# THROMBOTIC COMPLICATIONS IN CENTRAL VENOUS CATHETERIZATION WITH LONG-LIFE CATHETERS IN PEDIATRIC CHRONIC HEMODIALYSIS

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**Abstract**

Pediatric chronic hemodialysis has been significantly improved by the usage of long-life catheters. A frequent cause of catheter dysfunction is thrombosis in various forms. We present a case series of three pediatric patients with thrombosis of the long-life central venous catheters, illustrate the various evolutions of this complication, and, in consequence, the necessity of a multidisciplinary team approach in order to achieve the best permanent access pathway.

**Keywords:** thrombosis, long-life central venous catheter, children, ens stage renal disease.

**Introduction**

Recent data indicates that end stage renal disease (ESRD) incidence for pediatric patients (ages 0-18) has doubled in the last two decades. Similarly the prevalence has increased threefold in the same period.[1] Hemodiaysis continues to be the most frequently used renal replacement therapy. The number of chidren undergoing hemodialysis is higher than the sum of kidney transplant and peritoneal dialysis.[1] Vascular access is considered to be the backbone of the method. In children this implies an unique challenge for the medical team and the dialysis service provider mainly because of the small blood vessel diameter and of the vascular hiperreactivity.

**Patient presentation**

The clinical experience of the pediatric hemodialysis unit of St. Marry Emergency Hospital for Children of Iași showcases most of the aforementioned complications within three different patient evolutions. In our center we assure renal replacement therapy by hemodialysis for 14 children, 5 of which have long life central venous catheters. During their treatment, all 5 of these patients have experienced catheter malfunction and for 4 out of 5, catheter replacement was needed. Two cases associated severe renal osteodystrophy, with calciphylaxis lesions caused by the chronic hemodialysis. Two cases associated thrombosis and catheter infection.

*Patient 1* - S.A., 4 years old. He has been treated in our service from the age of 7 days by peritoneal hemodialysis for autosomal recessive polycystic kidney disease within a genetic syndrome (Mekel Gruber syndrome). After 18 months of apparently favorable evolution, the patient has developed multiple episodes of peritonitis. At the age of 3 years, the patient returns with peritoneal dialysis catheter dysfunction. We suspected sclerosing peritonitis, which was confirmed by biopsy. We stopped peritoneal dialysis and chose conversion to long life CVC hemodialysis. Arterio-venous fistula was not an option due to the patient's weight and age. At the age of 5 years, the patient is admitted for catheter dysfunction. Administration of Taurolok and Urokinase and tissue plasminogen activator – tPA (Altepaza – Actilyse) mildly and temporarily improved CVC functionality. As such CVC removal was recommended. Removal was practiced under vascular Doppler echography that indicated subclavian vein thrombosis. The initial recommendation was to place a new catheter on the left jugular vein, but the maneuver proved impossible. As such, a temporary central venous catheter was placed on the left femoral vein as insertion point. D-Dimer value was 1,4mcg/ml (0-0,3mcg/ml). The patient recieved anticoagulant therapy – Enoxaparin, in a dosage adapted to the renal insufficiency degree. After 6 months, control echography shows right internal jugular vein permeabilization. A new long life CVC was placed and the patient received oral anticoagulant the following 6 months.

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*Patient 2* – I.M.A., 10 years old. The patient has been monitored in our clinic since the age of one year with recurrent urinary tract infections in context of a posterior urethral valve that was discovered at a late stage, with association with secondary bilateral fifth degree vesico-ureteral reflux. In january 2014, at the age of 7 years, he began renal replacement therapy directly with hemodialysis with long-life catheter. During his therapy he developped two catheter disfunctions due to thrombosis and associated infection. Local treatment with Taurolok/Heparin (2014), followed by Taurolok/Urokinase (2015) has proven insufficient due to the added infections. Catheter removal and reimplantation was necessary. In june 2016, at the age of 9 years, he developped a new right internal jugular vein thrombosis confirmed by Doppler echography. D-dimer value at this time was 2314 ng/ml (0-250ng/ml).

