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Catheter related atrial thrombosis in an infant: A case report and review of the literature

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ABSTRACT

Catheter-related thrombosis is one of the potential major complications of the central venous access devices; main risk factors include catheter-related blood stream infection and hypercoagulable state such as malignancy and systemic infections. Catheter-related atrial thrombosis is an under-reported complication of venous access devices of unclear prevalence rate, predisposing factors, screening recommendations and management guidelines, usually diagnosed incidentally on echocardiogram and managed by systemic anticoagulation with or without catheter preservation.

Here we present the case of a 2700-g infant with catheter-related right atrial thrombosis who was successfully treated with anticoagulation therapy and preservation of the catheter. Potential risk factors for thrombosis in this case include dehydration caused by refractory diarrhea and feeding intolerance, urinary tract infection, and total parenteral nutrition containing dextrose. We have also performed a review of the literature on catheter-related atrial thrombosis in the pediatric age group.

1. Introduction

Central venous catheter device placement is common in children diagnosed with cancer or admitted to the intensive care unit, as well as in low birth-weight and small for gestational age neonates, to facilitate the administration of intravenous medications and parenteral nutrition, and for repetitive blood sampling [1].

Despite the fact that these devices have revolutionized the care of chronic patients of all ages, many potential complications have been associated with their placement and usage. Catheter-related atrial thrombosis (CRAT) is an under-reported complication of unclear prevalence rate and best management practices [2].

2. Case report

Herein, we present the case of a two-month-old girl who was born at full term (birth weight 3024 g) with no known neonatal or perinatal complications. The patient was transferred to our hospital for management of profuse watery non-bloody diarrhea (5–10 times per day) of four weeks duration, associated with reduced oral intake and non-bilious vomiting.

On admission, the patient was cachectic and weighed 2700 g. She could not tolerate oral intake, which prompted total parenteral nutrition administration, and had positive urine culture for Staphylococcus Epidermidis requiring intravenous vancomycin. The peripheral venous access was difficult and multiple attempts at inserting a peripherally inserted central venous catheter (PICC) failed. A size 6 French Polyurethane totally implantable venous access device was placed via the right internal jugular vein using an open technique under general anesthesia.

On postoperative day 7, an echocardiogram was performed to complete the medical workup; this uncovered the presence of a 1.4 × 0.8 cm homogenous echogenic mass in the right atrium, at the junction between IVC and tricuspid valve adherent to the diaphragmatic wall of the right atrium, suggestive of a previously unsuspected catheter-related right atrial thrombosis (CRAT). The rest of the medical work-up was negative and the patient was diagnosed with intractable diarrhea of infancy.

In light of the extreme difficulty in securing a peripheral venous access for the patient and because the clot was stable and adherent to the atrial wall on echocardiogram and was asymptomatic, we decided to

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preserve the line that remained functional throughout the hospital course. Therapeutic low molecular weight heparin (Enoxaparin) was started at a dose of 1 mg/kg subcutaneously every 12 hours, Anti-Xa level was utilized to adjust the dose; 2.3 mg/kg was required to achieve a therapeutic level of Anti-Xa of 0.5–1 IU/mL. The patient maintained a normal platelet count throughout.

Serial echocardiograms were performed on postoperative days 10, 17, 25, 45, 66, 96, and 153 showing gradual resolution of the right atrial thrombus with no hemodynamic obstruction to the inferior or superior vena cavae at any point in time, with complete resolution of the clot on postoperative day 96 (Table-1) (Fig. 1), (Fig. 2a–b), and (Fig. 3). Of note, the patient did not have any anatomic cardiac abnormality and no detectable patent foramen ovale.

On postoperative day 23, the patient developed fever; blood culture from the catheter grew Staphylococcus Epidermidis. She received a ten-day course of intravenous vancomycin, after which repeat blood cultures were negative. Screening tests for thrombophilia were negative. The device was removed 5 months after insertion whereby the patient's clinical condition improved significantly and the catheter was not needed any longer. The patient remained on therapeutic subcutaneous Enoxaparin until complete resolution of the right atrial thrombus was achieved (three months); she was then placed on prophylactic dose of Enoxaparin for two months until the catheter was removed. Our case is an example of provoked thrombosis hence anticoagulation was not indicated after catheter removal. We based our management decisions on the American society of hematology guidelines and Young (2017) [3,4].

