Cases **report**

MISSED DIAGNOSES IN PRENATAL EVALUATION BY ULTRASOUND: A RETROSPECTIVE ANALYSIS OF FOUR CASES FROM A TERTIARY CENTER FOR FETAL MALFORMATIONS

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Prenat Cardio 2016 Jan; 6(1):56-66
DOI: 10.1515/pcard-2016-0008

Abstract

Four cases of missed prenatal diagnosis by an experienced ultrasonographer and a fetal cardiologist from a tertiary teaching hospital are presented: 3-mm peri-membrane ventricular septal defect; hypoplastic aortic arch requiring prostin infusion after delivery; esophageal atresia with tracheal fistula; and right-sided diaphragmatic hernia. Freezed frames and cine loops of the prenatal ultrasound scans indicated that the missed anomalies were not visible in midgestation, suggesting that in the future, repeat ultrasound scans should be performed before delivery to reduce the occurrence of such diagnostic errors.

Key words: *diagnostic errors, prenatal ultrasound, fetal echocardiography*

INTRODUCTION

The vast majority of data in the published literature tout the success of ultrasonography in prenatal diagnoses. By contrast, there are far fewer publications about errors, mistakes and false-positive or false-negative interpretations. The goal of this report, based on the retrospective evaluation of prenatal ultrasound scans in four cases, is to address the possible reasons for diagnostic errors and how to avoid similar mistakes in the future.

CASE REPORTS

The prenatal and postnatal findings of each of the four cases are summarized in Table 1. It is noteworthy that all four cases had normal first trimester scans and had no chromosomal abnormalities.

Case no. 1

A 26-year-old primigravida was referred to our tertiary center due to a "bright spot" in the left ventricle, detected at 24 weeks of gestation by screening obstetrical ultrasound. At 12 weeks of gestation, nuchal translucency was 1,8 mm, and ductus venosus (DV) tracing and triple test were normal. And at 28 weeks, targeted

How to cite this article:
Respondek-Liberska M.
Missed diagnoses in prenatal evaluation by ultrasound: a retrospective analysis of four cases from a tertiary center for fetal malformations.
Prenat Cardio 2016 Jan; 6(1):56-66

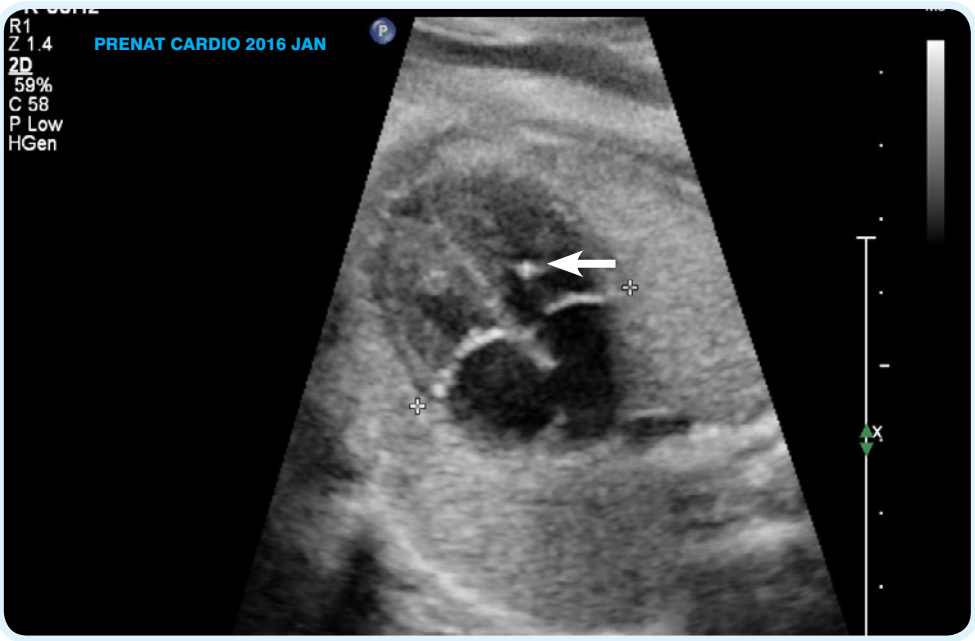

Fig. 1-1. Four-chamber view with bright spot in the left ventricle (arrow).

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Submitted: 2016-11-30; accepted: 2016-12-01

fetal echocardiography confirmed the "bright spot" with no other abnormalities detected (Fig. 1-1). However, due to maternal complaints of genital infection (genital warts), she was advised to return for a targeted echo scan to rule out functional abnormalities later on in gestation, at 34 weeks. Again, fetal echocardiography confirmed normal heart anatomy and normal intracardiac flow (Fig. 1-2 and 1-3). Fetal biometry was 34/33 weeks of gestation. At 39 weeks, there was spontaneous rupture of membranes and a baby girl was delivered, with birth weight of 2900 g and Apgar of 10/10. On day 4 after delivery, a heart murmur was detected, and neonatal echocardiography revealed a 3-mm peri-membrane ventricular septal defect (VSD). The baby was discharged from the hospital on day 6 with recommendation for outpatient follow-up and echocardiography at two months of age.