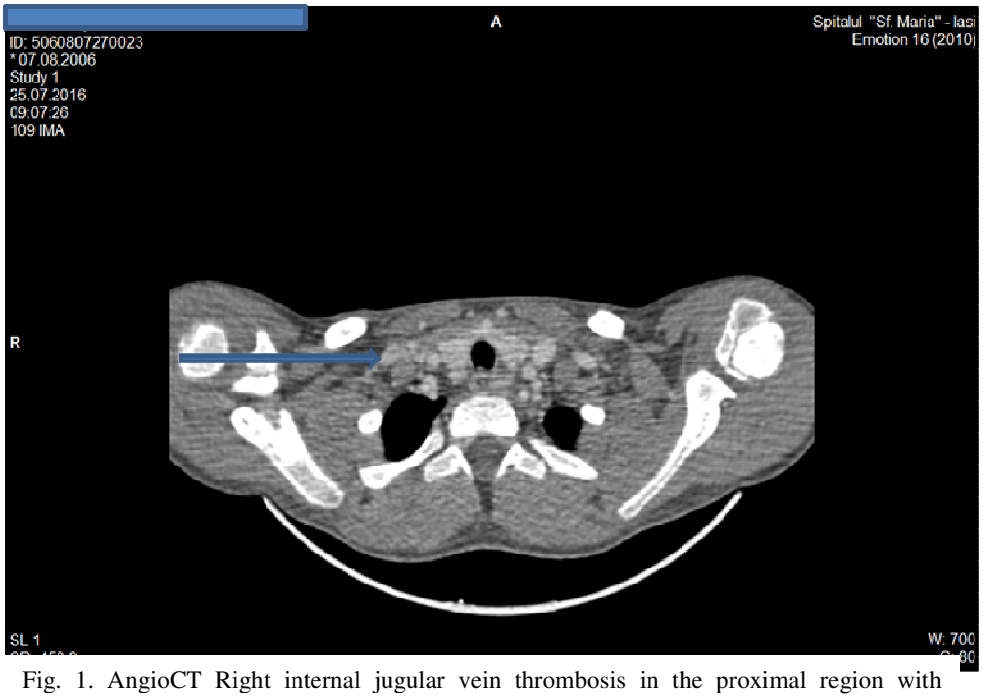


Fig. 1. AngioCT Right internal jugular vein thrombosis in the proximal region with extension to the superior vena cava. Colateral vein thrombosis is associated.

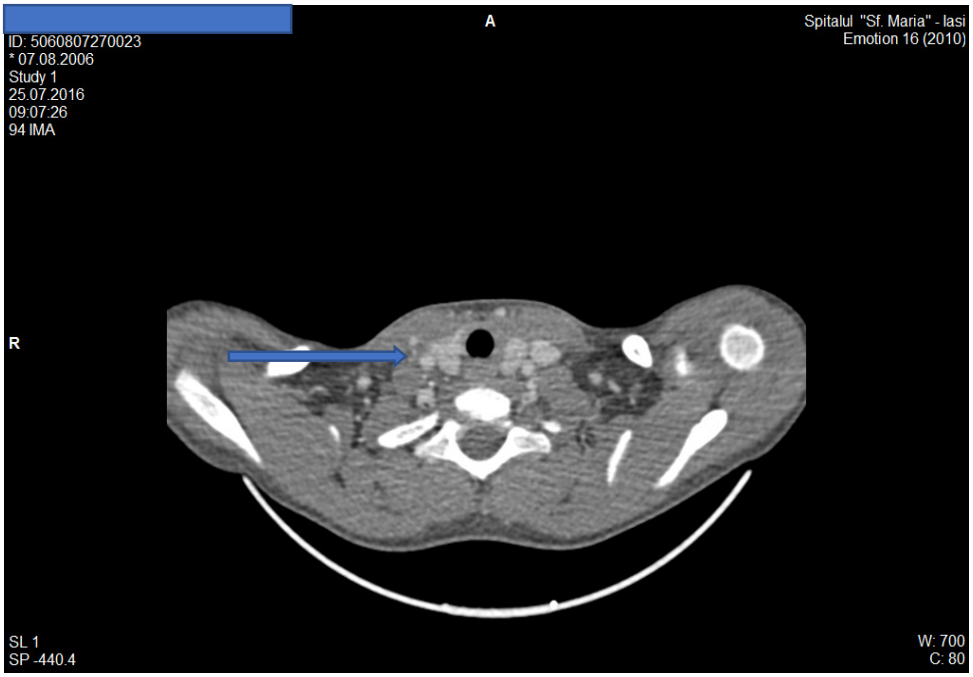


Fig. 2. AngioCT Right internal jugular vein thrombosis in the proximal region with extension to the superior vena cava. Colateral vein thrombosis is associated.

