Thrombophilia: A unique case of venous and arterial thrombotic complications in congenital protein C deficiency in newborns

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Congenital protein C deficiency is a hereditary coagulation disease characterized by venous/arterial thrombosis secondary to the reduction of protein synthesis and/or activity. It is well known that severe congenital protein C deficiency can occur with thrombosis severe, systemic symptoms, sometimes immediately after birth, with poor prognosis.1 We present a case in which the finding of thrombosis of the renal vein and renal infarction in two newborns (2015 and 2017), has subsequently allowed to diagnose an unknown deficiency of functional protein C in the mother with a history of obstetric complications.

Key Words: *Thrombophilia; Protein C deficiency; Renal vein thrombosis; Renal arterial thrombosis.*

INTRODUCTION

Renal vein thrombosis (RVT) is the most common non-catheter related venous thromboembolism (VTE) in newborns and is responsible for approximately 10% of all VTE in newborns [1-3]. Almost 80% of all RVT present within the first month and usually within the first week of life. Some newborns developed RVT *in utero*. Incidence in males and females is similar, both sides are affected equally and RVT occurs bilaterally in 24% of newborns. Number of large studies have confirmed that heterozygous protein C deficiency does not usually present with thrombosis during early infancy [4,5]. Despite the low absolute risk, numerous case series and cohort studies suggest that there is an increased prevalence of protein C heterozygosity in newborns and infants with TE [6,7]. The majority of these infants had clinical risk factors that "unmasked" the congenital defect. The diagnosis of heterozygote protein C deficiency in newborns is particularly difficult as physiologic values for protein C at birth may be as low as 17% of adult levels [8].

CASE REPORT

In November 2017, a patient of 40 years old was sent to our department; she presented a history of obstetric complications characterized by both pregnancies (one in 2015 and one in 2017) from severe intrauterine growth restriction (IUGR) and changes in cardiotocographic monitoring that made it necessary to carry out a caesarean section.

It was also reported that both infants at birth had complications. The one born in 2015 (newborn 1) had renal thrombosis and the one born in 2017 (newborn 2) had renal infarct; both of them reported a complicated clinical picture related to their prematurity as well.

The newborn 1 presented at birth with IUGR, sepsis and thrombosis of the right renal vein; renal ultrasound was performed and that showed a renal parenchyma of preserved thickness but with a marked increase in echogenicity, in line with the nephropathic state. The newborn 1 was treated with heparin.

The newborn 2 appeared at the premature, jaundiced birth. Macro hematuria appeared one month after birth. Renal ultrasound was then performed and it showed a hydronephrosis for stenosis for the left kidney and pathological kidney with loss of cortico-medullary differentiation, swollen appearance, and multiple hypoechoic areas for the right kidney. The color-doppler showed a blood flow reduced to more than half compared to the contralateral and compatible with partial thrombotic effect on the right renal artery. To complete the investigation, CT was also performed and that confirmed the structural subversion of the right kidney and made the framework compatible with renal infarction. We did not perform thrombophilic screening on newborns. At this point it was decided to perform a thrombophilic study of the mother which showed a functional protein C deficiency of 42%; this datum was re-confirmed on second sample (functional protein C 39%). The remaining thrombophilic screening showed a level of free protein S of 79%, antithrombin III of 89 %; the search for IgG anti-cardiolipin antibodies was positive; the factor V Leiden mutation was absent (resistance to activated protein C 3.02). A family study was also performed and a protein C deficiency was found in the brother.

DISSCUSSION AND CONCLUSION

Thromboembolism of protein C deficiency has been described in the neonatal period. Affected women characteristically may not have thromboembolic manifestations. Our case report suggests that thrombophilia should be suspected both in women with obstetric complications and in women with newborns with thrombotic disease. This case is unique because the newborn 1 was affected by venous thrombotic complication while the newborn 2 by arterial thrombotic complication. We believe that in case of thromboembolism in a neonate, with no trivial cause such as an indwelling catheter or sepsis, mother or both mother and infant should be tested for the presence of protein C deficiency, even when mother never had a history of thromboembolic events.

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