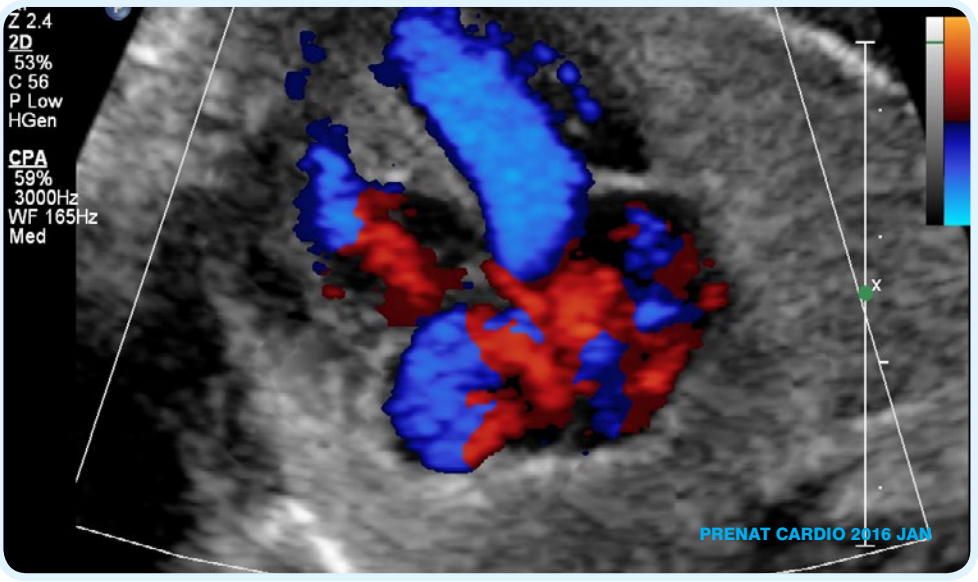


Fig. 1-2. Normal intracardiac flows in color Doppler

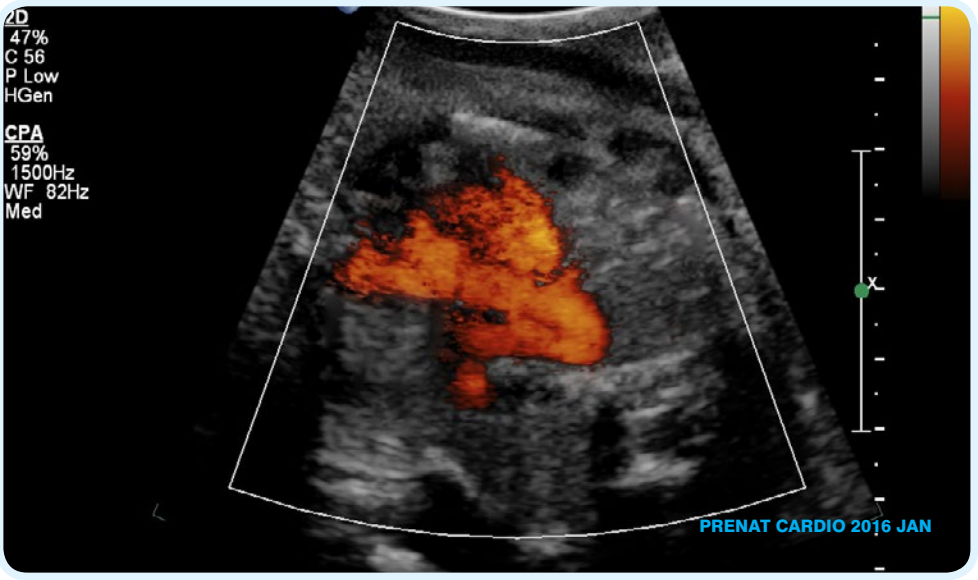


Fig. 1-3. Normal upper mediastinum in power angiography

Case no. 2:

A 28-year-old woman, the mother of a healthy two-year-old infant, in her second pregnancy, who had normal first trimester, with NT at 13 weeks of 1,9 mm, normal triple screen, and normal anomaly scan at 20 weeks of gestation, was referred to our unit at 31 weeks due to four-chamber disproportion (Fig.2-1). By targeted fetal echocardiography, the disproportion was confirmed. However, the intracardiac flows were normal, as were biometry and amniotic fluid index (AFI). A second fetal echocardiography was recommended. At 36 weeks of gestation, a similar disproportion was present (Fig 2-2, cine); however, in the long-

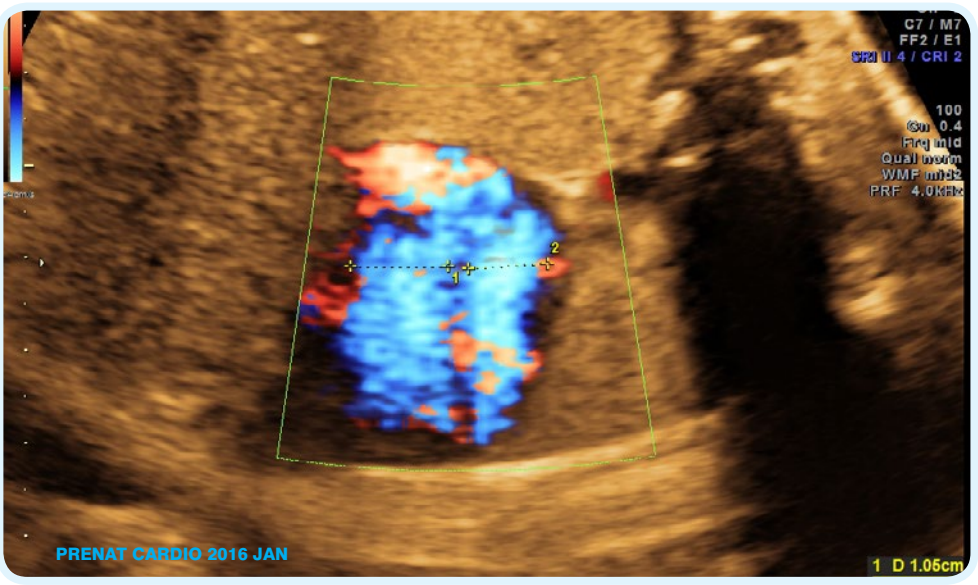


Fig. 2-1 Disproportion at 4 th chamber view in 31st week of pregnancy

axis view, there was bidirectional flow at the level of the aortic arch and ductal arch (Fig.2-3). It was also seen temporary in color Doppler, but later on the flow in both arches was normal (in the same direction) . The interpretation of these finding was "functional" and vaginal delivery at the local hospital was recommended. Three weeks later, she delivered a baby girl whose birth weight was 3000 g and Apgar was 10. However, on day 2, due to low oxygenation of 88%, neonatal echocardiography was performed, revealing hypoplastic left heart syndrome. The neonate was transferred to our Pediatric Cardiology and Cardiac Surgery Department on prostin infusion. On day 28, she had banding of the pulmonary artery and repair of the hypoplastic aortic arch. The postoperative period was uncomplicated.

Fig, 2-2 (Clne): Disprortion - 31 wks

Play the movie directly in the pdf by clicking on the content

At the age of 4 months, the infant was in good clinical condition. However, her echocardiography revealed small left ventricle (Fig 2-5, cine), small aortic valve annulus (4 mm), small mitral valve, narrow aortic isthmus with gradient up to 80 mm Hg, moderate right ventricular hypertrophy with tricuspid valve regurgitation up to 2 m/sec (Fig. 2-6).