Treatment with Actilyse was initied. Due to the degree of thrombosis extension and technical issues in catheterisation of the left internal jugular vein, the decision was made to insert a temporary CVC on the right femural vein. The patient recieved anticoagulant therapy – enoxaparin – in dosage adapted to creatinine clearence. Two months later Doppler echography showed maintenance of the clot on the right internal jugular vein. The vascular surgeon decided to insert long life CVC on the left internal jugular vein, that is functional to the present day. Enoxaparin therapy was maintained. D-dimers decreased but their value is constantly high, regardless of the anticoagulant therapy (1120 ng/ml).

*Patient 3* - A.E., 20 years old, has been treated in the clinic since the age of three years old for impure nephrotic syndrome with poor evolution towards end stage renal disease. Renal replacement therapy was initiated in 2001 at the age of 3 years old with continuous ambulatory peritoneal dialysis (CAPD). After 13 years, at the age of 16 years of peritoneal dialysis he developped sclerosing peritonitis (figure 3), requiring conversion to chronic hemodialysis in 2014. In evolution he developped severe renal osteodystrophy that required parathyroidectomy. The surgical intervention only partially controlled the secondary hiperparathyroidism. In this context, the patient associated calciphylaxis, clinically manifested by skin lesions, vascular rigidity and metastatic calcifications (that were demonstrated by angio CT, echocardiography and histologically by peritoneal biopsy).

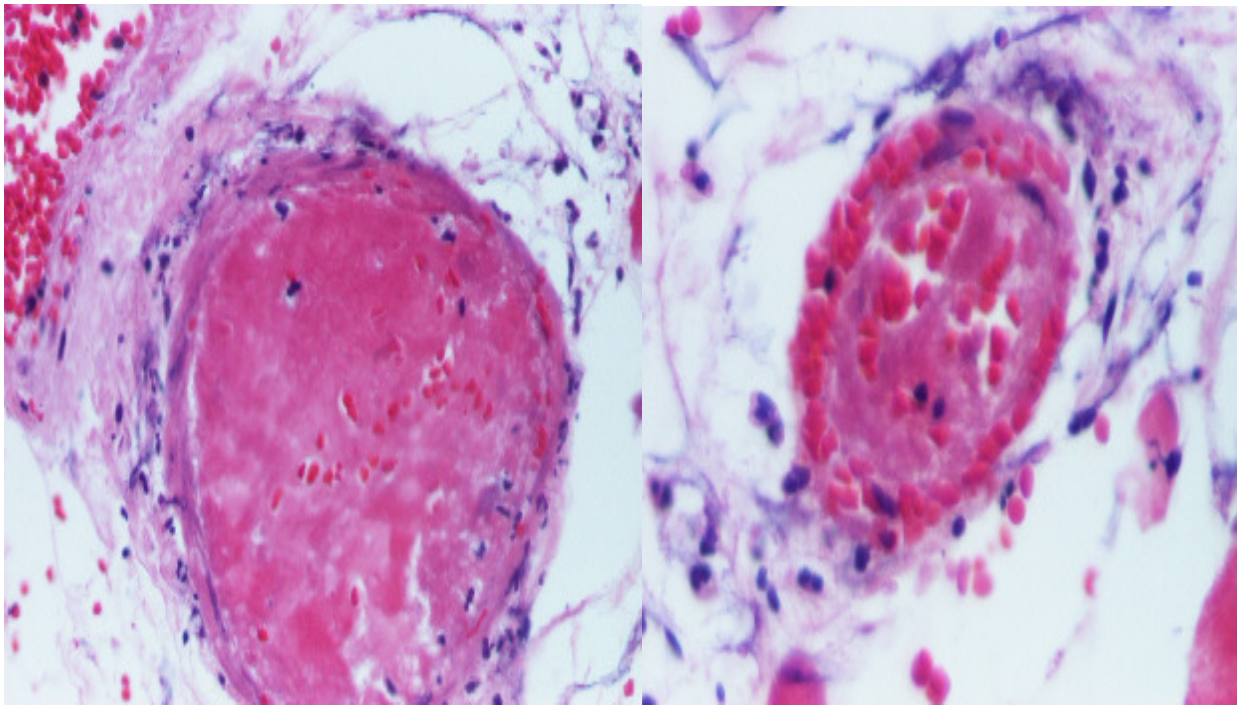

Fig. 3. Peritoneal biopsy - perivascular calcifications and thrombosis of the small peritoneal vessels.