The catheter removal procedure was smooth and uncomplicated. During the most recent follow-up visit, a week after catheter removal, the patient remained symptom-free and a repeat echocardiogram was negative for recurrence of the thrombosis.

3. Discussion

Since their introduction in the early 1980's [5] totally implantable venous access devices (TIVADs) have significantly improved the quality of care of patients, of all age groups, who require long-term venous access for administration of intravenous medications and multiple blood withdrawals [6].

A long list of potential complications of central venous access have been described in the literature including pneumothorax, hemothorax, air embolism and cardiac arrhythmias in the immediate postoperative phase, as well as late complications such as infection, catheter migration or disconnection, vascular erosion and catheter-related thrombotic complications [6]. Thrombotic complications are common with an incidence rate ranging between 14% and 36% within 1–2 years of catheter placement [7]. They may remain asymptomatic, result in catheter dysfunction, or even dislodge and cause life threatening thromboembolic events. Potential locations of the thrombus include the catheter itself, the central vein harboring the catheter, or even in the right atrium or the superior vena cava [8].

3.1. Prevalence rate

Different studies have reported a wide range of prevalence rates of catheter-related right atrial thrombosis [9]. Korones et al. reported a prevalence rate of 8.8% in children with oncologic conditions, all of which were asymptomatic and diagnosed on routine echocardiograms [10]. The prevalence rate in neonates varies between 0.7% and 67% [11]. Table 2 summarizes data on catheter-related atrial thrombosis in children.

Table-1
CRAT Dimensions on follow-up echocardiograms.

Post-operative Day	Length (cm)	Width (cm)
10	1.4	0.6
13	1.4	0.6
17	1.2	0.5
25	1.2	0.5
45	0.9	0.4
66	0.8	0.3
96	<0.1	<0.1
153		

3.2. Clinical presentation

Though mostly asymptomatic, patients with CRAT may present with catheter malfunction [12]. CRAT can be life threatening with reported mortality rate of up to 18.3% mainly due to potential cardiac arrest and pulmonary thrombo-embolism; systemic embolization is possible in cases of coexisting patent foramen ovale [13].

3.3. Risk factors

Multiple risk factors have been linked to the development of CRAT including hypercoagulable state such as malignancy and hyperviscosity due to dehydration; catheter-related blood stream infection, as well as catheter tip location [7,8,12,13].

The positive correlation between catheter-related infection and CRAT development has been explicitly discussed in the literature [14]. Intra-atrial thrombogenic process may be triggered by an infectious nidus at the tip of the catheter, or the clot itself may predispose to infection [15]. Systemic infectious diseases have also been associated with thrombotic complications by increasing cytokine levels such as TNF-alpha and interleukin-1 and 6, which stimulate the production and release of plasminogen activator inhibitor type I (PAI-1) thus impairing fibrinolysis and precipitating thrombotic events [16]. Our patient had positive urinary culture; this may have contributed to the development of thrombosis.

Long-standing stress has been linked to thrombotic complications via increasing platelet aggregability and serum levels of factors VIII, VWF and fibrinogen. Plasminogen activator inhibitor type I (PAI-1) levels are also increased by stress secondary to hypercortisolemia [17]. Our patient had long-standing diarrhea and undernutrition causing stress thus possibly contributing to her thrombotic complication. Hyperinsulinemia caused by intravenous hypertonic glucose administration has also been associated with thrombotic events due to secondary elevation in plasminogen activator inhibitor type I (PAI-1) levels [18]. Our patient was not on supra-physiologic levels of glucose infusion and she did not develop hyperglycemia during her hospital stay.

In regards to the catheter tip location, The National Kidney Foundation - Kidney Disease Outcomes Quality Initiative (NKF)-KDOQI guidelines, last updated in 2006, recommend placing the tip of long-term catheters within the right atrium both in children and adults to achieve optimal blood flow necessary for hemodialysis [19]. On the other hand,

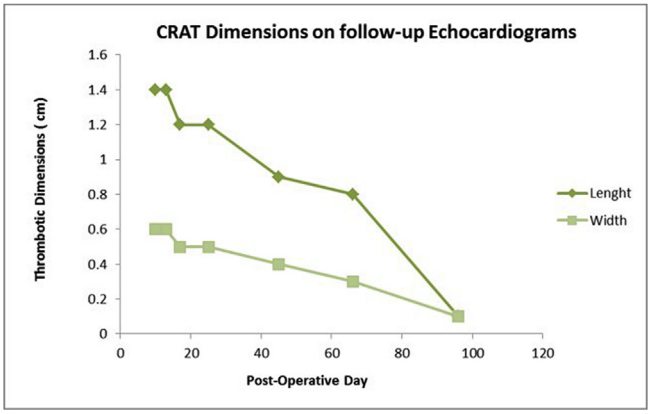

Fig. 1. CRAT Dimensions on follow-up Echocardiograms.

