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Case report

Concomitant effects of late fetal growth restriction and intra-cytoplasmatic sperm injection on fetal cardiac remodelling: a case report

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Abstract

Fetuses conceived by intra-cytoplasmatic sperm injection (ICSI) and complicated by fetal growth restriction (FGR) are characterised by a different phenotype of cardiac remodelling. We present a case in which both conditions, ICSI and late FGR, were present. An echocardiographic study of the fetal cardiac geometry showed the presence of a globular heart with sphericity indices of both ventricles values < 5th centile, not associated with dilated heart, as present in ICSI fetuses. The possible pathophysiological changes of these findings are discussed.

Key words: intra-cytoplasmatic sperm injection, fetal growth restriction, fetal cardiac geometry, fetal cardiac remodelling, echocardiography, sphericity index.

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Introduction

Distinct phenotypes of fetal cardiac remodelling have been shown in pregnancies complicated with fetal growth restriction (FGR) from those obtained by intracytoplasmic sperm injection (ICSI) [1-4]. Fetal growth restriction fetuses are characterised by a globular heart, as expressed by a low sphericity index (SI) in both ventricles [1, 2], while in fetuses obtained by ICSI the changes in SI are associated with dilated atria [3, 4].

The identification of different cardiac phenotypes in FGR and ICSI pregnancies has been suggested to be useful in the diagnosis and long-term cardiovascular prognosis of these fetuses and children [5].

We describe a case of pregnancy obtained by ICSI and complicated by late FGR, in which cardiac function was assessed by fetal echocardiography.

Case report

We present case of a 44-year-old woman, gravida 1, para 0, with pregnancy achieved by ICSI, and developing late FGR. Pregnancy resulted from the transfer of a single frozen embryo obtained using a donor egg. Before transfer a preimplantation diagnosis was performed, showing absence of aneuploidies. Her body mass index before pregnancy was 21.5, and she was treated with low-molecular-weight heparin, being a carrier of

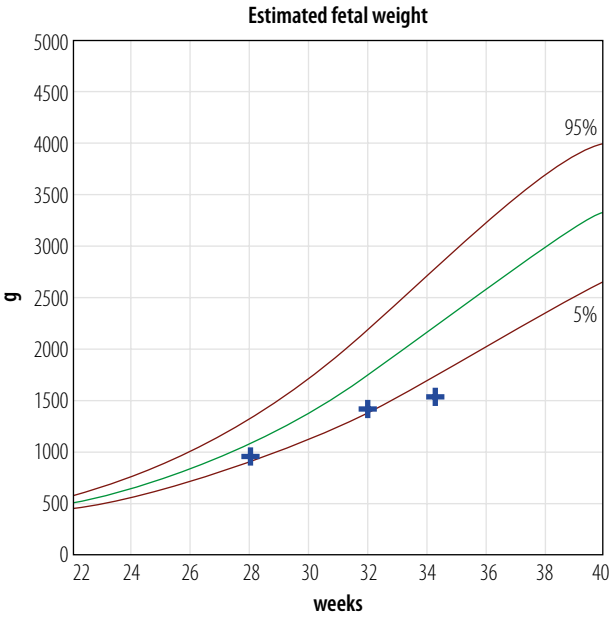

Figure 1. Serial changes in estimated fetal weight. Data are plotted against our reference limits for gestation [7]

factor V Leiden mutation and for a previous history of post-traumatic deep venous thrombosis.

An ultrasound at 8 weeks + 2 days revealed a single intrauterine pregnancy in normal evolution. The first trimester screening ultrasound performed at 13 weeks and 1 day showed a crown rump length of 65 mm, nuchal translucency of 1.4 mm, nasal bone presence, tricuspid valve Doppler without regurgitation and ductus venosus waveforms with a Pulsatility Index (PI) of 1.0. At the patient's request non-invasive prenatal testing was performed that showed a low risk for aneuploidies, a male fetus, and a free-fetal DNA fraction of 8%.

At the second trimester screening ultrasound, performed at 21 + 0 weeks, the assessment of fetal anatomy and uterine artery Doppler was normal with mean PI of 1.2 [6]. Fetal biometric evaluation showed a biparietal diameter, head circumference, and abdominal circumference (AC) appropriate for gestational age and a short femur length of 30 mm (3rd centile) according to our reference limits for gestation [7].

