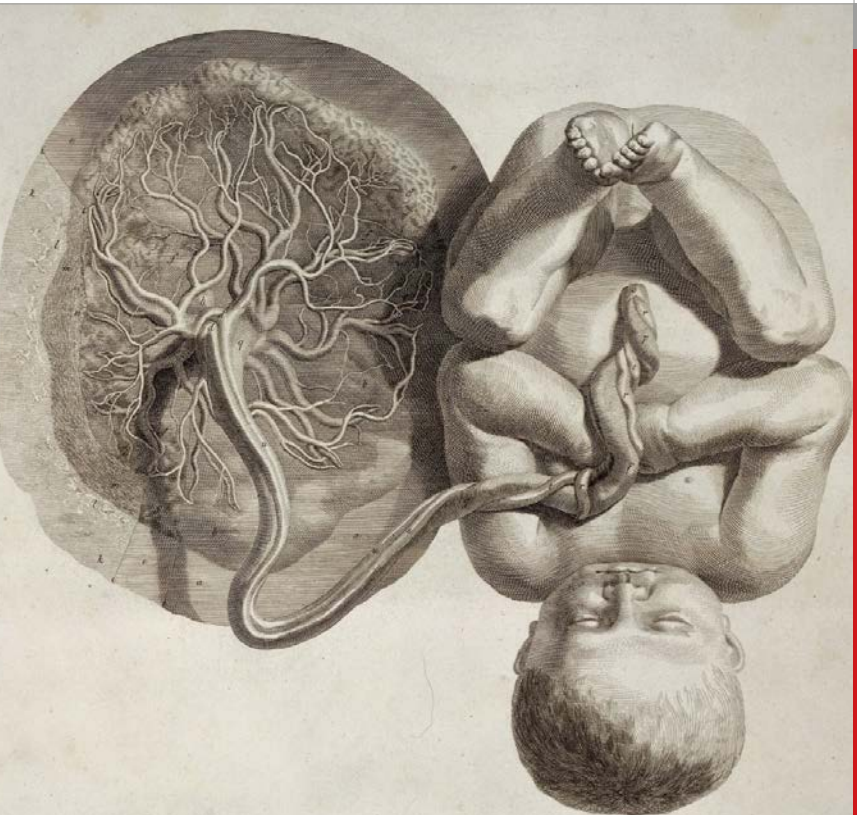
SWISS SOCIETY OF NEONATOLOGY

Neonatal renal and inferior vena cava thrombosis associated with fetal thrombotic vasculopathy



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Title figure:
Fetus with placenta (source: www.wikimedia.org)

Most neonatal thromboembolic events (TEs) are related to catheterization and most of their discoveries are secondary to clinical manifestations (1). Fetal thrombotic vasculopathy (FVT) is a placental disorder associated with adverse perinatal outcomes. It may also predispose children to somatic TEs.

A full-term male neonate was delivered at 39 weeks of gestation by urgent Caesarian section due to fetal heart rate decelerations, after a failed attempt of vacuum-assisted vaginal delivery. The pregnancy of the 30-year-old G4/P2 mother had been uneventful. The mother had previously experienced two spontaneous abortions of unclear etiology. Family history was negative for coagulopathies.

The neonate was asymptomatic at birth, with a good transition to extra-uterine life. Initial physical examination revealed no pathologic findings. Apgar scores were 7, 9 and 9 at 1, 5 and 10 minutes of life, respectively, and arterial cord pH was 7.24. Body weight was 3420 g, body length 52 cm and head circumference 34 cm. Neurological examination revealed no abnormalities.

The obstetrician reported difficulties in clamping and cutting the umbilical cord, which appeared edematous and showed signs of clotting and hematoma formation (Fig. 1). Macroscopically, the placenta showed signs of FTV. Histologically, thrombosis of several fetal vessels of the chorionic plate and avascular terminal villi, including macroscopic visible thrombosis of the umbilical artery in an edematous umbilical cord, were demonstrated (Fig. 2, 3).

Despite the normal clinical appearance of the neonate, an abdominal ultrasound was performed to rule

out any conditions potentially related to placental FTV. This examination revealed a hyperechoic oval structure (measuring 8.5 × 4 mm) inside the inferior vena cava (IVC) near the conjunction of the renal veins, suggestive of an intraluminal caval thrombus (Fig. 4). Of note, cranial ultrasonography revealed no abnormalities.

The neonate was admitted to the neonatal unit for clinical monitoring and observation. After consultation with the pediatric hematologist, anticoagulation with low-molecular-weight heparin (enoxaparin) at a dose of 1.5 mg/kg 12-hourly was started, targeting an anti-Xa between 0.5 and 1.0 U/ml (2).