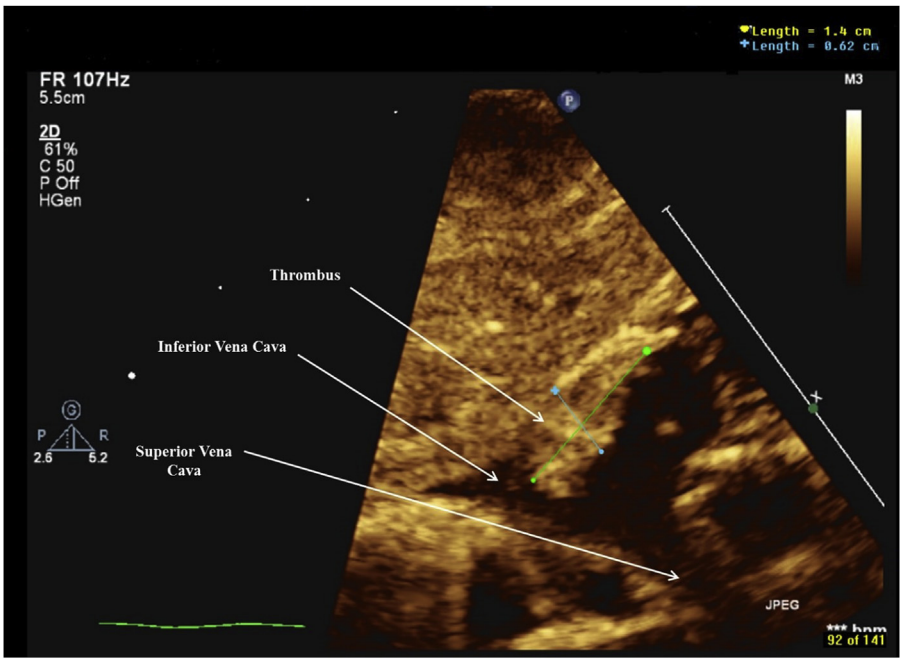

Fig. 2a. Echocardiography post-operative day 10.

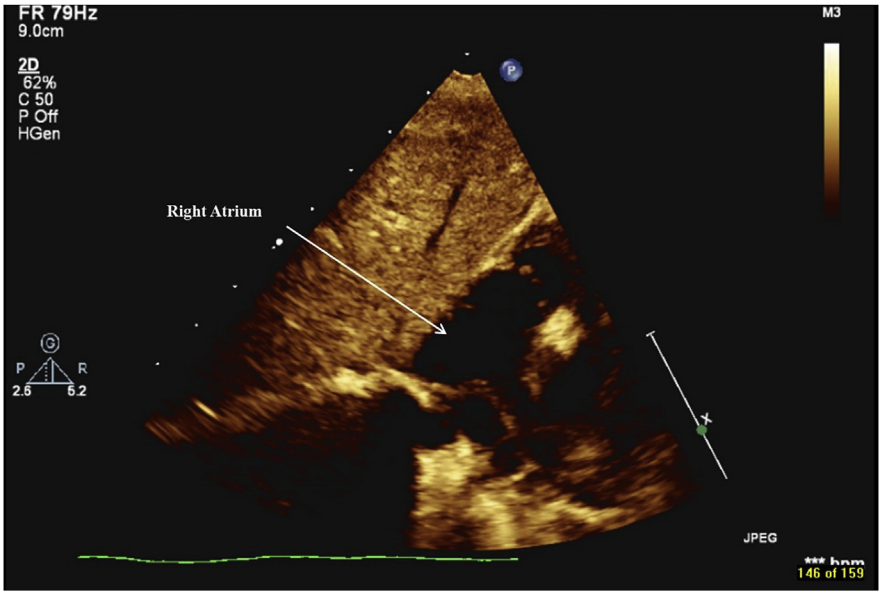

Fig. 2b. Echocardiography post-operative day 96.

