction in silhouette mode highlights the structure of the cervical tumor (white arrows), its exact extension and the relation with the other viscera.

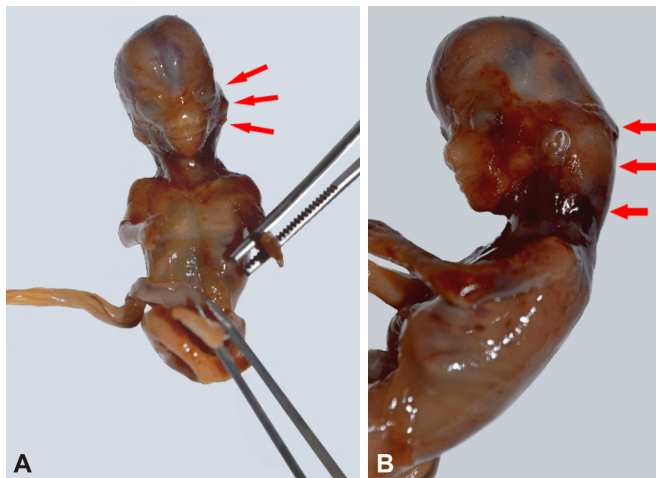
### Case No. 2

We also report the case of a 23-year-old nulliparous woman, with no relevant obstetrical or pathological

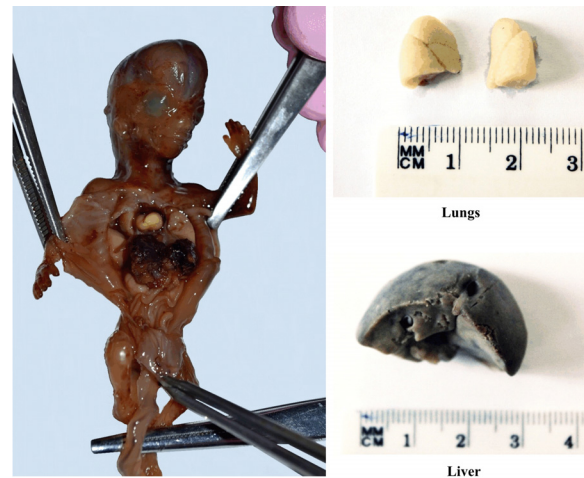
history who was diagnosed with cervical hygroma, in the Department of Obstetrics and Gynecology of the University Emergency Hospital in Bucharest, Romania. The diagnosis was established in the 11<sup>th</sup> week of pregnancy due to specific features detected during the ultrasound examination (Figure 3). No other structural anomalies were observed. The patient performed a non-invasive prenatal test and was diagnosed with Down syndrome. After genetic counseling, the patient decided to terminate the pregnancy. The fetus was expelled after prostaglandin treatment. With the consent of the patient, the product of conception was send to the Department of Anatomy of “Carol Davila” University of Medicine and Pharmacy, Bucharest, for a morphological analysis. The embryo had a cranial-caudal length of 45 mm and a weight of 9.3 g. In the nuchal region, we detected a well-delimited tumor, with regular borders of 4.1/3.2/3.5 mm that extended laterally towards the left side (Figure 4). During the morphological dissection, we detected important parietal edema, peritoneal and pleural effusion, mild hepatomegaly and bilateral lung hypoplasia (Figure 5).



**Figure 3 – 2D ultrasound examination of fetus 2:** (A) In the transverse section through the cephalic extremity, note a large hypoechoic mass, with small septa inside and regular borders located in the posterior region of the neck extending laterally towards left; (B) In the sagittal section, note the same large hypoechoic mass and a nuchal translucency of 3.04 mm.



**Figure 4 – (A and B) External aspect of fetus 2.** Note the cervical hygroma (red arrows) – a well-delimited tumor, with regular borders that extends laterally towards the left side.