Two days later, a second ultrasonography confirmed the presence of a thrombus of 7.5 × 4 mm, extending into the IVC from the right renal vein. The ipsilateral kidney was slightly more hyperechoic with respect to the left, suggesting parenchymal edema (Fig. 5). Magnetic resonance imaging confirmed the diagnosis. Creatinine reached a maximum value of 127 µmol/L on the same day. This value is high for neonatal age (3) suggesting initial renal vein involvement. Blood pressure was always normal.

A third ultrasonography performed on day of life 7 showed a reduction of thrombus size and normalization of the kidney structure. In parallel, serum creatinine concentrations decreased to normal values.

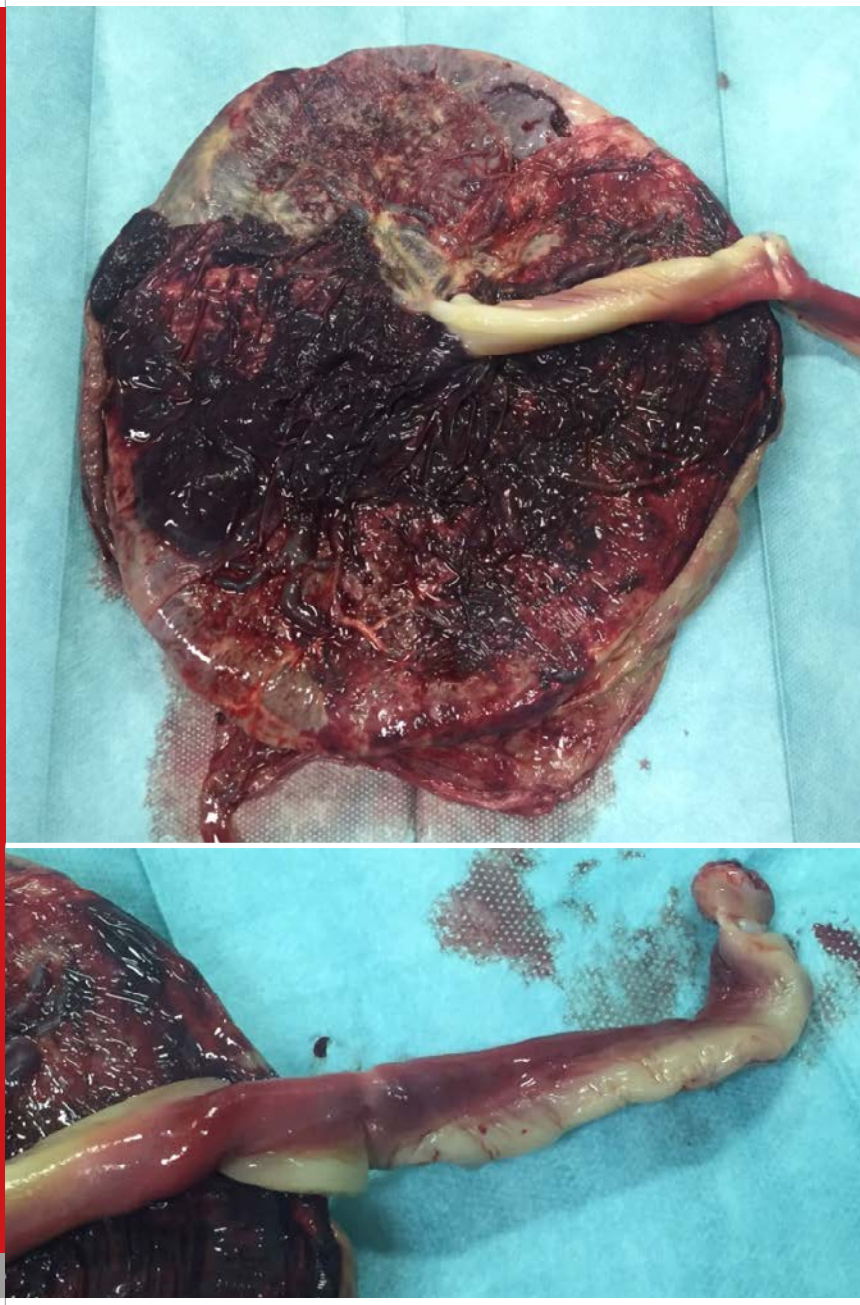

Fig. 1

Placenta (top) and umbilical cord (bottom) at birth.

