The clinical outcome after inferior vena cava thrombosis in early infancy

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Abstract The clinical outcome after inferior vena cava thrombosis in early infancy is unknown. We report the clinical long-term follow-up of 12 patients presenting inferior vena cava thrombosis within their first months of life (gestational age: 24–41 weeks; follow-up: 7 ± 3 years). Accompanying renal venous thrombosis occurred in 9, and adrenal bleeding in 4 patients. A central venous catheter was related to the thrombosis in only four patients. Heterozygous factor V Leiden mutation was found in two of the eight infants without central venous catheter. Thrombolysis was performed in seven and effective in three infants; one infant required surgical thrombectomy. In three of eight infants with ineffective or with no therapy, spontaneous recanalization occurred during follow-up. No patient died of the thrombosis. Although no long-term anticoagulatory prophylaxis was performed, none of the children with persisting occlusion (n = 5) or stenosis (n = 1) of the inferior vena cava developed symptomatic thrombo-embolic complications. However, extensive internal collaterals (n = 6), visible varicosis (n = 5), pain in the legs (n = 3) and persisting renal disease (n = 3) with arterial hypertension (n = 2) were observed during follow-up.

Conclusion Inferior vena cava thrombosis of early infancy frequently persists and may cause considerable long-term morbidity. New strategies for early and long-term therapy are necessary.

Key words Factor V deficiency · Infant · Thrombosis · Vena cava inferior

Abbreviations CVC Central venous catheter · IVC inferior vena cava · IVCT inferior vena cava thrombosis · RVT renal venous thrombosis

Introduction

The thrombotic occlusion of the inferior vena cava (IVCT) is a rare disease in early infancy which, however, may play an important part in the venous thromboses observed in neonates [18] and may occur in up to 29% of children and infants with central venous catheters (CVC) [13]. It may already occur in utero and lead to hydrops or congenital calcified IVCT [17, 21]. In adult patients with obstruction of the inferior vena cava (IVC) late-term complications like compression of the spinal cord and nerve roots by intraspinal collaterals and dilated paravertebral veins [4], bleeding from gastro-intestinal varices [10], destruction of pedicles of lumbar vertebral bodies secondary to venous collaterals [20], Budd-Chiari
syndrome [14], varicosity, leg ulcers and pulmonary embolism [8] have already been described. In contrast, the long-term outcome after IVCT in early infancy is unknown. Few case reports provide outcome data describing a follow-up period of more than 1 year [1, 5–7, 9, 16, 21].

In the following investigation we summarize the clinical long-term outcome of 12 infants presenting IVCT within their first months of life.

**Patients and methods**

Between 1989 and 1997, 12 patients at Aachen University Children’s Hospital without preceding cardiac surgery or catherization presented IVCT during their first months of life (Table 1). In four patients the occurrence of IVCT was related to the insertion of a CVC into the inferior vena cava (IVC). In the remaining infants a heterogeneous combination of maternal (gestosis, HELLP syndrome, n = 1) or patient-associated clinical risk factors (infection, n = 2; asphyxia, n = 2; intra-uterine dystrophy, n = 2; arterial hypotension, n = 4; exsiccosis, n = 4; hyperbilirubinemia, n = 2) was present. No mother was suffering from diabetes mellitus or presented clinical symptoms of lupus erythematosus. Most patients presented symptoms of renal venous thrombosis (RVT; n = 9), whereas symptoms directly linked to IVCT, like limb swelling or visible collaterals, occurred in four infants only (patients 3, 4, 5 and 8). At manifestation, diagnosis was confirmed by ultrasound in all and by phlebography of the lower limbs.

Because of contra-indications, thrombolysis (urokinase or streptokinase, 1000–2000 IU/kg per h each after bolus injection) with accompanying heparinization (5000 IU heparin/m² and day) and ensuing short-term low-dose heparin therapy (2–10 days) was performed in seven infants only. In patient 5 thrombolysis was complicated by a first grade cerebral haemorrhage and could not be completed. In patient 2 a catheter-associated thrombosis extending from the IVC to the right atrium was surgically resected because it was suspected to be infectious. After resection colonization with *Aspergillus fumigatus* was confirmed.

Long-term follow-up was available for 11 patients. One patient with congenital heart disease had died from right heart failure at the age of 6 months (patient 12). Autopsy excluded any pulmonary embolism that might have caused right heart failure. Ten patients were investigated prospectively at our hospital (follow-up: 7 ± 3 years). Close-meshed follow-up data were available from three patients (patients 1, 11 and 12) whereas eight patients who had transiently been lost to follow-up after discharge from hospital were selectively re-examined after periods of up to 9 years (patients 3–10). Clinical investigation (including oscillometric blood pressure recording), two-dimensional and duplex ultrasound of the IVC, and of renal, iliac and femoral vessels, and basic laboratory screening for hereditary thrombophilia (protein C and S activity, APC ratio, thrombin time, antithrombin activity) and for renal function (urea, creatinine) were performed in all these children. Depending on these findings, more specific investigations like phlebography of the lower limbs (n = 4), CT (n = 3) and MRI of the abdomen (n = 1), electrocardiography and echocardiography (n = 6) followed. Limited data were available for patient 2 who was not investigated at our hospital during follow-up.

**Results**

IVCT persisted in five patients (Table 1). Although no long-term anticoagulation was performed, no patient contracted symptomatic peripheral venous thromboembolism or Budd-Chiari disease, and none presented electro- or echocardiographic signs of increased right heart pressure, indicative of major pulmonary embolism. However, occlusion or stenosis of iliac veins, extensive collaterals draining to the azygos, hemi-azygos, lumbar, intraspinal or mesenteric veins and clinical varicosity were documented in four patients with persisting IVCT (patients 3, 4, 5 and 10; Fig. 1) and in the patient with IVC stenosis after partial spontaneous recanalization of the IVCT (patient 8). In addition, occlusion of veins of the legs was found in four patients. Three of these patients were also suffering from chronic pain in the lower limbs (patients 3, 4 and 8) and from abdominal complaints (patient 4). In patient 1 no detailed documentation of internal collateral vessels was performed; however, clinical and sonographic findings also suggested the presence of extensive internal collaterals in this infant. Surprisingly, complete spontaneous recanalization of the IVCT occurred in two of the four infants in whom no therapeutic interventions had been performed at all (patients 9 and 11; Fig. 2).

During follow-up, therapy of renal complications was required for three of four infants who had initially suffered from bilateral RVT (patients 1, 10 and 11); patient 1 developed renal tubulopathy, progressive renal failure and arterial hypertension. At the age of 9 years, left-sided renal shrinking (no residual function/MAG-3 scintigraphy) with arterial hypertension and first-stage hypertensive retinopathy required nephrectomy in patient 10. Patient 11 (creatinine clearance normal) developed chronic renal tubular acidosis, which responded to potassium-sodium-citrate substitution.

In patient 8, whose stillborn brother had suffered from intra-uterine RVT, and in patient 6 the APC ratio was reduced. Both infants and their clinically asymptomatic mothers were confirmed as being heterozygous

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**Fig. 1** Enhanced CT scan of a 9-year-old girl (patient 5) with persisting IVCT: intraspinal collaterals (solid black arrows); dilated veins of the paravertebral plexus (open black arrows); mesenterial collaterals (white arrow)