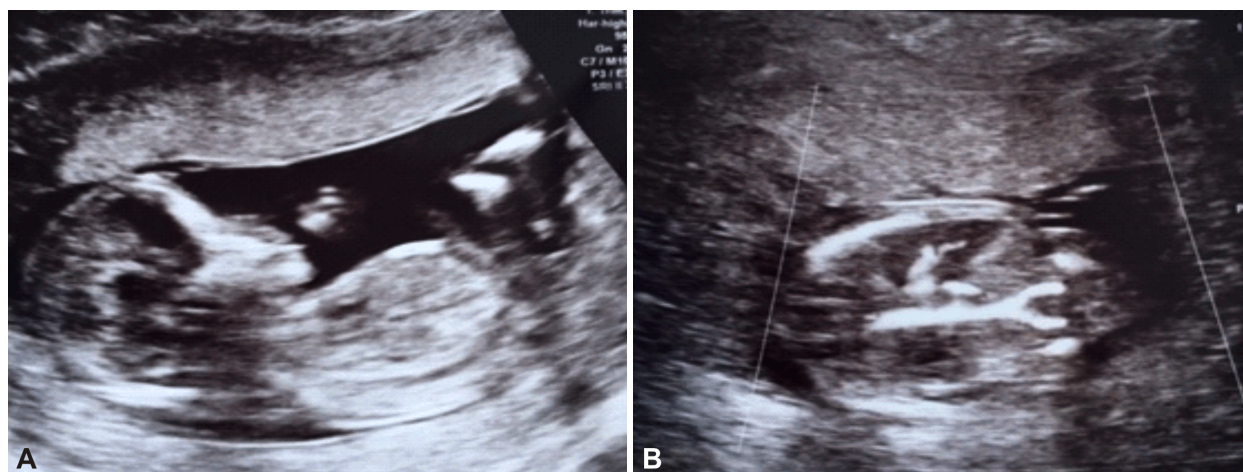
**Figure 5 – Morphological dissection of fetus 2.** Note important parietal edema, peritoneal and pleural effusion, mild hepatomegaly and bilateral lung hypoplasia.

### Case No. 3

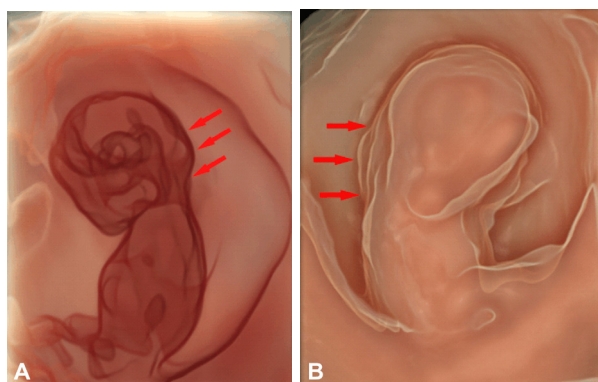
A 29-year-old nulliparous patient, with no relevant obstetrical or pathological history, was diagnosed with cervical hygroma in our Department. During the ultrasound examination at 14 weeks and one day of gestation,

we detected specific features of Down syndrome: the absence of the nasal bones, bilateral renal agenesis and nuchal translucency of 5 mm (Figures 6 and 7).

After genetic counseling, the patient decided to terminate the pregnancy.



**Figure 6 – 2D ultrasound examination of fetus 3: (A) Sagittal section through the cephalic extremity. Note the absence of the nasal bone and a nuchal translucency of 5 mm; (B) Frontal section through the abdomen and Doppler mode, note the agenesis of the renal arteries and kidneys.**

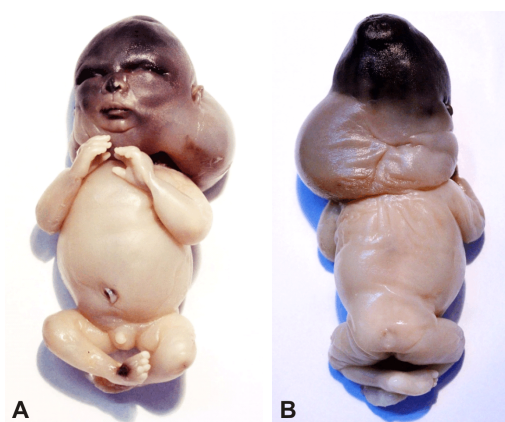


**Figure 7 – (A and B) 3D ultrasound examination of the fetus 3. The 3D reconstruction in silhouette mode highlights the cervical tumor (red arrows), its structure and its extension.**

