Acute Iliofemoral Venous Thrombosis in Patients with Atresia of the Inferior Vena Cava Can Be Treated Successfully with Catheter-directed Thrombolysis

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ABSTRACT

Purpose: To assess the effectiveness and clinical outcomes of catheter-directed thrombolysis in patients with atresia of the inferior vena cava (IVC) and acute iliofemoral deep vein thrombosis (DVT).

Materials and Methods: From 2001 to 2009, 11 patients (median age, 32 y) with atresia of the IVC and acute iliofemoral DVT in 13 limbs were admitted for catheter-directed thrombolysis. Through a multiple–side hole catheter inserted in the popliteal vein, continuous pulse-spray infusion of tissue plasminogen activator and heparin was performed. Thrombolysis was terminated when all thrombus was resolved and venous outflow through the paravertebral collateral vessels was achieved. After thrombolysis, all patients received lifelong anticoagulation and compression stockings and were followed up at regular intervals.

Results: Ultrasound or computed tomography revealed absence of the suprarenal segment of the IVC in two patients, and nine were diagnosed with absence of the infrarenal segment of the IVC. Median treatment time was 58 hours (range, 42–95 h). No deaths or serious complications occurred. Overall, complications were observed in four patients, one of whom required blood transfusion. Three patients were diagnosed with thrombophilia. Median follow-up was 37 months (range, 51 d to 96 mo). All patients had patent deep veins and one developed reflux in the popliteal fossa after 4 years. No thromboembolic recurrences were observed during follow-up.

Conclusions: Catheter-directed thrombolysis of patients with acute iliofemoral DVT and atresia of the IVC is a viable treatment option, as reasonable clinical outcomes can be obtained.

ABBREVIATIONS:

DVT = deep vein thrombosis, IVC = inferior vena cava, TPA = tissue plasminogen activator

Atresia, or absence, of the inferior vena cava (IVC) is a rare congenital anomaly that results from aberrant development in embryogenesis whereby three sets of paired veins fail to anastomose (1). Various abnormalities of the IVC have been described, including complete absence, partial ab-
bosis. The conventional treatment of deep vein thrombosis (DVT) among patients with anomalies of the IVC is anticoagulation therapy. Treatment with catheter-directed thrombolysis has been described in only a few cases, with various outcomes (11,17–19).

In the present study, we describe our experience with catheter-directed thrombolysis in patients with acute iliofemoral DVT and atresia of the IVC.

MATERIALS AND METHODS

In the period from December 2001 to September 2009, 11 patients with acute iliofemoral DVT in 13 lower limbs were admitted to our department as a subgroup of patients admitted for catheter-directed thrombolysis. The institutional review board at the hospital approved the treatment as a developing project, and all patients gave informed consent. Four women and seven men with caval atresia and with a median age of 32 years (range, 15–52 y) were treated. All patients presented with pain and swelling of their legs. Three patients had additional lumbar pain and two patients presented with pain especially in their inguinal region. Several years before their development of DVT, two male patients had symptoms of compromised venous blood flow: one had varicose veins and the other had varicocele testis and severe varices in his lower limbs. One male patient had a history of DVT in the contralateral leg 16 years earlier, and at that time he was diagnosed with atresia of the IVC. He was receiving oral anticoagulation with warfarin, but at the time of recurrent DVT, his International Normalized Ratio was not within the therapeutic range of 2–3.

In one male patient who was first admitted to a local hospital with back pain, retroperitoneal masses were suggested to be enlarged lymph nodes, and several biopsy specimens were taken from these structures because he was suspected of having malignant disease with tumor along the spine. A few days later, the patient’s leg became painful and swollen, and DVT was diagnosed. Pathologic evaluation of the biopsy specimens revealed no signs of malignancy, and a later computed tomography (CT) scan confirmed atresia of the IVC. The patient was admitted to our department, and catheter-directed thrombolysis was started 10 days after the biopsies were performed.

Catheter-directed thrombolysis for DVT has been used at our institution since 1999 and has previously been described (20,21). A total of 134 patients were treated with venous thrombolysis in the study period. Inclusion criteria for catheter-directed thrombolysis were iliofemoral thrombosis, symptom duration shorter than 14 days, distal popliteal vein without thrombus, and age younger than 60 years. Exclusion criteria were cancer and previous ipsilateral DVT. Initially, atresia of the IVC was an exclusion criterion for thrombolysis as well, but as catheter-directed thrombolysis became a standardized treatment in the department, it was decided to treat patients with caval atresia and acute iliofemoral DVT as well. Thrombophilia screening was performed in all patients and included factor V Leiden mutation, protein C, protein S, prothrombin mutation, antithrombin, lupus anticoagulant, anticardiolipin antibodies, and homocysteine. Thrombophilia was not a contraindication to treatment.