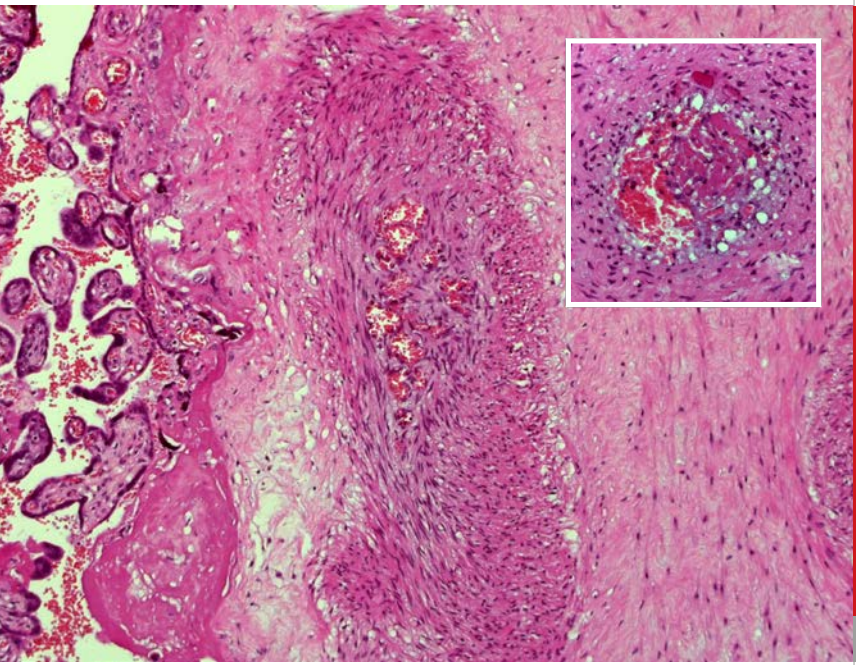

Fig. 2

Organized thrombus and recanalized stem villus; thrombus not completely organized (insert).

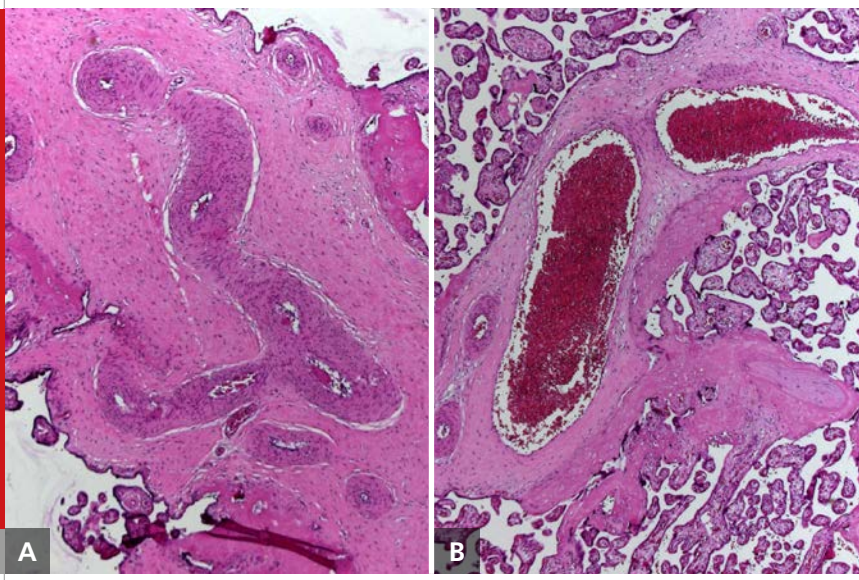

Fig. 3

A: Stem villous vessels with thrombus;

B) normal stem villous vessels for comparison.