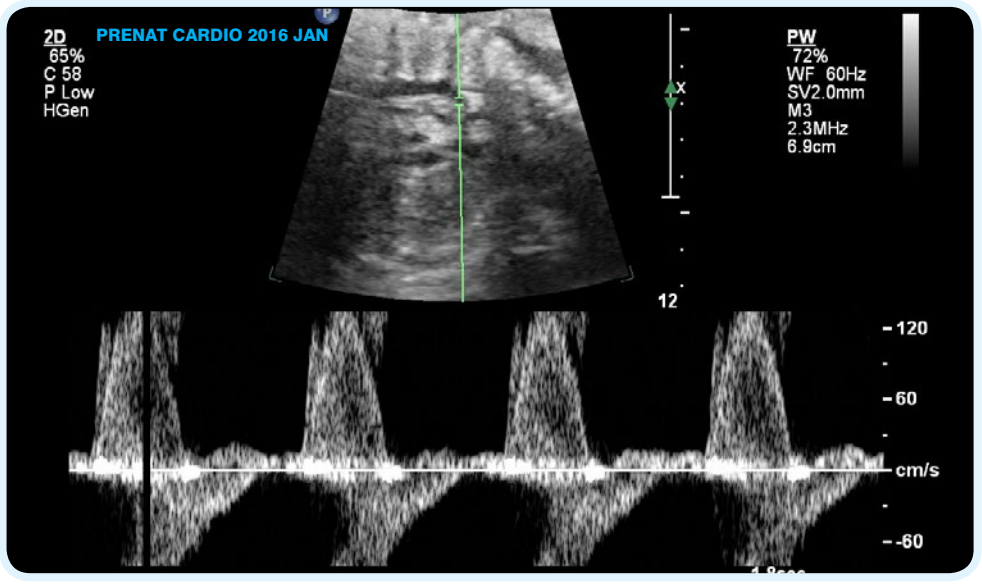
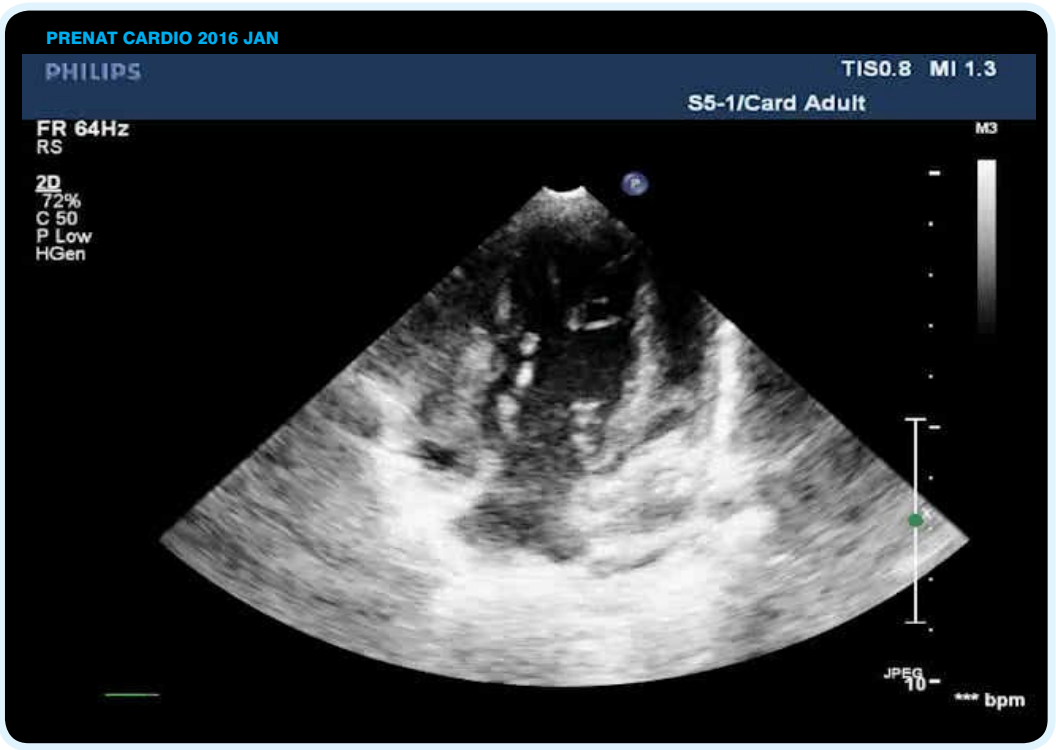


Fig. 2-3. Bidirectional flow in hypoplastic aortic arch in 36th week of pregnancy

Case no. 3

A 32-year-old primigravida had an ultrasound scan at 13 weeks of gestation, showing NT of 2,6 mm, but normal triple screen. Her risk for trisomy 21 was calculated as 1:619, for trisomy 18 as 1:19404 and for trisomy 13 as 1:78269. At 27 weeks, she was treated with antibiotic for 10 days for urinary tract infection. At 31 weeks, obstetrical ultrasound revealed cardiomegaly, single umbilical artery, and left pyelectasis. Due to fetal cardiomegaly she was referred to our unit for targeted fetal echocardiography. Heart to chest area ratio was 0,47, with normal four-chamber view (Fig. 3-1), normal mediastinum view (Fig. 3-2) and normal long- axis scan (Fig. 3-3). There was left pyelactasis up to 6 mm and ureter dilatation up to 5 mm (Fig. 3-4). The right kidney was ectopic in the pelvis behind the bladder. AFI was 15 and biometry was normal, fetal gender was female. A follow-up scan, performed at 37 weeks of gestation, showed similar cardiac findings as at 31 weeks: normal heart anatomy and mild cardiomegaly, cardiovascular profile score (CVPS) was 9/10 (minus 1 for borderline cardiomegaly). The fetal stomach was about 20 mm long (Fig. 3-5), with echogenic amniotic fluid. The fetus was



Fig, 2-5 (Clne)

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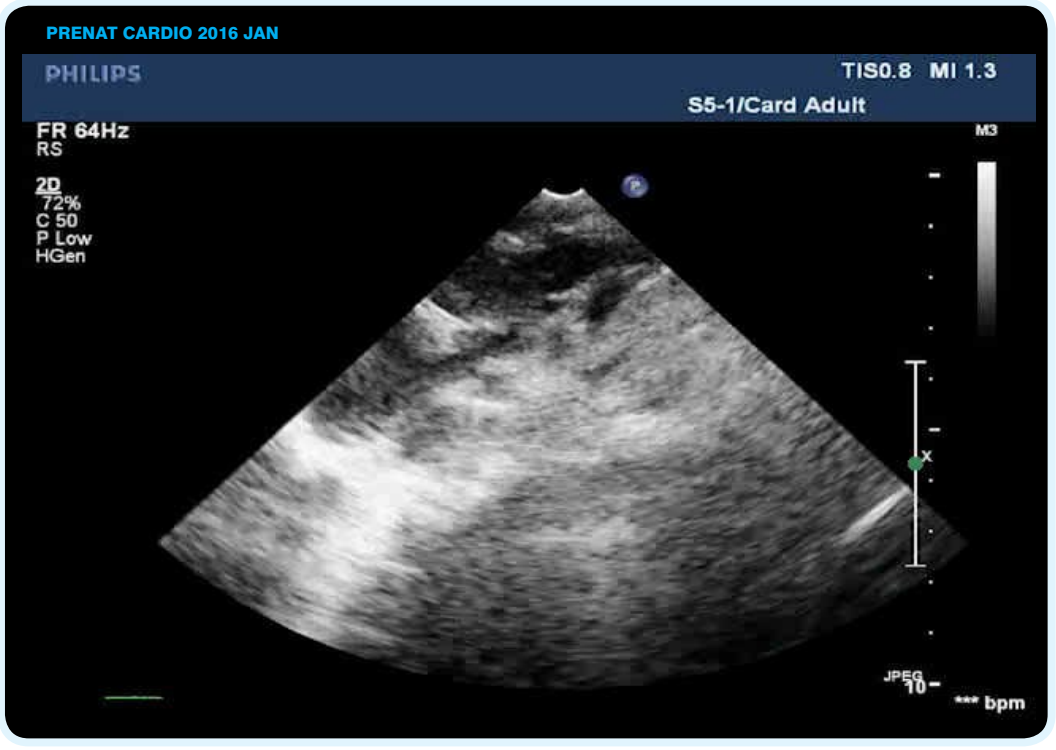

Fig, 2-6 (Clne)