### Case No. 4

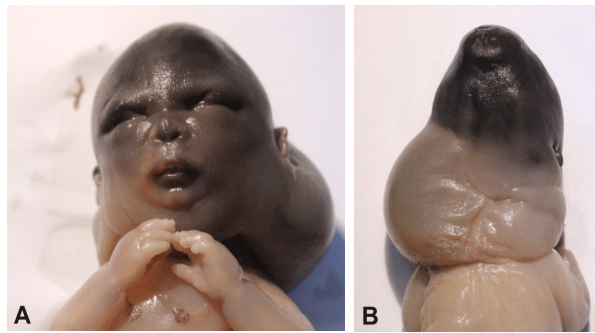
We also report the case of a 33-year-old patient, in the 18<sup>th</sup> week of pregnancy, hospitalized in the Department of Obstetrics and Gynecology of University Emergency Hospital in Bucharest for abundant metrorrhagia and pelvic pain. The ultrasound examination revealed an inferior implantation of the placenta and also hydrops fetalis and a large left cervical cystic tumor. The obstetrical history of the patient revealed a full-term pregnancy at 29-year-old and a miscarriage in the first trimester of pregnancy at the age of 31 years. The routine screening tests were unremarkable, but we detected increased serum levels of anti-Rh antibodies. Screening for fetal aneuploidies revealed an increased risk for Down syndrome. The patient spontaneously aborted four days after the admission in our Department. With the consent of the patient, the product of conception was sent to the Department of Anatomy of the “Carol Davila” University of Medicine and Pharmacy, Bucharest, for an extensive

morphological analysis. The fetus had a general edematous aspect, a weight of 385 g, a length of 19.1 cm and a large cervical tumor with a circumference of 7.1 cm (Figure 8). The cephalic extremity had characteristic signs of Down syndrome: micrognathia, small and low-positioned ears, short neck with an excess of skin on the back neck, oblique palpebral fissures, nasal bridge, small nose and a round face (Figure 9). During the morphological dissection, we detected important parietal edema, peritoneal and pleural effusion and mild hepatomegaly and splenomegaly, which confirmed the diagnosis of hydrops fetalis. We also encountered a large dilatation of the thoracic duct in its superior segment. The cervical tumor was well delimited, it had regular borders and it contained a yellow liquid with relative viscous consistency. After this extensive morphological analysis, we established the diagnosis of cystic hygroma associated with hydrops fetalis and Down syndrome.



**Figure 8 – External aspect of fetus 4: (A) Anterior aspect; (B) Posterior aspect. Note the presence of a large cervical tumor that extends from the nuchal region towards laterally, especially on the left side and the general edematous aspect of the specimen.**





**Figure 9 – Detail of the cephalic extremity of fetus 4 [(A) Anterior aspect; (B) Posterior aspect] that highlights the characteristic signs of the Down syndrome: micrognathia, small and low-positioned ears, short neck with an excess of skin on the back neck, oblique palpebral fissures, nasal bridge, small nose and a round face. Note also the external aspect of the cervical hygroma.**

## Discussion

Cervical hygroma is usually identified during the first trimester screening ultrasonography as mass-like tumor located at the fetal neck [4, 22, 23]. In the first three cases reported, we have established the diagnosis of cervical hygroma, at the end of the first trimester, after a complete ultrasound examination.

Determining the dimension of the nuchal translucence is an important step in evaluating the risk of cervical hygroma. The nuchal translucence (nuchal fold) is a hypo-echogenic area located between the fetal skin and the nuchal fascia [4, 24]. The nuchal fluid arises from paracervical lymphatic system that should drain towards the internal jugular vein *via* the large lymphatic ducts; however, in cystic hygroma the sequestration of segments from the primitive lymphatic sacs determines accumulation of lymph at this level but also important mesenchymal edema [17, 24]. This is why elevated nuchal translucence (2.5–3 mm) is a common ultrasonographic sign is numerous aneuploidies, however when the dimensions exceed 5 mm the diagnosis of cervical hygroma should always be presumed [4, 23, 24]. In Case No. 2, the nuchal translucence was 3.8 mm, but the aspect of the cervical tumor was characteristic in the transverse section.