The fetal growth assessment was repeated at 28, 32, and 34 weeks of gestation, and the estimated fetal weight (EFW) was computed with the Hadlock 4 formula [8]. There was a progressive deterioration of fetal growth with the EFW at 34 weeks of 1553 g below the 3rd centile, as shown in Figure 1. Concomitant Doppler studies revealed a progressive increase of umbilical artery PI and decrease in middle cerebral artery PI resulting in an abnormal placental cerebral artery ratio at 34 weeks of gestation (Figure 2). According the criteria of the 2016 Delphi consensus on fetal growth restriction [9], the fetus fulfilled the criteria of late FGR and was managed according to our unit protocol. In particular, the umbilical vein flow (UVBF) was evaluated and corrected for fetal AC, and the UVBF/AC result was below the 5th centile for gestational age (Figure 3) [10]. A cardiac morphometric evaluation was performed to evaluate the presence of cardiac remodelling. The SI of both the

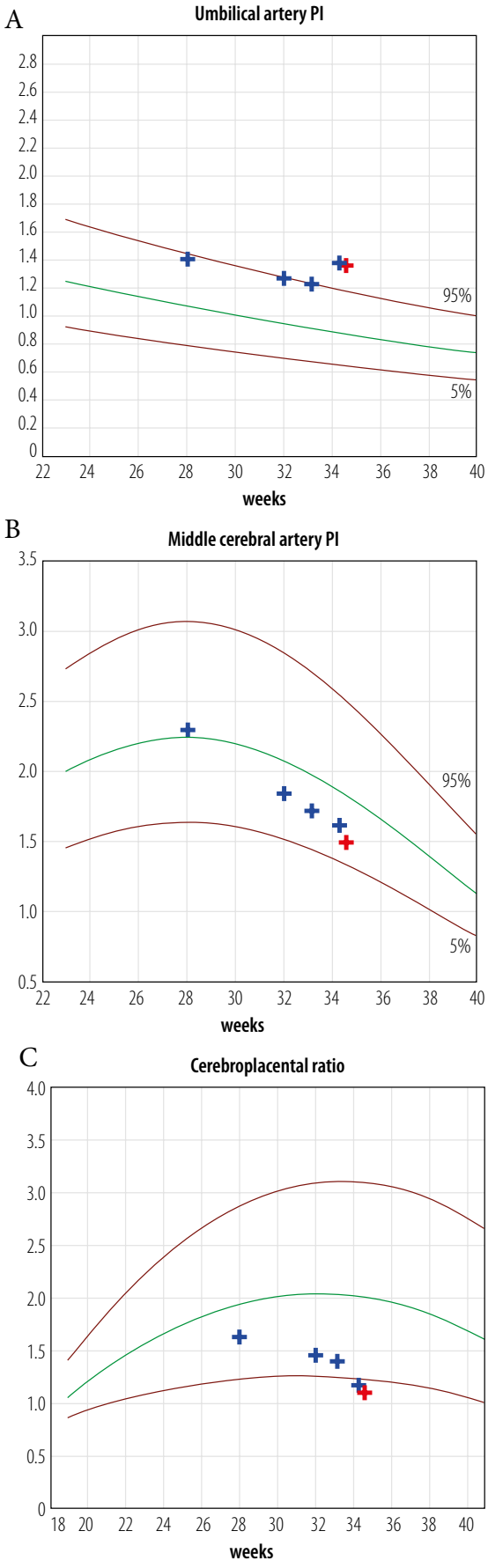

Figure 2. Serial changes of Doppler PI from umbilical artery Pulsatility Index (PI) (**A**), middle cerebral artery PI (**B**), and cerebroplacental ratio (**C**). Data are plotted against our reference limits for gestation [6]

left and right ventricle result was below the 5th centile (left SI = 1.21; right SI = 1.32) while right and left atria values were within normal ranges (Figure 4). Pregnancy was followed by serial fetal heart rate monitoring, which was normal, and Doppler recordings from fetal circulation, which remained stable. At 36 weeks and 0 days an elective Caesarean delivery for breech presentation was performed and a male newborn was delivered, weighting 1550 g, placental weight 200 g, Apgar score of 10 at 5', umbilical cord arterial pH 7.30, and Base Excess 2.0 mmol/l. The newborn was admitted to a neonatal special care unit with an uneventful postnatal course and was discharged 20 days after admission. A postnatal cardiac evaluation is in progress.

Discussion

In this case report we described the cardiac changes occurring in a fetus conceived by IVF and complicated by late FGR. Both conditions could independently alter cardiac geometry by different mechanisms, and they were concomitantly present in our case. In such a fetus the typical cardiac phenotype of fetuses conceived by ICSI characterised by dilated atria and more spherical ventricles was not present, while the SI were markedly reduced in both ventricles. As a consequence the cardiac phenotype of FGR was dominant in our case.