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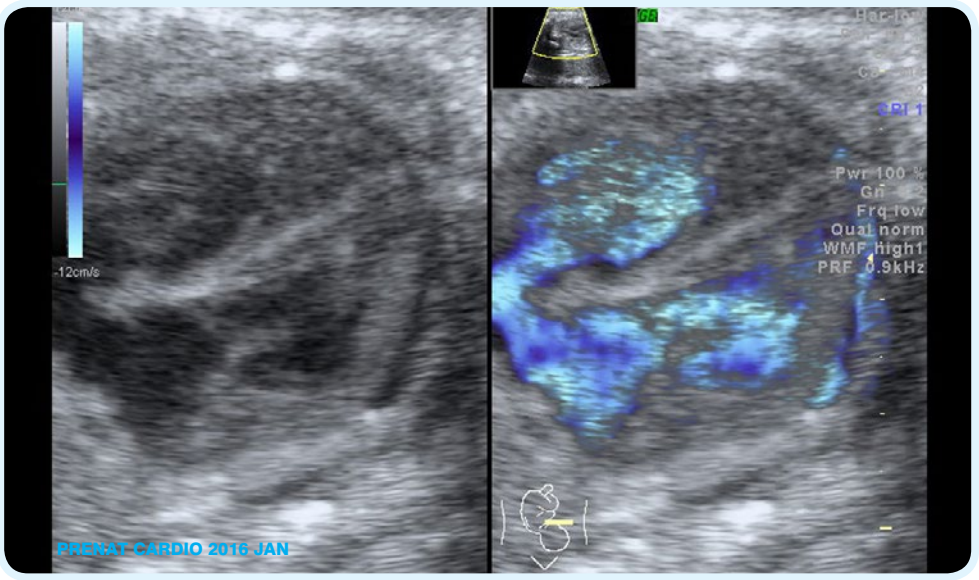

Fig. 3-1. Normal 4 chamber view at 31st week of gestation in 2D and in power angio.

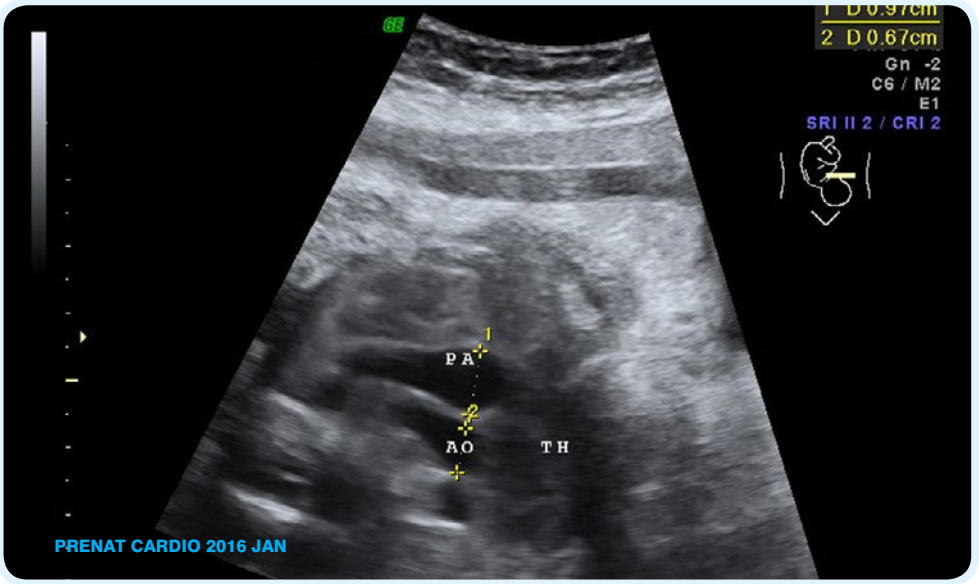

Fig. 3-2. There was normal 3 vessels view and thymus

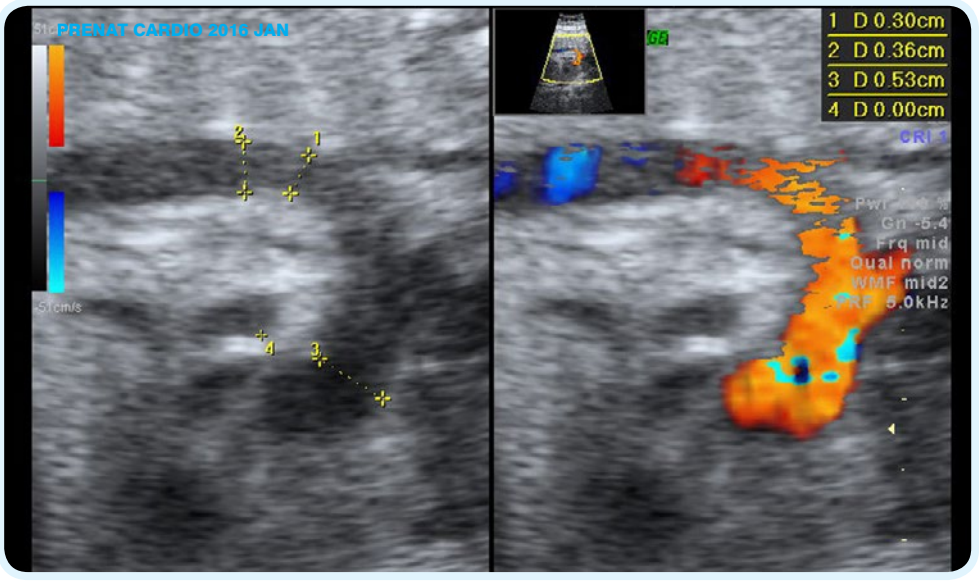

Fig. 3-3. Normal aortic arch in long axis scan in 2D and color Doppler

small for gestational age (Fig. 3-6), however his fetal cardiac function was preserved and Doppler tracings in umbilical arteries and vein, in ductus venosus, as well as in middle cerebral artery were normal.

Two weeks later, due to abnormal cardiotocogram, a baby girl, was delivered by cesarean section with birth weight of 2750 g and Apgar of 9/10. On the delivery ward, nasal tube was inserted and esophageal atresia was suspected and confirmed by chest X-ray with contrast (Fig. 3-7). Surgery was performed on the second day after delivery and esophageal reconstruction was performed with closure of the tracheal fistula. The postoperative course was without complications. Postnatal renal check-up confirmed mild vesico-uretral reflux on the left and ectopic right pelvic kidney, which did not require any interventions in the first six months of postnatal life.

Case no. 4

A 36-year-old pregnant woman with an obstetrical history of C1 – 2000 healthy boy, C2 – 2002 7-week miscarriage, C3 – 2003 – healthy boy, had a normal first trimester of the current pregnancy with NT of 1,8 mm. However, amniocentesis, performed because of maternal age, showed 46XY. And she was referred for fetal echocardiography to our center. At 23 weeks of pregnancy, the fetus was vertex position, stomach and apex on the left side, heart anatomy was described as normal, there was no functional abnormalities, biometry and AFI were normal, as well as 3D fetal assessment (Fig. 4-1 to 4-6). Three months later, a baby boy, delivered by cesarean section, weighed 2600 g with