In may 2015, at the age of 17, she developped catheter dysfunction for which local thrombolytic therapy (urokinase) was inefficient. Catheter replacement was required. CT examination describes right internal jugular vein thrombosis, tracheal calcification – in context of calciphylaxis (figure 4 and figure 5). Vascular calciphylaxis manifestations were associated. The degree of calcific uremic arteriolopathy was severe, leading to ventricular fibrilation and generalised non-epileptic seizures. The patient required cardio-pulmonary resuscitation, that was succesful. Hemodialysis on the new catheter was performed with difficulty as it was associated with multiple thrombotic recurrences. Actilyse and low molecular weight heparin therapy was associated. In july 2016 she was transferred in an adult hemodialysis service. The severe calciphylaxis lesions led to her death a few years later.

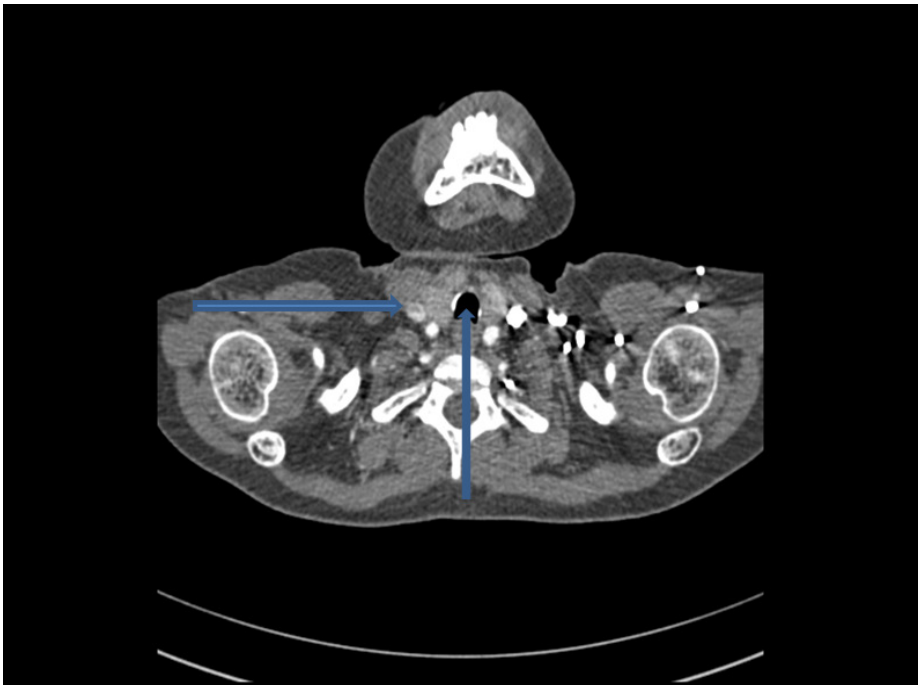

Fig. 4. AngioCT Right internal jugular vein thrombosis (left arrow) tracheal calcification – in context of calciphylaxis (middle arrow).

