Antenatal bilateral renal vein and vena cava thrombosis in dichorionic twin pregnancy

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ABSTRACT

Introduction: Antenatal renal vein thrombosis is a rarely described diagnostic finding, with variable consequences on kidney function. Case Report: We present the unusual case of a dichorionic twin pregnancy in 34 weeks of gestation with one affected fetus, showing already intrauterine a bilateral hyperechoic kidneys with a left kidney increased in size and cardiotocographic signs of fetal distress, while dichorionic male co-twin was healthy. At birth, there was no heartbeat of the affected fetus despite resuscitation. Clinical examination of the stillborn showed that both kidneys were bulky. At autopsy, it was a stillborn boy, with enlarged hemorrhagic kidneys, and thrombosis of the renal and adrenal veins, extending to the inferior vena cava, with no sign of fetal hydrops except for a moderate pleural effusion. Histological examination confirmed the presence of hemorrhagic infarction by massive bleeding with thrombosis of both renal veins and suprarenal vena cava. The postnatal thrombophilia investigations revealed a heterozygous mutation in the MTHFR gene with no associated hyperhomocysteinemia. Conclusion: There are still many unresolved issues regarding antenatal vein thrombosis. Diagnostic possibilities and prognostic probabilities still show large discrepancies.

Keywords: Antenatal thrombosis, Inferior vena cava thrombosis, Thrombosis of renal veins, Twin pregnancy

INTRODUCTION

Antenatal renal vein thrombosis is a rarely described diagnostic finding, with variable consequences on kidney function. Its prevalence ranges from 2.2 to 50 per 100,000 births [1]. Renal vein thrombosis is particularly serious and can occur insidiously during pregnancy. It is difficult to define a group of patients at risk or a standardized approach to monitoring, surveillance and prevention, given the small number of cases. In the antenatal period, the condition is usually unknown to sonographers and it is mainly diagnosed after birth. We present the unusual case of a dichorionic twin pregnancy in 34 weeks of gestation with one affected fetus.

CASE PRESENTATION

The mother was a nulliparous female without medical family or personal history. The pregnancy was after in...
vitro fertilization. Two embryos were implanted, resulting in a twin dichorionic diamniotic pregnancy. Her first and second trimester ultrasounds were normal. A third trimester ultrasound, performed at 33 weeks, detected an abnormality in the first twin’s scan, which consisted of bilateral hyperechoic kidneys with the left kidney increased in size; no abnormalities had been noted in the previous scans (Figure 1). This renal abnormality was not initially linked with disease of the renal veins. After birth by cesarean section, the first twin had acute fetal distress and no heartbeat whereas the second twin was clinically normal. Clinical examination of the stillborn showed that both kidneys were bulky. Birth weight was 2060 g (fifth percentile for the term). A prenatal examination had not evoked the renal pathology. Therefore, a diagnosis of late-onset renal-vein thrombosis was suspected as a possible cause of per partum death. An autopsy revealed enlarged hemorrhagic kidneys, distension of the Gerota’s fascia (Figure 2), and thrombosis of the renal and adrenal veins, extending to the inferior vena cava, with no sign of fetal hydrops except for a moderate pleural effusion.

Histological examination confirmed the presence of hemorrhagic infarction from a massive bleed with thrombosis of both renal veins and the supra-renal vena cava (Figures 3–5). The stillborn’s placenta weighed 315 g (10th percentile). A comparative study between both placentas showed that the stillborn’s had moderate central fibrinoid necrosis and congestion of the villous veins without thrombosis, whereas the second twin’s placenta was normal. There were no signs of placental vasculopathy in either case. The cord of the stillborn’s placenta had a marginal insertion.

A review of thrombophilia was carried out in the parents and the neonate including the search for Factor V or Factor II mutations, protein S deficiency, antithrombin III, and protein C, as well as a mutation 2 in the MTHFR gene; revealed a heterozygous mutation in the MTHFR gene with no associated hyperhomocysteinemia in either the mother or neonate.

**DISCUSSION**

Neonatal renal vein thrombosis was first described by Rayer in 1837 and is a rare event that went undiagnosed for many decades until its discovery during surgery or post-mortem. Its incidence varies from 0.5‰ of admissions to neonatal intensive care units to 0.5% in autopsy series [2]. Its presence in a dichorionic twin pregnancy obtained by in vitro fertilization does the originality of our case report. Some cases may occur in the antenatal period. Most authors agree that thrombosis begins in the small veins of the renal parenchyma and expands towards the large venous trunks up to the renal vein or inferior vena cava. Furthermore, compression of the left renal vein by the aorta is also linked to a higher prevalence of thrombosis of the left renal vein, in its unilateral form [3]. Any maternal and/or fetal condition promoting hyperosmolarity may cause the development of renal vein thrombosis. The risk factors for thrombosis can be classified into three types: biological, amnestic and clinical. Biological risk factors include: protein C, protein S and antithrombin-III deficiencies; Factor II or
Factor V mutations; hyperhomocysteinemia linked to a homozygous mutation in the MTHFR gene; homozygous sickle cell disease; anti-cardiolipin antibodies; and circulating lupus anticoagulant in the mother’s blood and transmitted to the fetus in utero [4]. Identified anamnestic and clinical risk factors include: cesarean section; male gender; per-natal anoxia; maternal history of thrombosis; pregnancy-induced hypertension; gestational diabetes; premature birth; dehydration; shock; and any cause of increased osmolarity. Nearly, 50% of cases will demonstrate thrombophilia [5].