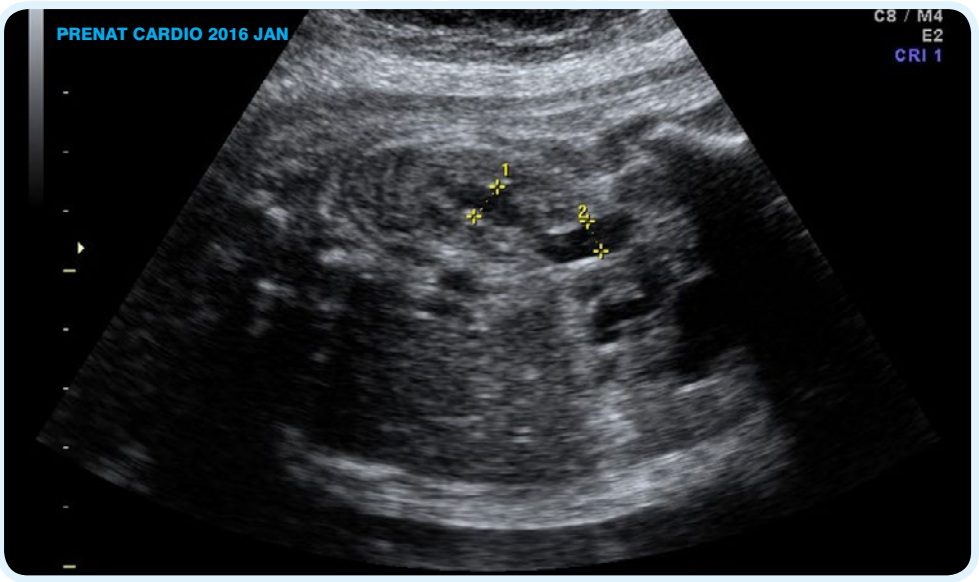

Fig.3- 4. Left 6 mm pyelectasis and ureter dilatation up to 5 mm.

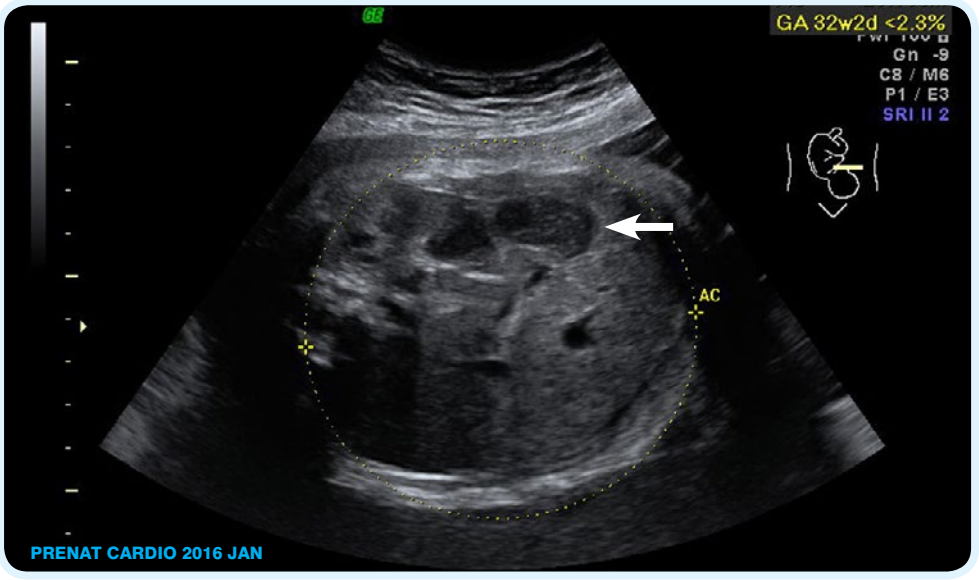

Fig.3- 5 Abdominal circumference at 37 weeks of gestation, suggesting hypotrophy / small gestational age . Stomach was well seen with echogenic amniotic fluid.

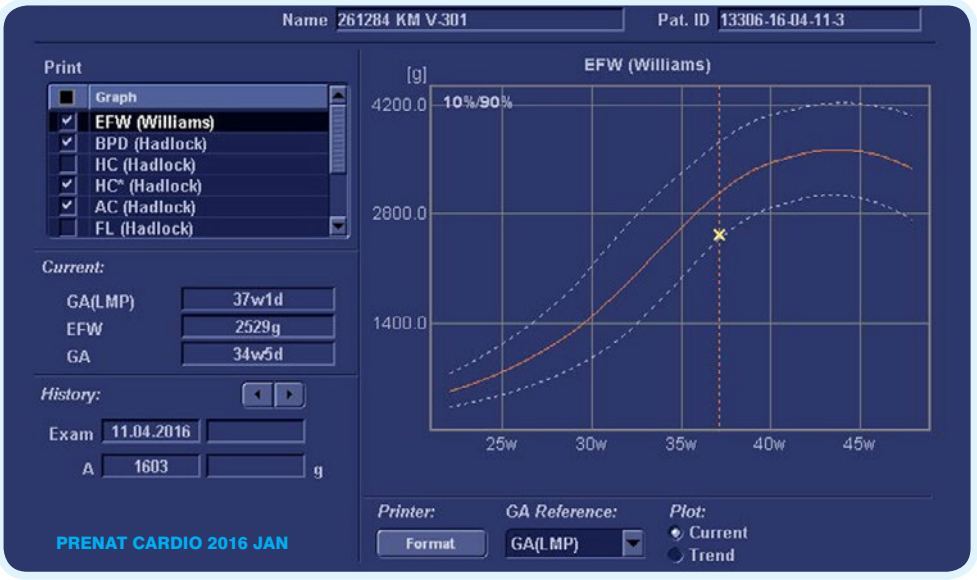

Fig.3- 6 Fetal estimated weight 2529g – 34 w 5 d and 37 w 1d (LMP) suggesting mild hypotrophy

Apgar of 1/5. He required intubation and ventilation. An emergency chest X ray showed a right-sided diaphragmatic hernia (Fig. 4-7). The baby died 26 hours later. The autopsy confirmed hypoplasia of both lungs, a 30-mm central hole in the right diaphragm, and liver segments within the chest.

DISCUSSION

There are few published reports about errors in prenatal diagnoses or misinterpretation. In our unit, since its inception, there has been a standing rule to verify prenatal and postnatal diagnoses. This is possible due to the placement of our Department in research institute combining delivery wards, intensive care units, neonatology, pediatric surgery, pediatric cardiology, cardiac surgery and autopsy departments, as well as by systematic double checking of prenatal findings by postnatal evaluation, usually after discharging the baby after delivery.

Prenatal ultrasound evaluation and echocardiography are very demanding fields of medicine and each mistake may significantly impact fetal and neonatal life. Proper and accurate diagnosis may save fetal/neonatal life, may prolong life, and may hasten postnatal intervention. It is also very important in counselling parents and referring physicians. In our referral center of 1300-1500 fetuses per year, with at least a couple of fetal malformations every week and a huge video library from the past, the expertise and track records are excellent. Therefore, from time to time, we have been asked for a second opinion in difficult cases, and formal medical opinions in cases of malpractice.