Catheter-directed thrombolysis was performed with a multiple-side hole catheter (Uni*Fuse; AngioDynamics, Queensbury, New York) inserted from the popliteal vein with ultrasound (US)– guided puncture and local anesthesia. The catheter (5-F) with tip occlusion was placed in the thrombus as proximal as possible to central venous outflow, in the iliac vein or a large collateral vein. A bolus of 10 mg tissue plasminogen activator (TPA) was used to load the thrombus, and then pulse-spray thrombolysis with 1.2 mg TPA per hour and 1,200 IU heparin per hour was administered. Continuous pulse-spray infusion was employed with the use of a mechanical injector (AngioDynamics), with 0.5 mL injected every 15 seconds to achieve a total of 120 mL/h (Fig 1). The dosage of heparin was titrated to achieve a partial thromboplastin time between 80 and 100 seconds. Patients with bilateral thrombosis had bilateral placement of infusion catheters and half the total dose was infused in each catheter, corresponding to a total dose of 1.2 mg TPA per hour and 1,200 IU heparin per hour. Every patient had an intermittent pneumatic compression device placed on the calf and thigh while in bed to maximize the venous flow through the previously thrombosed vein. CT scans were obtained in the event that the US examination left any doubt regarding the diagnosis of caval atresia. US and CT diagnostic criteria for caval atresia were no venous structure at the normal site of the IVC, ascending lumbar veins and paravertebral collateral vessels anastomosing

![Figure 1. Atresia of IVC and several paravertebral collateral vessels is seen before catheter-directed thrombolysis. Thrombus is present in the common iliac vein.](image-url)
with the iliac vein, and a well developed azygos/hemiazygos system.

Venography was performed daily to visualize the degree of thrombus regression, and in case of considerable residual thrombus, a bolus of 10 mg TPA was given by pulse-spray technique to load residual thrombus. Continuous pulse-spray infusion was continued with the same volume of 120 mL/h, and therapy was terminated when all thrombus was resolved and a satisfactory venous outflow through the collateral vessels was achieved (Fig 2). The regimen used for treatment of patients with caval atresia did not differ from our treatment of patients with normal caval anatomy. After thrombolytic was completed, all patients immediately commenced anticoagulation treatment with low molecular weight heparin for 14 days and warfarin, along with long graduated class II compression stockings. The target therapeutic International Normalized Ratio range was 2–3. Because of the strong association between caval atresia and iliofemoral thrombosis, warfarin was given indefinitely. Follow-up with clinical examination combined with US was performed after 6 weeks and 3 and 12 months, and annually thereafter.

RESULTS

Two patients had bilateral iliofemoral DVT, eight had left-sided thrombosis, and one had right-sided thrombosis. In four patients, the diagnosis of caval atresia and iliofemoral thrombosis was confirmed by a thorough US examination, and in seven patients it was confirmed by an additional CT scan. In two patients, of whom one had bilateral thrombosis, absence of the suprarenal segment was identified, whereas the others were diagnosed with absence of the infrarenal segment. All patients had collateral veins in the pelvis, some of which had thrombus. In one patient, it was not possible to place the catheter in the common iliac vein and it was positioned in a collateral vein. In six patients, the thrombus was located in the iliac, common femoral, and femoral vein, whereas three patients had further involvement of the proximal part of the popliteal vein. Two patients had thrombus exclusively in the iliac veins. All patients had considerable dimensions of the paravertebral collateral veins connecting to the azygos and hemiazygos system. No attempts were made to place stents. No concomitant visceral defects were detected in any of the patients.

Median treatment time was 58 hours (range, 42–95 h). No deaths occurred. Overall, complications were observed in four patients (36%): one patient (9%) with bilateral DVT experienced major bleeding that required blood transfusion, with hematuria and bleeding observed from both puncture sites. Three further patients (27%) experienced minor bleeding, which was managed in two cases with local compression of the access site. The third patient had hematuria for a few hours but did not require any intervention. None of the patients experienced pulmonary embolism while undergoing thrombolysis, but one young male patient had hemoptysis before treatment and a later ventilation/perfusion scintigram identified small visible emboli in both lungs. No patients developed recurrent thromboembolism during follow-up.

Thrombophilia screening revealed three patients with factor V Leiden heterozygosity. Other risk factors for DVT were identified in an additional two female patients. One had given birth 8 weeks before the acute DVT episode, and the other had been taking oral contraceptive agents and had a long flight (approximately 12 h).