Korones et al. [10] showed a statistically significant higher incidence of CRAT in patients in whom the tip of the catheter was positioned in the right atrium as opposed to the superior vena cava (20% versus 2%, P = 0.004). Other authors have shown even higher incidence (up to 46.2%) of CRAT development associated with catheter tip positioning in the right atrium [20]. This phenomenon may be attributed to the continuous mobility of the catheter within the right atrial cavity caused by the beating heart, resulting in right atrial wall endothelial damage thus initiating the thrombogenic process [1,21]. Chen et al. explained that in children the tip of the catheter may not stay in its place after placement under fluoroscopic guidance due to physical activity; this catheter-tip movement contributes to catheter thrombosis; the authors suggest positioning the catheter in the superior vena cava to minimize catheter tip movement in children [22].

In the present case, central blood culture grew Staphylococcus Epidermidis, the tip of the catheter was positioned within the right atrium, the patient had urinary tract infection, dehydration, and was in a state of physiologic stress; all of the above factors may have contributed to the development of CRAT.

3.4. Diagnosis

As in the present case, CRAT is usually diagnosed incidentally on echocardiograms [9]. Echocardiograms may be prompted by catheter dysfunction or other signs such as arrhythmia. Cardiac magnetic resonance imaging may be useful when echocardiograms are not conclusive to rule out other pathologies such as intra-atrial tumors [23].

CRAT may develop early after central line placement. Similar to our

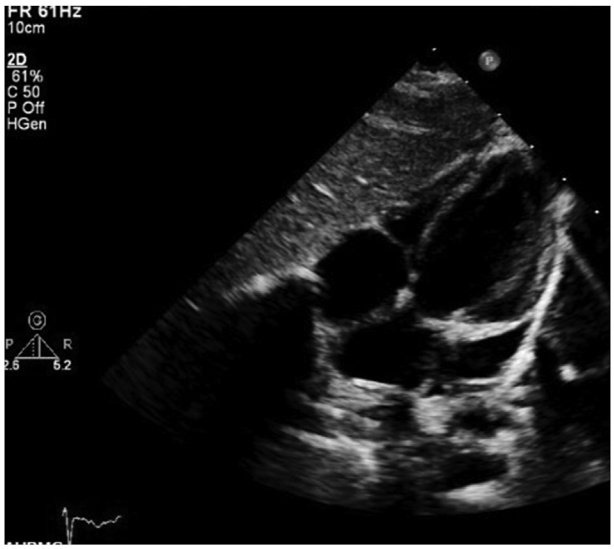

Fig. 3. Echocardiography post- catheter removal.

case, Gilon et al. [20] documented CRAT development in less than a week after insertion, whereas other studies documented cases diagnosed up to a year after removal of the catheter [10].

3.5. Management

Classically, catheter-related thrombosis is managed by catheter removal and long-term anticoagulation therapy [24,25]. Due to the paucity of high-level evidence, most of the management strategies of catheter-related thrombosis in neonates and children are extrapolated from the adult literature [11,26]. Yang et al. [12] reported successful management of 20 adult hemodialysis patients with anticoagulation and catheter replacement whereby the tip of the new catheter is located at a different location than that of the clot. Thrombolysis of the atrial clot has also been reported in the literature [27]; however, risk of fragmentation of the clot resulting in pulmonary embolism [28] or systemic embolism in the presence of patent foramen ovale remains a major concern [29]. Prompt thoracotomy and excision of the thrombus is indicated when anticoagulation is contraindicated, in hemodynamically unstable patients, or in cases of large thrombi [13]. The medical literature remains indecisive when it comes to comparing the outcomes of medical and surgical management options in patients with CRAT [13]. In our case, despite the fact that the dimensions of the right atrial clot were 1.4 × 0.8 cm, which is smaller than the reported cut-off for surgical intervention (2 cm) [28], the patient weighed only 2700 g and the largest dimension of her right atrium was 1.9 cm as measured on echocardiogram. That said, and because the line was legitimately needed and the clot was asymptomatic, we elected to preserve the catheter and treat by anticoagulation only.

In their meta-analysis of 71 CRAT cases in hemodialysis adult patients, Stavroulopoulos et al. [13] concluded that the removal of central venous catheter in patients diagnosed with CRAT is mandatory because of the high mortality and complication rates associated with retaining the catheters in place. The authors attributed this high correlation between keeping the lines and worse outcomes to the mechanical trauma inflicted on the atrial wall by the catheters' tips, particularly when the later are located in the right atrium rather than the distal superior vena cava, as well as the potential bacterial colonization of the catheters.