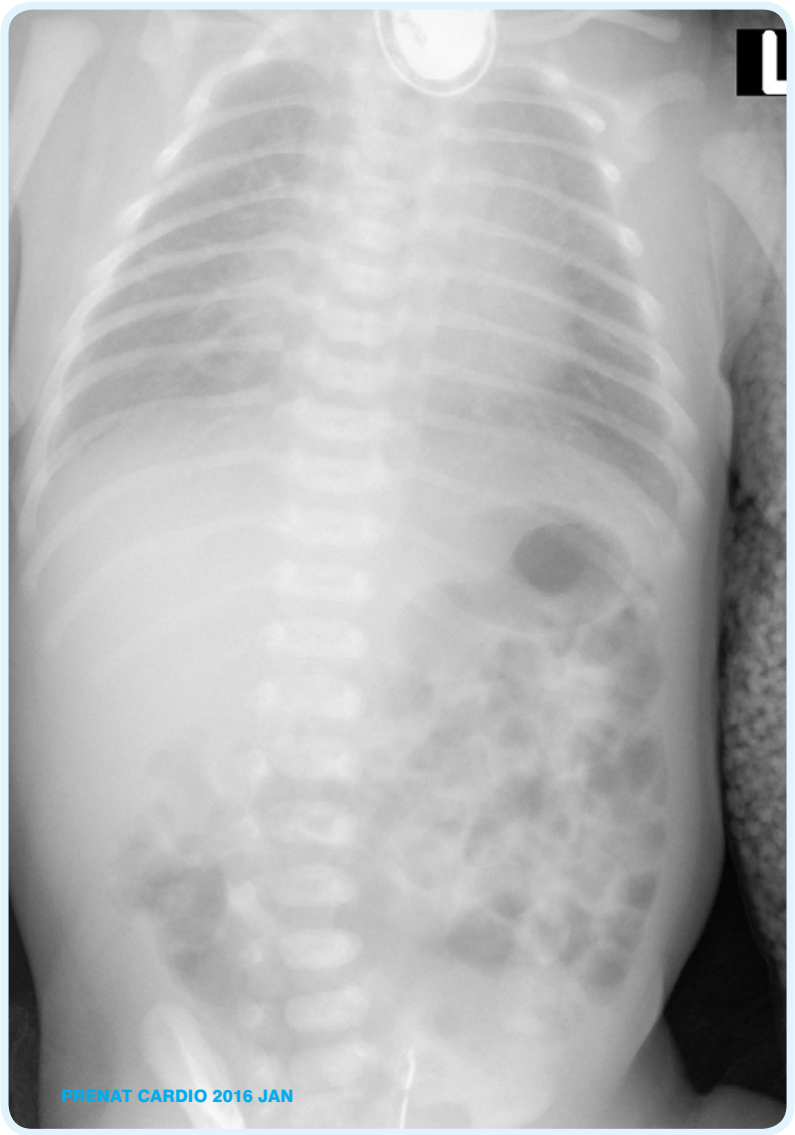

Fig. 3-7. Chest Xray after delivery showing esopahgeal atresia with stomach on the left.

Even with increasingly powerful technologies, years of experience and improved organizational infrastructure, we cannot forget that there is no individual or institution which has a perfect record of medical prenatal diagnosis. Mistakes, unintended errors or misinterpretations might occur even for highly skilled and experienced specialists. Based on retrospective analysis of questionnaires, administered to parents whose neonates with congenital malformations had been treated at our hospital, fetal cardiologists proved to be the most effective in detecting congenital malformations (up to 89,3 %)[1,2]. In this report, we presented some of our mistaken diagnoses in hopes that lessons will be learned to reduce such occurrences and to improve our skills and protocols for the future.

From our previous publications, it was clear that the cause of one of the mistakes in perinatal management could be "fast reading"[3]. The prenatal diagnosis of levo- or L-looped transposition of the great arteries (l-TGA) was correct, but it was read by the neonatologist as d-TGA and prostin infusion was started. The pediatric cardiologist stopped the treatment on the following day. From our previous publications, it was also emphasized that despite NT measurements, biochemical tests, anomaly scan, fetal echocardiography, prenatal detection and diagnosis of Down Syndrome is still challenging and many false negative cases are recorded[4].

HLHS, the most common congenital cardiac anomaly in the Polish Fetal Cardiac Registry, is still better and better detected[5] . However, we were able to prove that a normal four-chamber view and normal three-vessel view in mid-gestation do not guarantee that HLHS will not develop in the second half of pregnancy[6]. We also pointed out already that by focusing on one fetal anomaly, one might overlook another anomaly. We described the prenatal evaluation of a fetus with tumor that first was suspected as sacrococcygeal teratoma, turned out to be mature teratoma, which did not cause any cardiac failure and was successfully operated after delivery. However, both ultrasound and magnetic resonance imaging MRI (and three separate departments in two different hospitals) missed prenatally the right forearm agenesis[7]. We also published about misinterpretations regarding our system of evaluation of the heart defect that are within the Polish Registry for Fetal Cardiac Anomalies[8,9]. Usually the differences were related to poor visualization of the fetal heart anatomy or to using old pediatric classifications instead of current ones dedicated to fetal cardiology[10]. The misinterpretations of prenatal findings are very important, especially nowadays as we try not only to establish the diagnosis but also develop a perinatal care plan based on the projected prognosis[11].

We have widely accepted the detection of anomalies during the first and second trimesters of pregnancies, particularly in referral centers, but we can not forget that during the second half of pregnancy, the fetus is still changing and malformations may also change. We had proven this in Apert Syndrome[12] and in ectopia cordis[13], as well as in HLHS[6]. As presented in Table 1, the reason for missing peri-membrane VSD (Case no. 1) could be fetal heart physiology and equal pressure of the RV and LV at 34 weeks of gestation. Maybe the difference of the pressure could be seen later on, for instance after 37 weeks. However, in this case, prenatal diagnosis would not change the perinatal care, as a 3-mm VSD has no clinical significance both for fetus and neonate. The future outcome depends on the pressure gradient and amount of blood flow across the defect. In some cases, this VSD might be closed by tricuspid septal valve leaflet and the defect may not require any surgical closure. In other cases, it may grow along with the baby and in such case it should be closed usually by cardiac

Fig. 4-1 and 4-2. In 3D, no dysmorphia, normal legs.

surgeon during infancy. An additional observation from our previous study suggested that in cases of a "bright spot" in the four-chamber view, one may expect low birth weight[14] (< 3000g), which was confirmed in this case.

The reason for the error in Case no. 2 was probably not enough attention paid on the reversal flow at the level of ductus arteriosus and aortic arch. Despite not significant disproportion in the four-chamber and three-vessel views, reversal flow at 36 weeks of gestation should alert the specialist about ductal-dependent flow and necessity for prostin administration for the neonate. This mistake can best be classified as "human error" and misinterpretation.

The prenatal detection of esophageal atresia in Case no. 3 (coexisting with mild uropathy) was very difficult, as the stomach was well seen and the AFI was normal. However, echogenic fluid in the fetal stomach, by retrospective analysis, was "strange" and could alert other differential diagnosis. Fetal cardiomegaly was interpreted as one of the features of mild uropathy (assuming similar prenatal mechanism to postnatal changes in patient's heart involvement in case of "nephropathy") , but we know that esophageal atresia with tracheal fistula could be also a reason for slower lung and chest development and taking part in pathogenetic mechanism of small for gestational age in the third trimester in this case.