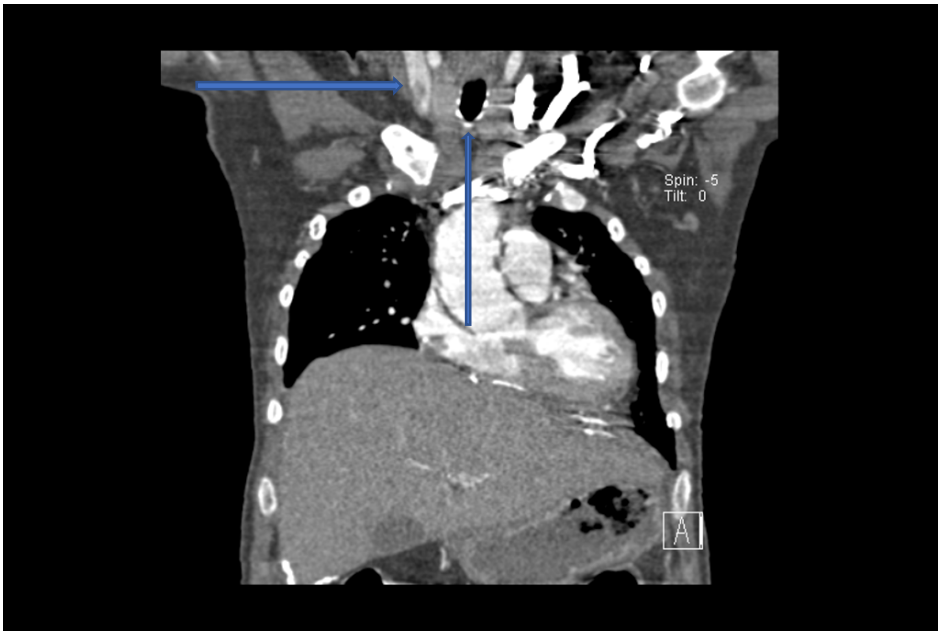


Fig. 5. AngioCT Right internal jugular vein thrombosis (left arrow) tracheal calcification – in context of calciphylaxis (middle arrow).

**Discussions**

During long term utilisation of a chronic dialysis catheter there are some foreseed trombotic complications such as fibrin coating, mural thrombosis, venous thrombosis and intraluminal clot formation.[2][3][4] After placing the central venous catheter, fibrin coating of the catheter may occur. Fibrin sheath development has been reported in 47% of CVC placed patients. This, in itself is a benign complication, but it may cause catheter malfunction, facilitating infection and mural thrombosis.[2] Mural thrombosis is usually found near the entrance of the catheter in the vessel or at great vein jonction. There are many risk factors for thrombosis, such as CVC biocompatibilty, the positioning of the tip of the catheter or its insertion, the insertion point, thrombofilia and CVC-related infections. [2] Endothelial lesion, part of the Virchow

triad (along with hipercoagulability, hemodynamic changes), also plays an important part. Vessel distruction may be caused by a variety of factors, such as mechanic lesion of the venous endothelium, the CVC insertion type, the number of vein perforation and the irritation of the vascular wall by medication. [2] The placement of the tip of the catheter in the vascular system is also an important risk factor in developing CVC-associated thrombosis. Incidence is greater in patients where the tip of the catheter is inserted in the innominate vein or proximal superior vena cava and less so in distal superior vena cava or cavo-atrial junction. [2] Patients with venous obstruction supposition must undertake venography, Doppler echography or computed tomography in order to localize the thrombus. [2] A strong association between thrombosis and infection has been suggested by multiple studies.[1][5][6]As such all practitioners from hemodialysis units must prove extreme vigilance when using CVC. There are studies that suggest that prophylactic washing of the catheter with urokinase will improve catheter permeability. CVC should be regularly washed either with urokinase or heparinized saline solution to reduce thrombotic occlusion of the catheter.[6]Aside from showcasing different clinical constelations of thrombosis, these three patients also illustrate the importance of the vascular wall in the progress of the disease. In all cases catheter dysfunction was related to thrombosis demonstrated by medical imaging and high value of D-Dimers. All of these patients required catheter replacement, but for different reasons. Thrombolytics did not mantain the catheter, but association of thrombolytics and low molecular weight heparin allowed for good recovery and fast reinsertion of the new catheter. Finally, calciphylaxis associated with thrombosis is a negative prognosis marker. These patients also demonstrate the necessity of interdisciplinary collaboration. Decision of catheter insertion point and insertion maneuvers require both an experienced anaesthesiologist as well as a vascular surgeon. Interventional radiologists are mandatory for evaluation of catheter placement and competent medical imaging interpretation of the complications. The pathologist was crucial in the calciphylaxis diagnosis. Obviously a great role is played by the nephrologist who needs to suggest the plan and, alongside the specialised nursing staff, to monitor the patient's evolution.

**Conclusions**

- Central venous catheter is a viable vascular pathway for the small child when peritoneal dialysis cannot be performed, even if it is associated with multiple complications.
- When catheter permeabilty is reduced by partial thrombosis, tissular plasminogen activator, urokinase and even heparin can have successful results.
- Vascular pathway management requires adequate planning. Interdisciplinary teams must collaborate (nephrologists, anaesthesiologists, dialysis-specialised nursing staff, surgeons and interventional radiologists) in order to achieve the best permanent access pathway.
- It is imperative for the practitioners of this field to have morbidity reduction as the long term premesis in this special category of patients.

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