Valenzuela et al. [11] recently compared the cardiac geometry in a cohort of IVF fetuses divided according to the presence of appropriate fetal growth or below the 10th percentile and found a combination of the features between the two phenotypes in small fetuses. Moreover, in this series fetuses were mainly small and without severe FGR as in our case, and this may explain this discrepancy.

The intrauterine environment did not allow us to obtain direct evidence on the mechanisms causing the cardiac changes in these two conditions. However, it is possible to speculate that in both conditions a small placenta is present, which may induce similar changes in ventricular shape. On the other hand, the reduction in cardiac preload, as expressed by reduced UVBF, present only in FGR (2), may explain the differences in atrial area between the two conditions.

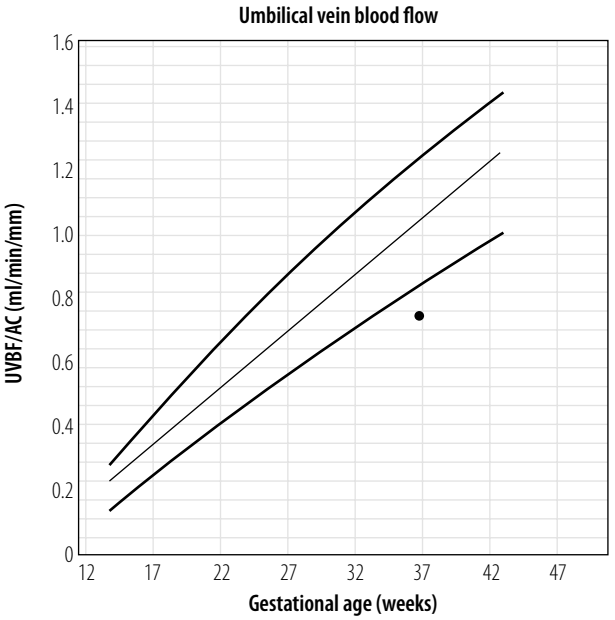

Figure 3. Umbilical vein flow corrected for abdominal circumference plotted on our reference limits for gestation [10]

Irrespectively of these speculations, our report confirms the findings that FGR and conception with ICSI were associated with distinct patterns of fetal cardiac remodelling, supporting the concept that they are independent causes of cardiac programming.

Conclusions

Although the underlying mechanisms for these changes remain to be elucidated, the existence of different cardiac remodelling in ICSI and IUGR fetuses suggests the need for long-term cardiovascular follow-up of both FGR and ICSI fetuses

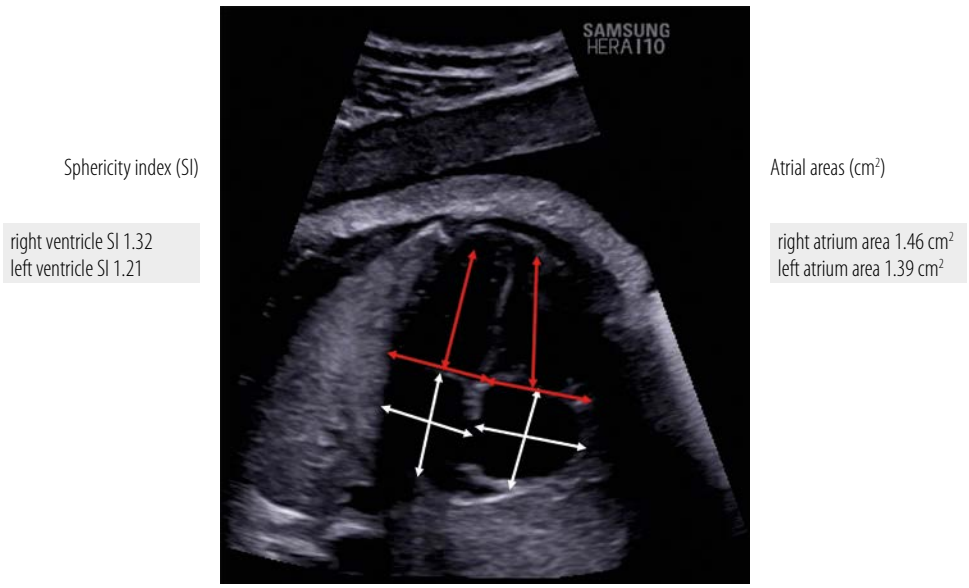

Figure 4. Four-chamber view of the fetal heart at end diastole with the calculated values of atrial areas and ventricular sphericity index

and opens a window of opportunity to monitor and potentially improve cardiovascular health in these children.

Conflict of interest

The authors declare no conflict of interest.

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