The most dramatic diagnostic error related to Case no. 4, who had anomaly scan in our center at 24 weeks of pregnancy without follow-up scan and despite normal four-chamber view and normal lung echogenicity. Sixteen weeks later, the baby was born with right-sided diaphragmatic hernia and died in our intensive care unit on the second day after delivery. Autopsy revealed a significant hypoplasia of both lungs. In our center, diaphragmatic hernia is not a rare disease[15]. In 2005, in our unit, we had 17 fetuses with different types of diaphragmatic hernia. Usually it is a left-sided anomaly with the stomach within the fetal chest cavity and diagnosis is straightforward. Surgical-correction results of diaphragmatic hernia from our center are good, especially for babies delivered at term. The mistake in this instance confirmed that in selected cases the diagnosis of diaphragmatic hernia may be difficult, particularly those on the right side, when a normally sited stomach below the

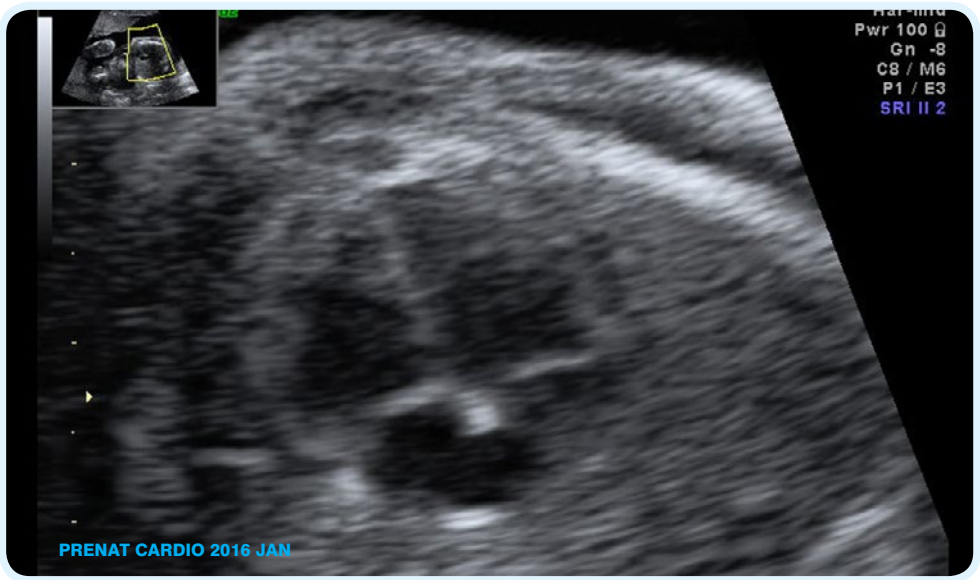

Fig. 4-3. Four-chamber view, showing normal heart axis, similar echogenicity on the both sides of the thorax.

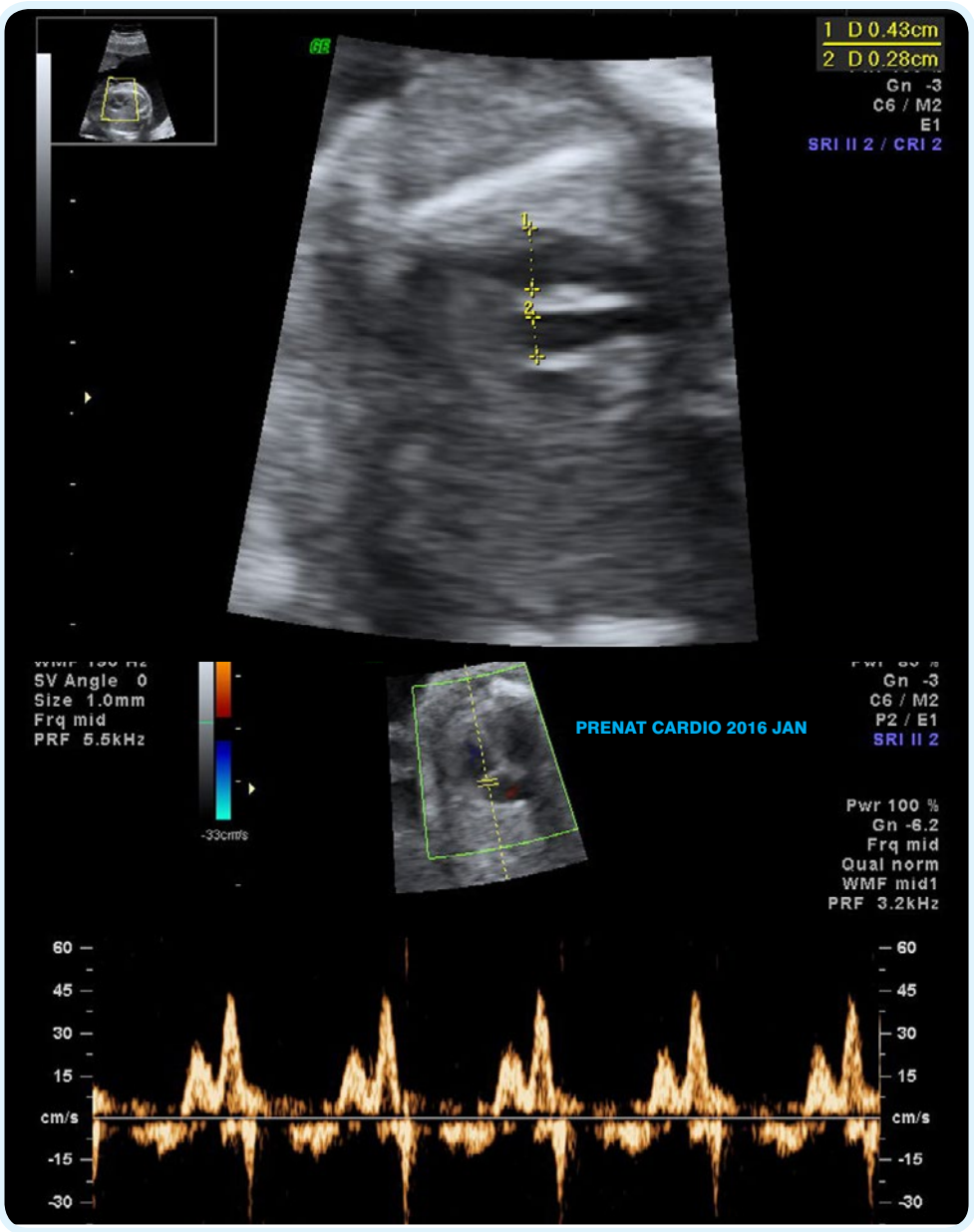

Fig.4-4 Normal mediastinum and fig. 4-5: normal intracardiac flows - tricuspid valve inflow

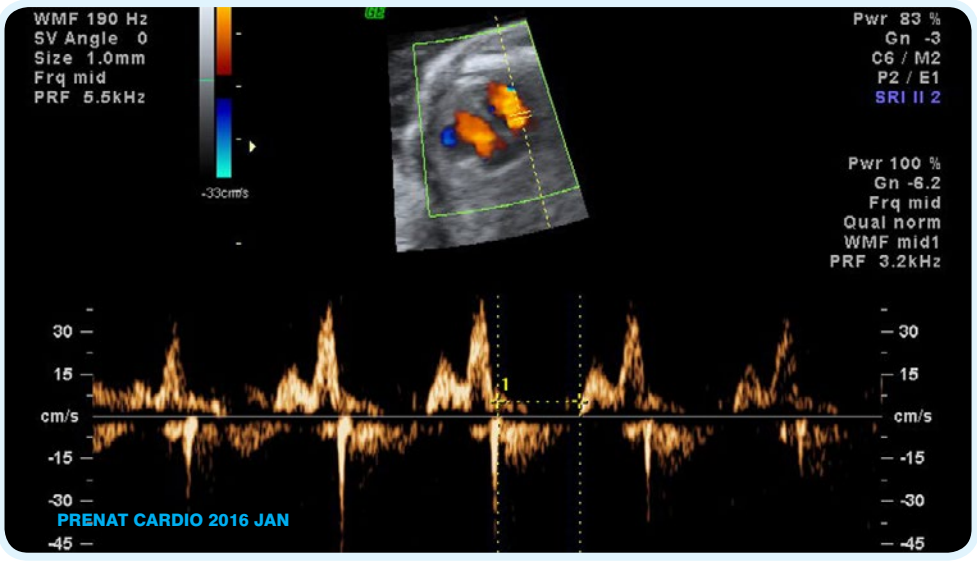

Fig. 4-6. Normal intracardiac flow - mitral inflow

diaphragm may mislead the ultrasonographer. Prenatal diagnosis of diaphragmatic hernia coexisting with heart defect is much more difficult, but extremely important due to different counselling and usually conservative management[16,17].