At a median follow-up of 37 months (range, 51 d to 96 mo), all 11 patients had patent iliofemoral vein segments including opened collateral veins. One patient developed incompetent venous valves in the popliteal fossa 4 years after treatment and had some edema and pigmentation of his leg, which was categorized as clinical class C4 per clinical/etiology/anatomy/pathophysiology classification (22,23). Three patients were diagnosed with symptomatic insufficiency of their great saphenous vein and have been offered surgery. The others were asymptomatic.

DISCUSSION

The results of the present study indicate that catheter-directed thrombolysis can be recommended as the treatment of choice for acute iliofemoral DVT in patients with atresia of the IVC, as this treatment can achieve satisfactory clinical outcomes, including patency of deep veins. Only small case series of this treatment in this patient group have been reported thus far (11,17–19). Dean et al (17) reported successful outcomes in two patients treated with catheter-directed thrombolysis; rethrombosis was reported within 10
days in one patient, and a new attempt at thrombolysis with adjunctive mechanical thrombectomy and stent placement restored venous perfusion. Long-term anticoagulation was recommended in both patients. Mechanical thrombectomy and stent placement were not attempted in the present series. Even though May–Thurner syndrome (24) could have been considered a complicating factor in the present series, we did not attempt adjunctive stent implantation, mostly because of caution. Ly et al (18) reported unsuccessful outcomes in three patients with atresia of the IVC treated with catheter-directed thrombolysis and therefore recommended against the use of this treatment in these patients. The reason for the unsatisfactory outcome in some studies may be the longer duration of symptoms before initiation of thrombolysis, resulting in a lower degree of thrombus resolution. Additionally, thrombus may have had further extension than in our study, from which patients with calf vein thrombosis were excluded. In addition, we have used more “aggressive” dosing regimens of TPA (1.2 mg/h), which was infused by continuous pulse-spray technique, and heparin, which was titrated to achieve partial thromboplastin times of 80–100 seconds, which are higher than in other studies that reported times of 50–80 seconds (18). In addition, we used an intermittent pneumatic compression device during treatment to maximize venous flow through the previously thrombosed vein and to keep it patent. We continued venous thrombolysis until all thrombus was resolved.

The difficulty with catheter-directed thrombolysis in patients with atresia of the IVC is the poor venous outflow that results from collateral drainage. Therefore, it is very important to establish diagnosis of atresia of the IVC before treatment to guide the positioning of the catheter. It is of great importance to place the catheter as proximal as possible in the iliac vein system or in the tortuous collateral vessels to recanalize the paravertebral collateral vessels and achieve the best venous outflow possible. Positioning of the catheter in these tortuous collateral vessels complicates the technical procedure, which is why the diagnosis of caval atresia before treatment is of utmost importance. As shown, the chronic collateral drainage around the nonexisting or occluded IVC is an acceptable substitute for a patent IVC in patients undergoing thrombolysis. Reasonable outcomes can be obtained.

Atresia of the IVC is rare: it is detected in approximately 0.15%–0.5% of otherwise healthy individuals (2,12). However, among young patients with DVT, atresia is seen in as many as 5% of cases (14,25). Bilateral DVT in patients with atresia of the IVC has been reported in more than 50% of cases (14). In the present study, the frequency of bilateral thrombosis was 18%, which might be lower than expected because these patients were selected with regard to duration of symptoms.

The coexistence of thrombophilia and atresia of the IVC has been described in the literature, with most cases representing mild thrombophilia such as factor V Leiden heterozygosity (14,26–28). Factor V Leiden heterozygosity was found in three of 11 patients in the present study.

The presence of pulmonary embolism in patients with DVT and atresia of the IVC is rare. However, it has been described, and might occur through the well developedazygos/hemiazygos system to the pulmonary circulation (29,30). This was thought to be the case in one of our patients who had small visible emboli in both lungs confirmed by a ventilation/perfusion scintigram.

As patients with anomalies of the IVC and thrombosis are at higher risk of thrombotic recurrence, we believe it is important that they receive anticoagulation on a lifelong basis (29,31,32). All the patients in the present study were treated with lifelong anticoagulation, and none have developed new thromboembolism as of the time of manuscript submission. Wearing graduated compression stockings is recommended for at least 1 year to minimize postthrombotic syndrome (33).

Limitations of the present study include the small number of patients and the fact that it is a retrospective study.

In conclusion, when people present with thrombus of the pelvic and femoral veins or with bilateral DVT, atresia of the IVC must be considered. Therefore, diagnostic imaging of the IVC must always be performed in patients with iliofemoral thrombosis. Aggressive treatment of patients with acute iliofemoral DVT and atresia of the IVC with catheter-directed thrombolysis is a viable option. An obliterated IVC does not preclude successful venous thrombolysis, as a recanalized IVC is not necessary for clinical improvement after successful thrombolysis.

REFERENCES