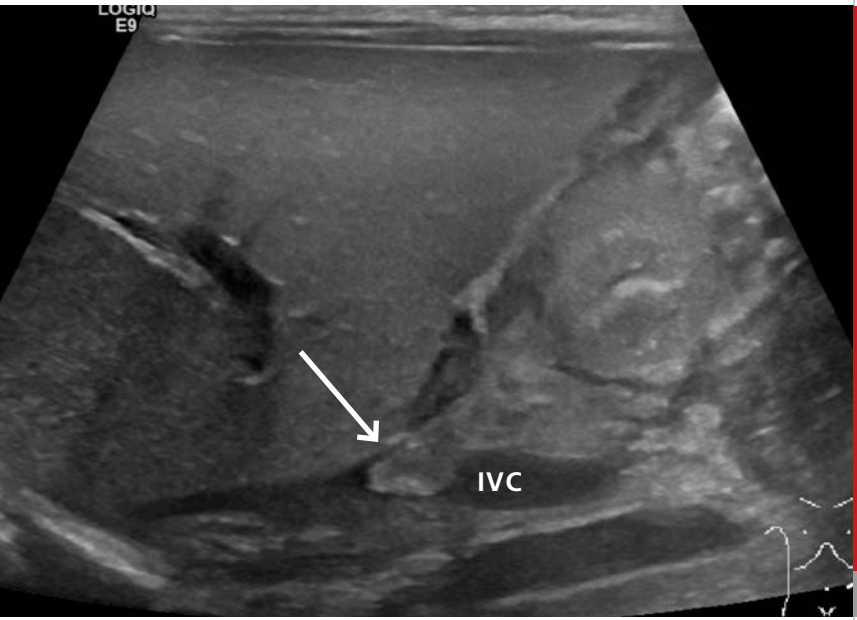

Fig. 4

Hyperechoic oval structure (8.5 × 4 mm) (arrow) at the level of the IVC near the entry of the renal veins suggestive of an intraluminal caval thrombus.

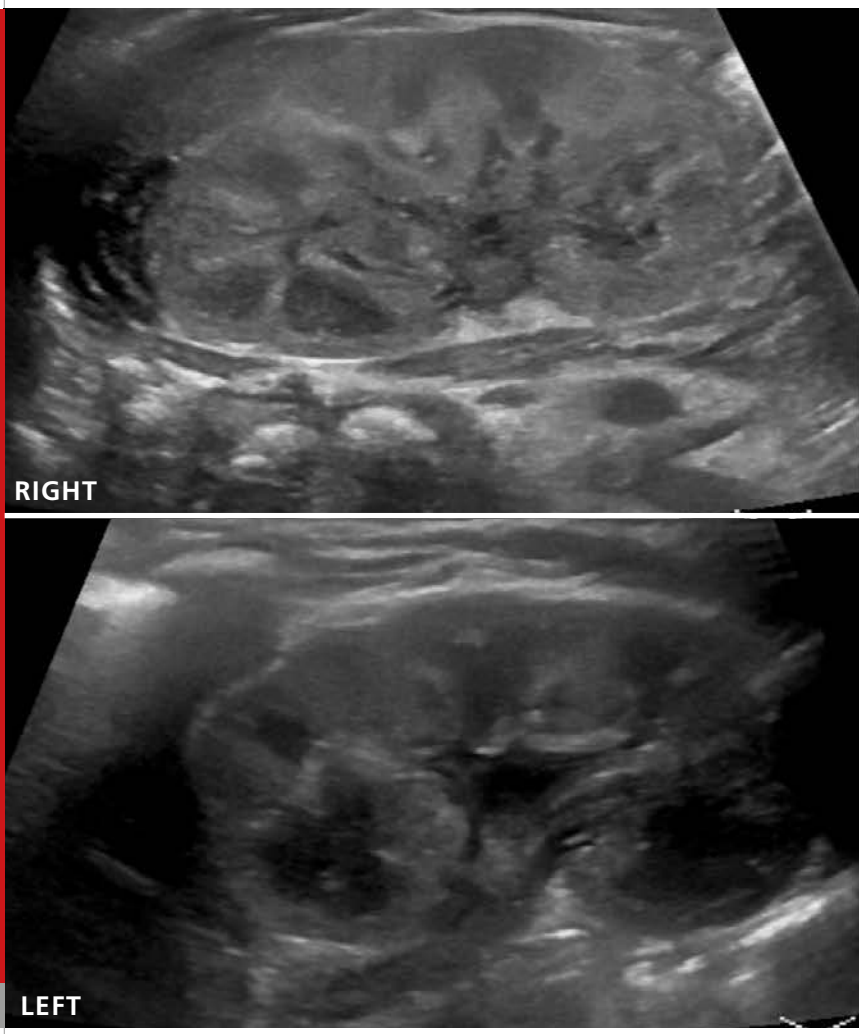

Fig. 5

Right kidney parenchyma appears more hyperechoic than the left.