In the case reported here, the mother and child were both heterozygous for the MTHFR gene mutation with no associated hyperhomocysteinemia. Nevertheless, the prevalence of heterozygous MTHFR mutation is estimated around 30–40% in the general population. Therefore, it seems as an unlikely cause. A marginal umbilical cord insertion was present in our patient, providing an anatomic predisposition to umbilical blood flow restriction. Few manuscripts address the relationship between placental fetal vascular thrombosis and renal vein thrombosis. If expanded to include other visceral lesions, manuscripts highlighting placental fetal vascular thrombosis and cerebral, pulmonary and/or hepatic thromboemboli/infarction can be added to this relatively short list [6].

Typical postnatal symptoms of renal vein thrombosis include an abdominal mass, bloody urine, and thrombocytopenia. The diagnosis is achieved though ultrasound. Doppler ultrasound is the gold standard to confirm renal vein obstruction and to detect its extension to the contralateral kidney, inferior vena cava, and adrenal glands. The ultrasound findings depend on the stage of thrombosis. Initially, the interlobar and interlobular furrows appear hyperechoic. Quickly, the kidney becomes globular and hyperechoic with hypoechoic pyramids, with the eventual loss of corticomedullary differentiation. Doppler (done in postnatal studies) reveals the disappearance of venous flow, an elevated resistance index in the artery, with, occasionally, the appearance of reverse flow [7].

The symptoms can be difficult to identify in utero, especially as suggestive signs such as bloody urine are missing. Moreover, there can be technical obstacles (unfavorable position of the fetus, multiple pregnancies, and lack of echogenicity of some patients). There is also the possibility of false positives or spontaneous recovery. A prenatal ultrasound diagnosis can be suggested in cases of a large hyperechoic kidney, hyperechogenicity following the path of the interlobular veins, thrombus in the inferior vena cava, and Doppler indexes in the renal artery with reverse flow. There is a prognostic relation between kidney size and postnatal consequences: the larger the kidney, the worse the prognosis [8]. Patients with a family or personal history of thrombosis, thrombophilia or autoimmune disease, diabetes, fetal growth restriction or hypotrophy should be subjected to additional ultrasounds. In these patients in particular, an extra focus on kidney examination is recommended.

Medical management of renal vein thrombosis includes aggressive hydration and anti-coagulation. Nevertheless, previous studies report conflicting data regarding the benefit of anticoagulation with regard to long-term renal function, particularly in cases of bilateral renal vein thrombosis [3]. Thrombolytic therapy may be considered in cases of bilateral renal vein thrombosis, especially if there is concomitant renal failure [9]. Definitive surgical treatment consists of nephrectomy and thrombectomy on a non-urgent basis, provided there is no caval extension and obstruction. Thrombectomy for bilateral renal vein thrombosis with caval involvement and obstruction has been described once before, but with subsequent unilateral nephrectomy [10]. Recently, Lee et al. [4] showed that bilateral renal vein thrombosis can be successfully managed with early surgical thrombectomy without the need for nephrectomy, thereby avoiding the
significant morbidity associated with infant dialysis and renal transplantation. Successful restoration of renal function after surgical thrombectomy in his patient illustrates an encouraging treatment option. However, the relatively small number of reported cases and lack of prospective trials have opened up debate regarding the best way to manage this condition [11].

CONCLUSION

To date, there are still many unresolved issues regarding antenatal vein thrombosis. Diagnostic possibilities and prognostic probabilities still show large discrepancies. It would be ideal to hold a register on a large scale, to collect different cases of reported antenatal renal vein thrombosis, from different obstetric teams. A standardized approach for monitoring, surveillance and prevention for subsequent pregnancies is yet to be defined. It is essential to learn to diagnose it, as is it necessary to update obstetric ultrasound books and teaching methods for obstetricians.

Author Contributions
Moez Kdous – Substantial contributions to conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Revising it critically for important intellectual content, Final approval of the version to be published
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Guarantor
The corresponding author is the guarantor of submission.

Conflict of Interest
Authors declare no conflict of interest.

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