The risks of removing a central catheter due to thrombosis or infection include embolization and dissemination of bacteria [29]. Medical management of CRAT with anticoagulation only and preserving the catheter has been successfully attempted in stable and asymptomatic patients. In their retrospective review, Chick et al. reported a 92% rate of catheter preservation in cases of incidentally discovered catheter-related thrombosis [30]. There are also reports in the literature of managing patients with incidentally discovered small asymptomatic CRAT located at the catheter tip by observation only without anticoagulation or catheter removal, both in children and adults [10,30] [Table 2]. Our patient was incidentally diagnosed with CRAT around one week after central venous device placement, was successfully managed with anticoagulation while preserving her catheter.

3.6. Prophylaxis

Despite the fact that some authors have suggested the utilization of heparin prophylaxis to prevent peripherally inserted venous catheter-related thrombosis in infants [31], its use has been associated with significant albeit rare adverse events such as bleeding and heparin-induced thrombocytopenia [32]. In their systematic review of literature and meta-analysis, Vidal et al. analyzed over 3000 pediatric patients including newborns and concluded that thromboprophylaxis using heparin, warfarin, or other potential agents do not reduce the risk of catheter-related thrombosis [33]. Our patient was not placed on thromboprophylaxis at the time of catheter placement, as we believe that the risk-versus-benefits of thromboprophylaxis does not justify its use in neonates.

3.7. Recurrence

Recurrence of CRAT after successful treatment is extremely rare; it has so far been reported in two patients, an adult [22] and a child [34] both of which were originally treated via anticoagulation and surgical excision of the clot. The adult patient was a 39-year-old woman on hemodialysis who had high serum homocysteine levels [22], and the other patient was a 12-year-old child with non-Hodgkin lymphoma and factor-V Leiden mutation [34]. Our patient's serum homocysteine level was 2.5 μ mol/L (reference range: 5–15 μ mol/L) and no evidence of inherited coagulopathy.

Table-2
List of reported CRAT cases in children.

Reference	Study methodology	Number of cases	Age range	Management	
Chen et al. (2016) [1]	Retrospective	6	Not available	Not available	
Corapçioğlu et al. (2005) [34]	Case report	1	12 years	Atriotomy and clot excision	
Kornoes et al. (1996) [10]	Retrospective	13	2 years–20 years	Approach	Number of patients
				Atriotomy and clot excision	2
				Anticoagulation and pulling back of the catheter	1
				Anticoagulation only	3
				Observation only	7
Ross et al. (1989) [35]	Retrospective	16	3 weeks–15 years	Approach	Number of patients
				Atriotomy and clot excision	2
				Thrombolysis	8
				Catheter removal	3
				Observation only	3

3.8. Screening

The gold-standard screening for central-line-related thrombosis has yet to be defined. Some authors have suggested routine echocardiograms in all patients with long-term central venous catheters to avoid potential significant complications of asymptomatic CRAT [21]. Other published suggestions include obtaining echocardiograms only in patients with dysfunctional catheters [28], or in patients with high-risk profile such as catheter tip in the right atrium or recipients of known thrombogenic chemotherapeutic agents such as L-asparignase [34].

4. Conclusion

We have presented a case of 2700 grams-infant with CRAT who was successfully treated with anticoagulation therapy with preservation of the catheter; At this point in time, current data are not sufficient to recommend how to screen and treat central venous catheter-related atrial thrombosis.

Human rights

The described work has been carried out in accordance with The Code of Ethics of the World Medical Association(Declaration of Helsinki) for experiments involving humans; the patient's parents were consented to present the following case report. Their permission (parents' permission) was granted to post all Echocardiography related image.

Author contributions

Ahmad Zaghal proposed the study.

Mariam Arabi and **Rana Sharara-Chami** contributed equally to this paper and are both first authors.

Ahmad Zaghal, Joelle Hassanieh, performed the research and wrote the first draft.

Ahmad Zaghal, Joelle Hassanieh, collected and analyzed the data.

All authors contributed to the design and interpretation of the study and to editing of the manuscript.

Ahmad Zaghal is the guarantor.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

List of abbreviations

NKF-KDOQI	The National Kidney Foundation - Kidney Disease Outcomes Quality Initiative
CRAT	Catheter-related atrial thrombosis
MTHFR	Methylenetetrahydrofolate reductase
PFO	Patent foramen oval
PICC	Peripherally inserted central catheter
POD	Postoperative day
TIVAD	Totally implantable venous access device

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