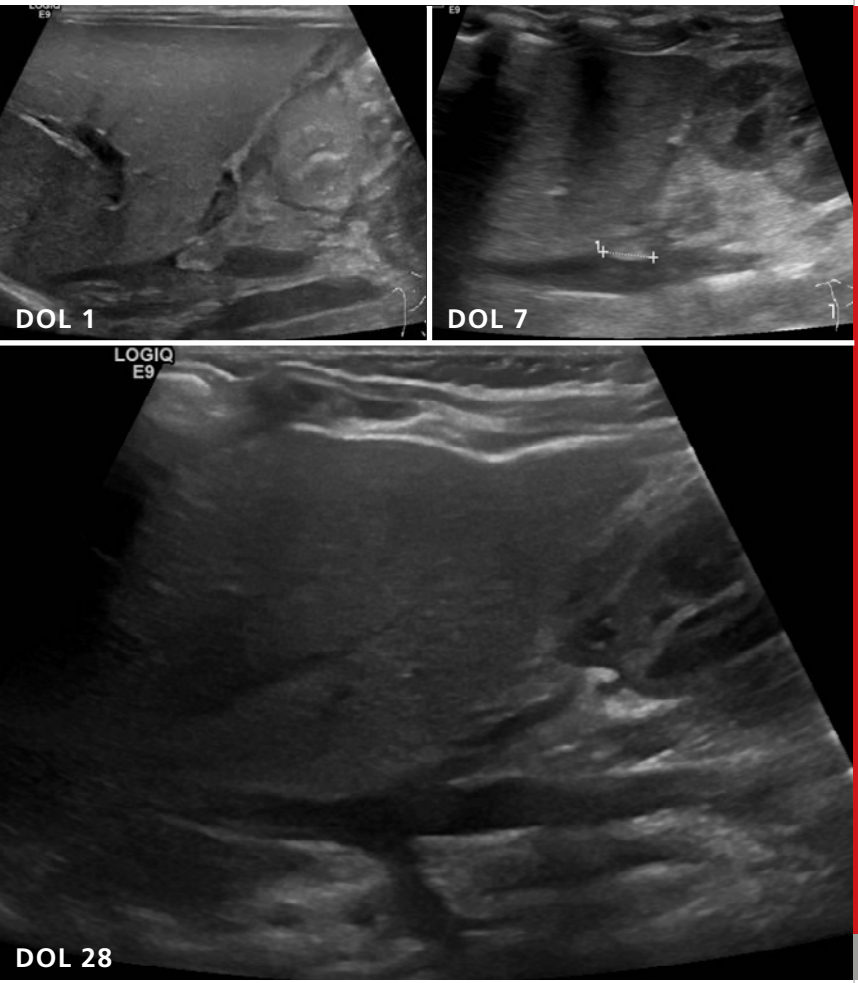

Fig. 6

Evolution of the thrombus: top left: thrombus on day of life 1; bottom left: regression by day of life 7; right: complete regression of the thrombus by day of life 28.

The neonate was discharged in a good clinical condition on day of life 8. Enoxaparin was to be continued for 3 months. An additional ultrasound examination on day of life 28 showed almost complete resolution of the thrombus (Fig. 6).

Thrombophilia screening in the mother showed a prothrombin gene G20210A heterozygous mutation. Thrombophilia screening in the child was performed at 3 months of age with normal results. The baby is in excellent clinical condition at one-year follow-up and thriving normally.

Both arterial and venous TEs in infancy are rare but associated with high morbidity and mortality risks. It has been suggested that neonates are particularly susceptible to such thrombotic complications as they have decreased levels of anticoagulants and lower levels of fibrinolytic components.

In the literature, the reported incidence of symptomatic venous TEs ranges from 0.07 – 0.14/10'000 children, and 24/10'000 patients in neonatal intensive care units (4 – 6). While the clear majority of venous TEs in neonates and children are associated with the presence of a central venous lines, renal vein thrombosis represents the most common non-catheter-related venous TEs occurring during the neonatal period (1). The etiology of renal vein thrombosis is not precisely known. Reported risk factors include perinatal asphyxia, maternal diabetes, and infections (1).

FTV is a placental abnormality characterized by clusters of not adequately vascularized villi, often related to upstream thrombosis in placental fetal vessels (7, 8). Microscopically, FTV is diagnosed by the presence of one or more thrombosed fetal vessels. The incidence of FTV varies from 1 % to 6.4 % (9). Some conditions, such as hypercoagulable states, endothelial damage, blood flow stasis, maternal diabetes and thrombophilia have been associated with FTV (10). Obstructive cord abnormalities, such as excessively long or hypercoiled cord, entanglement, true knots,

marginal/membranous insertion, decreased Wharton's jelly, cord diameter < 8 mm are closely associated with FTV and consequently with neonatal thrombosis (7, 11).

Even though there is no consensus on the causes of FTV, the adverse outcomes of this vasculopathy have been well recognized. Intrauterine growth restriction, fetal demise, intestinal atresia, and TEs in the fetal circulation affecting liver, heart and central nervous system have been described (12).

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