Another characteristic element in determining the diagnosis of cervical hygroma during the screening first trimester ultrasonography is the presence of an intact nuchal ligament that is compressed by the large multilocular tumor [24]. Thin hyperechogenic septa can be identified in the structure of the tumor in both sagittal and transverse section [4, 22–24]. Cases Nos. 1 and 2 reported by us highlight this specific feature.

Screening for aneuploidies and hydrops fetalis between the 11<sup>th</sup> and 14<sup>th</sup> weeks of pregnancy is also mandatory due to the frequent association between cervical hygroma and congenital anomalies [7, 12–17, 25]. Therefore, determining the serum levels of human chorionic gonadotropin, unconjugated estriol and  $\alpha$ -fetoprotein are recommended in screening for fetal aneuploidies [25]. Fluorescent *in situ* hybridization (FISH) method, non-invasive prenatal test

or amniocentesis may aid the diagnosis [25]. All the cases reported by us were diagnosed with Down syndrome after screening for fetal aneuploidies.

During the second trimester of gestation, specific characteristics of other congenital anomalies may be detected during the periodic ultrasound examinations [4]. In Case No. 3 during the ultrasound examination at 14 weeks and one day of gestation, we detected specific features of Down syndrome: the absence of the nasal bones and bilateral renal agenesis.

In 2005, in a study that included 38 167 patients, 134 (0.35%) were diagnosed with cervical cystic hygroma [34]. In this study, authors mention that 67 (50%) fetuses had chromosomal anomalies [34]. We report a case series of fetuses with cervical hygroma who were all diagnosed with Down syndrome.

In Case No. 4, after an extensive morphological analysis we established the diagnosis of cystic hygroma associated with hydrops fetalis and Down syndrome. We also detected mild signs of hydrops fetalis (parietal edema, peritoneal and pleural effusion, hepatomegaly) in Case No. 2. Has, in a review of 30 cases, demonstrated that non-immune hydrops fetalis is accompanied by structural anomalies in 83.3% of the cases and of chromosomal aberrations in 47.3% of the cases [35]. We report a particular case of cervical hygroma, associated with hydrops fetalis, which may have double cause, non-immune and immune, due to the fact that anti-Rh antibodies were detected in maternal serum.

The management of an antepartum-diagnosed fetus with cervical hygroma depends mainly on the karyotype and the associations with other malformations [1, 4, 25, 26]. Descamps *et al.* recommend termination of pregnancy if the karyotype is abnormal [28]. However, if the karyotype is normal the pregnancy should be carefully followed-up and terminated only if there is no regression until 20 weeks of gestation [28]. At the same time, Fisher *et al.* state that termination of pregnancy should be carefully managed due to the potential error in establishing the diagnosis by conventional 2D prenatal ultrasound [36]. In the first three cases reported by us, we highlighted the importance of 3D reconstruction, especially in silhouette mode in establishing an accurate diagnosis of cervical hygroma.

Postpartum management of patients with cervical hygroma depends on the dimensions of the tumor [2, 5, 6]. The gold standard is complete surgical excision, however the moment should be carefully established [1, 2, 5, 27, 37]. The surgical intervention requires a well-trained multi-disciplinary team in order to minimize the intraoperative risks (injury of the facial, hypoglossal, recurrent laryngeal nerves or injury of the internal jugular vein) and postoperative complications (lymph leakage, infections, poor wound healing or tongue edema) [1, 2, 9, 37–39].

## Conclusions

Cervical cystic hygroma is a congenital condition of variable expression in terms of both morphology and

chronology. A complete ultrasound examination, performed by an experimented specialist in maternal-fetal medicine is essential in establishing the diagnosis of cervical hygroma. Screening for aneuploidies, between the 11<sup>th</sup> and 14<sup>th</sup> weeks of pregnancy is also mandatory due to the frequent association between cervical hygroma and congenital anomalies.

### Conflict of interests

The authors declare that they have no conflict of interests.

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