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Asymptomatic catheter-related venous thrombosis in a child with cystic fibrosis: When to treat?

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The use of central venous catheters (CVCs) in patients with cystic fibrosis is associated with an increased incidence of right atrial thrombosis. Practically, the management of CVC-related right atrial thrombosis presents a challenge as there are no clinical trials or systematic reviews in pediatric patients with cystic fibrosis. We describe a case of a 5-year-old child who presented with a CVC-related infection due to Candida parapsilosis. *Echocardiogram revealed the presence of an incidental thrombus, measuring 1.4 cm × 0.4 cm, at the tip of the catheter, adherent to the right atrial wall and discrete from the tricuspid valve leaflets. Imaging was performed at monthly intervals and showed spontaneous resolution of the thrombus after six months. Follow-up blood cultures were negative, and the course of the patient was uneventful.* (J Vasc Nurs 2018;37:43-45)

The use of central venous catheters (CVCs) is important in the management of pediatric patients with cystic fibrosis (CF) for the administration primarily of antibiotics. The use of CVCs has considerably impacted the quality of life in these patients. However, CVCs are associated with an increased risk of venous thromboembolism (VTE) and systemic infection.[1] The presence of a CVC is the most important risk factor for the development of VTE in children. Reports estimate that CVC-related VTE occurs in 6.6% of pediatric patients with CF.[2] This compares favorably to other pediatric patient populations such as children with cancer, children admitted to intensive care units, and children receiving long-term total parenteral nutrition. The reported incidence in pediatric patients ranges from 5% to 44% depending on age, the primary condition, and therapies received via the CVC, as well as the type (tunneled CVC, e.g., Hickman and implantable central venous access ports [portacath]) and site of CVC placement.[3] In most instances, CVC-related VTE is an incidental radiographic finding related to the catheter tip position. Recommended treatment options include observation with or without removal of the CVC, anticoagulation, systemic thrombolysis, and surgical thrombectomy.[4] There are, however, limited evidence-based guidelines for the optimal treatment approach in CF patients with CVC-related thrombosis. We describe the conservative management and successful outcome of a 5-year-old child with CF who was found to have a low-risk CVC-related right atrial thrombosis (RAT) on echocardiography.

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CASE REPORT

A 5-year-old Caucasian girl with CF (delta F508 homozygous) had a CVC (Celsite; Braun) inserted in the right subclavian vein for multiple courses of intravenous antibiotics after colonization by *Pseudomonas aeruginosa*. The CVC had been used for two years after insertion without complication. She presented to the emergency room with a one-day history of fever. Before this presentation, her CVC was flushed with heparin and saline at her routine checkup. On examination, she was normotensive with a temperature of 38.7°C and evidence of an upper respiratory tract infection. On auscultation of the chest, there were no crepitations, and air entry was equal bilaterally. Her chest was hyperinflated. Her weight and height when plotted gave a z-score of −1 on the world health organization growth charts.

Broad-spectrum oral antibiotics (co-amoxiclav) were started empirically for the upper respiratory tract infection. Blood cultures revealed a CVC-related bacteremia with the growth of *Candida parapsilosis*. Intravenous amphotericin B was started, and the CVC was removed percutaneously. Further investigations included an echocardiogram to exclude a septic thrombosis or endocarditis. The transthoracic echocardiogram revealed the presence of a nonmobile linear thrombus, 1.4 cm × 0.4 cm, classified as type B in the superior vena cava, extending into the right atrium at the CVC tip (Figure 1). The thrombus was adherent to the right atrial wall and discrete from the tricuspid valve leaflets. The right ventricle was normal. An inherited thrombophilia screening was performed at the discretion of the treating doctor, which was normal.

She showed a response to antifungal therapy and received 10 days of intravenous therapy via a peripheral line, followed by an additional 10 days of oral fluconazole. On follow-up, repeated blood cultures after CVC removal were negative, and she was clinically apyrexial. The RAT was managed supportively with serial radiologic monitoring. Imaging at one week and monthly intervals showed no extension or dislodgement of the RAT with spontaneous resolution of the thrombus after six months. The clinical course of the patient was uneventful.

DISCUSSION

VTE is a rare complication in children with CF, and therefore, outcome data are limited.[2] More recently, the significant morbidity and mortality associated with CVC-related thrombosis have been recognized.[5] This is associated with an increased risk of short-term complications that include CVC-related infection, CVC occlusion, the need for catheter replacement, and embolization. There are, however, few studies on the incidence of long-term complications. Complications such as no thrombus resolution, postthrombotic syndrome, VTE recurrence, and loss of venous access have been reported. The management of CVC-related thrombosis needs to be individualized with appropriate consideration of the risk-benefit ratio.