So far, in majority mistakes in prenatal diagnoses the discussions was focused on screening, maternal obesity, anterior placenta, skill of examiners [18,19]. In this paper we focus on the importance of the timing of diagnoses in 3rd trimester or before the delivery, as this problem is very rare in current literature [20].

Summarizing the current findings and diagnostic errors in these four cases emphasize that normal ultrasound scans in mid-gestation are insufficient to exclude the possibility of severe congenital defects at the time of delivery. Thus, a third trimester scan is justified and should be considered for wide-scale implementation. Such a routine practice might be challenging for health care organizations and might require additional funds, however, its seems important for our unborn patients. Thus, in conclusion: an anomaly detected in the fetal ultrasound examination might not be the only one; and so-called "normal" scans in mid-gestation do not exclude the presence of severe life-threatening anomaly in the third trimester.

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Fig. 4-7. Stomach on the left.

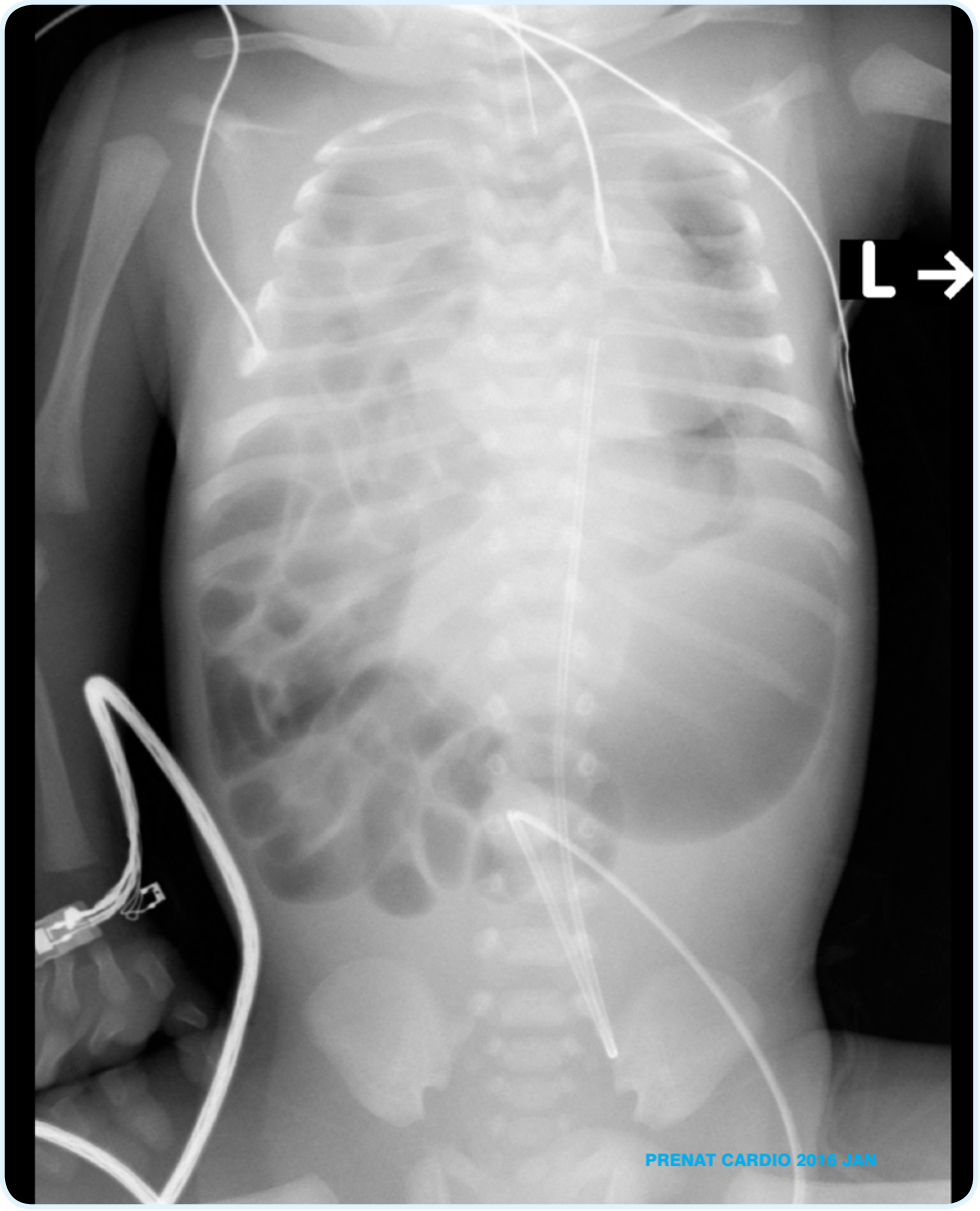

Fig.4- 8. Emergency chest X-ray showing right diaphragmatic hernia.

Case No.	Prenatal findings	Gestational age of the last echocardiography	Time to delivery	Postnatal diagnosis	Possible reason of mistaken diagnosis	How to avoid such a mistake
1	Bright spot, possible fetal infection	34 weeks	5 weeks	3-mm peri-membrane VSD	Equal pressure in left and right ventricle at 34 weeks and no flow	Fetal echo > 37 weeks
2	Disproportion (RA > LA, RV> LV and PA> Ao) Aortic arch hypoplasia	36 weeks	3 weeks	HLHS/ CoA Prostin & planned cardiac surgery	Misinterpretation of prenatal findings or progression of disease in the end of pregnancy	Fetal echo > 37 weeks
3	Mild uropathy, dilated ureter, ectopic kidney Good size stomach but with echogenic fluid	37 weeks	2 weeks	Esophageal atresia	Each fetal anomaly may be the first clue to look for other problems	?
4	"Normal anatomy scan"	23 weeks	16 weeks	R diaphragmatic hernia	Too short 20 - minutes scan in midgestation	3rd trimester scan

RA – right atrium, LA – left atrium, RV – Right ventricle, LV – Left ventricle, PA – pulmonary artery, Ao - aorta

Table 1: Summary of the presented cases. Prenatal and postnatal findings in four cases and the possible reasons for errors in diagnosis.

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Acknowledgements:

Conflicts of interest: none

Funding: There was no financial support for this research