

Original Research Article

Antenatal Bilateral Renal Vein and Vena Cava Thrombosis in Dichorionic Twin Pregnancy

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Background: Antenatal renal vein thrombosis have been a rarely described diagnostic finding, with variable consequences on kidney function. **Case report:** We present an unusual case of a dichorionic twin pregnancy in 34 weeks of gestation with one affected fetus, showing already intrauterine a bilaterally 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. Autopsy revealed enlarged hemorrhagic kidneys, distension of the Gerota fascia 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. Histologically, there was hemorrhagic infarction by massive bleeding with thrombosis of both renal veins and supra-renal 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: Thrombosis of renal veins, Inferior vena cava thrombosis, Antenatal thrombosis, 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 50/100 000 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. During 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 1st and 2nd trimester ultrasounds were normal. A 3rd 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 [Fig 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 2060g (5th 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 fascia [Fig 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 [Fig 3, 4, 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 hyper-homocysteinemia 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, amniotic 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 amniotic and clinical risk factors include: caesarean 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 to 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 through 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 cortico-medullary 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 renal vein thrombosis. There are still large discrepancies in diagnostic possibilities and prognosis. It would be ideal to keep a register of all cases of antenatal renal vein thrombosis, from different obstetric teams. A standardized approach for monitoring, surveillance and prevention in subsequent pregnancies is yet to be defined. It is essential to learn to how to diagnose this condition, as is it necessary to update obstetric ultrasound books and teaching methods for obstetricians.

CONFLICT OF INTERESTS

The authors declare that there is no conflict of interests regarding the publication of this paper.

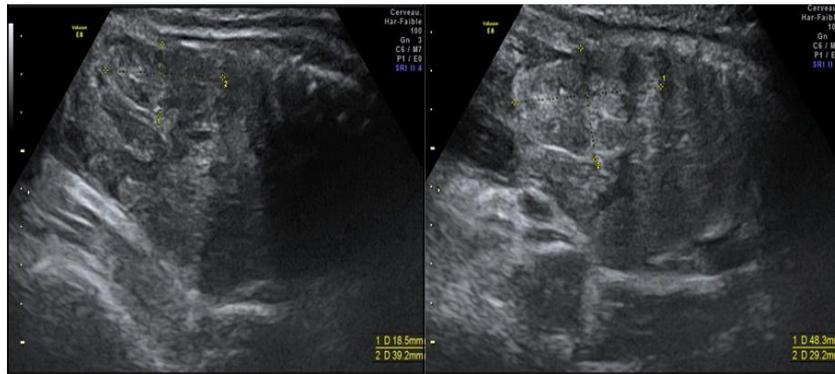


Figure 1. 1st twin's kidneys. The right kidney appears smaller and hyperechoic (The left kidney measured 49 mm (>90th percentile), the right kidney 39mm)

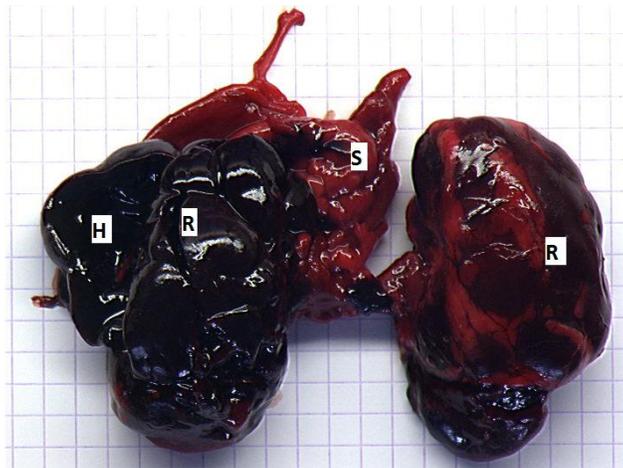


Figure 2: Macroscopic examination of the fetal kidneys recovering hemorrhagic infarction with renal vein thrombosis extended to the inferior vena cava. (H: Hematoma; R: Kidney; S: Adrenal gland).

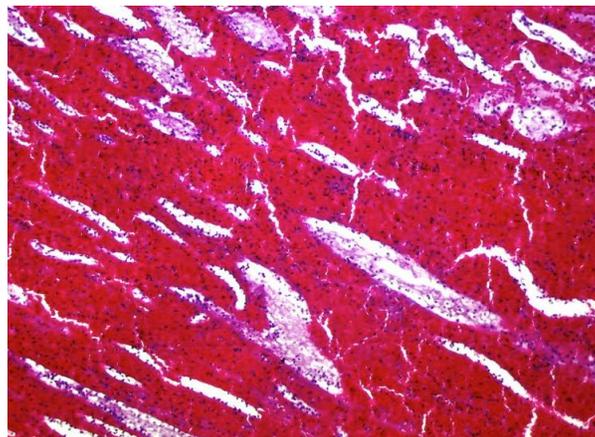


Figure 3. Medullary hemorrhagic infarction of the kidney.

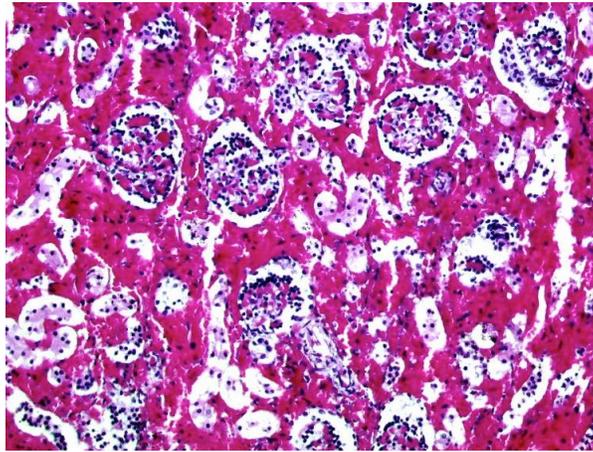


Figure 4. Renal hemorrhagic infarction of the cortex.

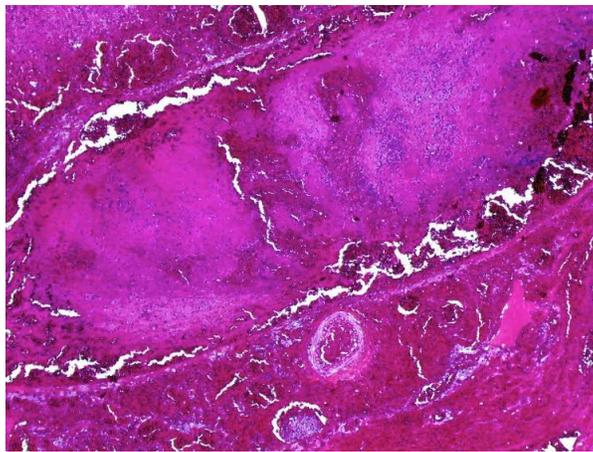


Figure 5. Recent thrombosis of the renal vein. The presence of calcifications confirms the antemortem thrombosis

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