The patient presented with a CVC-related infection and RAT. Atrial thrombi, in children with a CVC in the subclavian vein extending into the right atrium, usually present as asymptomatic.[6] The European Working Group of Echocardiography recommends risk-stratifying pediatric patients into high-risk or low-risk groups according to the presenting symptoms and the clot size, morphology, and mobility.[7] Clot size is dependent on the age and the size of the right atrium. The proband presented with a moderate-size nonmobile linear thrombus (type B) with no right-to-left intracardiac shunts and was thus classified as low risk. The current recommendation for low-risk CVC-related RAT, which is associated with a good prognosis, is removal of the CVC and anticoagulant therapy or supportive care with radiologic monitoring.[4] This case report adds to the body of evidence that it is therefore safe to manage an RAT that poses a low risk for embolization in a CF patient supportively with serial echocardiograms, without anticoagulant therapy. We recommended removal of the CVC if possible with radiological monitoring for such low-risk patients. There is a high reported incidence of thrombus dislodgement and pulmonary embolization at the time of CVC removal. Anticoagulant therapy for three to five days before removal is thus recommended.[4]

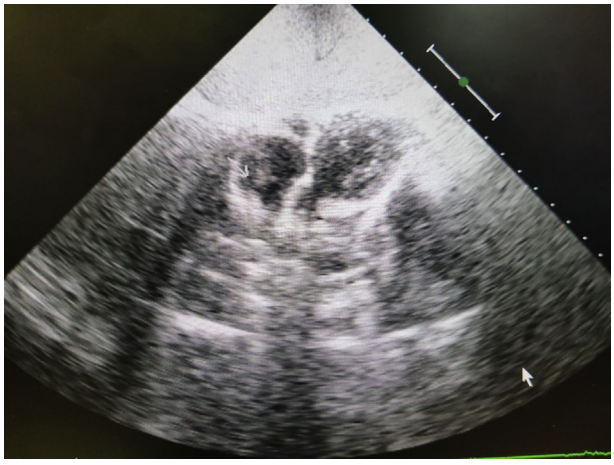

Figure 1. *Transthoracic echocardiography showing a thrombus (arrow) of dimension 1.4 cm × 0.4 cm.*

If there is extension of thrombosis during supportive care or the patient is classified as high-risk, anticoagulation is recommended.[4] Surgical thrombectomy or thrombolytic therapy carries a significant risk and should be considered individually in high-risk patients as experience with CF patients is limited. The choice of anticoagulant depends on the advantage and disadvantages of each of the locally available anticoagulants, namely low-molecular-weight heparin (LMWH), unfractionated heparin, and vitamin K antagonists (e.g., warfarin). LMWH offers several advantages such as superior bioavailability, minimal monitoring requirements, and predictable dose response and is therefore the mainstay of therapy. LMWH is administered subcutaneously, which can be difficult to manage in the outpatient setting. Furthermore, the available LMWH-prefilled syringes often need to be diluted with sterile water to administer the small doses required. New anticoagulant drugs in clinical trials have demonstrated improved safety and efficacy. However, it is still too early to recommend their use in pediatrics. The optimal duration of anticoagulant therapy has not been extensively studied and is an area of ongoing research. The current recommendation is three months for children in conjunction with radiological monitoring.[4] The patient's thromboembolic risk and risk for bleeding, e.g., hemoptysis, should also be considered. A raised D-dimer, >0.5 mg/mL, level and residual thrombus after three to six months of anticoagulant therapy are risk factors for recurrent VTE.[8]

In chronically ill children, acquired risk factors for VTE play a greater role than inherited thrombophilia. CF patients are at increased risk of VTE because of the higher frequency of acquired protein C and S deficiencies as a result of vitamin K deficiency or associated liver involvement.[9] Thrombophilia testing is currently not recommended in pediatric patients presenting with CVC-related VTE.[2] Testing, however, can be considered in the setting of recurrent CVC-related VTE or a family history.[10] If clinically indicated, testing of the parents can also be performed. It is advisable to perform the testing at least two weeks after discontinuation of anticoagulation therapy because the acute event and anticoagulant therapy will influence the results. Furthermore, the results of thrombophilia testing rarely influence

early management decisions and do not impact the duration of anticoagulant therapy.

CONCLUSION

The use of CVC in patients with CF is associated with an increased incidence of CVC-related VTE. The findings of this case report support the conservative management of CF patients with RAT who are hemodynamically stable and classified as low risk on echocardiography. We recommend close observation with radiological monitoring and removal of the CVC if possible.

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