Tunneled Catheter–Associated Atrial Thrombi: Successful Treatment with Chronic Anticoagulation

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Tunneled dialysis catheter–associated right atrial thrombus (RAT) is a rarely reported complication. We reviewed hospital records of 10 patients from a teaching hospital dialysis unit, in whom RAT was diagnosed by trans-esophageal echocardiography (TEE). Patients were treated with chronic anticoagulation (heparin followed by warfarin) and followed over time. The group included 7 women; 6 patients were African American, 3 were Caucasian, and 1 was Hispanic. The average age was 52.1 ± 15.3 years. The most common presenting symptom was poor catheter flow on hemodialysis followed by fever and chills. On average, the patients had had 3.4 ± 2.7 catheter insertions before diagnosis of RAT, and the tunneled dialysis catheter (TC) had been in place for a mean of 91 ± 89.4 days when the thrombi were diagnosed. Trans-thoracic echocardiography (2-D echo) was done in 4 patients, but it identified RAT in only 1 patient. The catheter tip was at the junction of the superior vena cava and right atrium (SVC/RA) in most patients.

Thrombolysis (unsuccessful) was attempted with urokinase in 3 patients, complicated in 2 patients by hemorrhage. After anticoagulation, 90% of the RAT resolved on repeated TEE. One patient had persistent RAT for 23 weeks and underwent surgical thrombolysis, but died postoperatively.

We conclude that RAT is a frequently missed complication of a TC. Positioning the tip of the TC at the SVC/RA junction may not prevent RAT. Trans-esophageal echocardiography is a more sensitive diagnostic tool than 2-D echo and should be obtained early. Most patients can be successfully treated with anticoagulation alone. Thrombolytic therapy and surgical thrombolysis have high morbidity and mortality.

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Key Words

Tunneled catheter, atrial thrombus, urokinase, anticoagulation

Introduction

Cuffed tunneled hemodialysis catheters (TCs) were developed in the 1980s as an alternative acute hemodialysis vascular access [1]. Initially intended as a bridge device to provide prolonged periods of temporary access, TCs have become permanent accesses for hemodialysis in many patients. Despite providing lower blood flows as compared with arteriovenous graft or fistula [2], the number of patients using this dialysis access is increasing. The United States Renal Data System (USRDS) incident sample indicates that between 1993 and 1996, the incidence of tunneled cuffed catheter use for dialysis at initiation and 60 days afterward increased to 12.9% from 9.7% [3]. Thrombosis is a common problem with TCs. A large intra-atrial thrombus may develop in association with the dialysis catheter. Although many reports exist of indwelling catheter–related right atrial thrombi in pediatric patients receiving total parenteral nutrition (TPN) and chemotherapy, relatively few case reports are seen of dialysis catheter–related right atrial thrombi [4–7]. The optimal therapy for this condition has yet to be established. The aim of the present retrospective study was to report our experience, at the Albert Einstein Medical Center dialysis unit, with tunneled catheter–related atrial thrombi.

Material and methods

The patients were followed at the teaching hospital dialysis unit at Albert Einstein Medical Center, Philadelphia, from March 1998 to March 2000. The dialysis unit followed 250 patients in that time, and 20% had a TC as the dialysis access. All of the catheters were double-lumen silicone rubber catheters with felt cuffs; most were the PermCath type (Kendall Healthcare, Mansfield, MA, U.S.A.). The catheters were inserted under fluoroscopic guidance at our institution by either the surgeons or the radiologists. When complications arose from accesses, the patients were admitted to hospital. Atrial thrombi were found by trans-esophageal echocardiography (TEE) during the diagnostic workup.

Chemical thrombolysis using 250,000 U urokinase in a continuous infusion was attempted in some patients. All the patients were treated with a standard anticoagulation regimen consisting of heparin followed by warfarin. Dosages of warfarin were adjusted to maintain a plasma international normalized ratio (INR) between 2.0 and 3.0. All patients suspected of catheter-related infection had routine blood cultures done at the time of admission to hospital. They were treated with vancomycin (1 g) and gentamicin (1 mg/kg) empirically, and switched to appropriate antibiotics after sensitivity profiles became available. Most patients had repeat TEE at weekly intervals to assess the size of the thrombus and its relation-

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ship to the catheter after anticoagulation therapy was begun. Catheters with non adherent thrombi were removed once therapeutic anticoagulation was achieved. Catheters with adherent thrombi were left in place and patients received dialysis via an alternative access for 6 weeks. The patients were followed through 31 December 2000.

Results

Within a 2-year period, 10 patients were diagnosed with right atrial thrombus (RAT) (Table I). In 8 patients, the TC was used as the permanent dialysis access because alternative accesses such as arteriovenous fistula (AVF) or polytetrafluoroethylene (PTFE) graft had been exhausted from numerous past failures. In 2 patients, the TC was a bridge access: one patient was waiting for an AVF to mature; the other patient was waiting for a living related kidney allograft transplantation procedure. The group included 7 women; 6 patients were African American, 3 were Caucasian, and 1 was Hispanic. The mean age was 52.1 ± 15.3 years. Diabetes mellitus was the cause of the end-stage renal disease (ESRD) in 40% of the patients. In 6 cases, the catheter was inserted through the right internal jugular vein; in 3, through the left internal jugular vein; and, in 1 case, the dialysis catheter was inserted through the right subclavian vein.

The most common reason for hospital admission was poor catheter blood flow on dialysis (n = 4). Dyspnea was experienced by 3 patients; however, radionuclide scintigraphy in these cases indicated low probability for pulmonary embolism. None of the patients had a history of coagulopathy; therefore, no work-up was done to identify a prothrombotic factor. Of the 4 patients with positive blood cultures, 3 showed mixed flora (Table I). On average, 3.4 ± 2.7 catheters had been inserted before the occurrence of RAT, and the catheters had been in place for a mean of 13 ± 12.8 weeks when the atrial thrombus was found (Table II). Four patients had transthoracic echocardiography (2-D echo) before TEE; however, the thrombus was visualized on 2-D echo in only 1 patient. On TEE, most of the clots originated in the superior vena cava (SVC) and extended into the right atrium (RA); 7 thrombi were adherent to the catheter. The average thrombus size was 3.6 cm^2 (range: 0.3 – 9.45 cm^2).

Chemical thrombolysis using urokinase was attempted in 3 patients (unsuccessfully). All patients received chronic anticoagulation therapy; the warfarin dosage was adjusted according to INR. Follow-up TEE results were available in 7 patients (Table III). One patient had to be withdrawn from anticoagulation therapy because of bleeding from a duodenal ulcer; this patient had persistent RAT for 23 weeks and underwent surgical thrombolysis, but died postoperatively. Of the other 6 patients in whom TEE was repeated between 10 weeks and 3 years, all were free of thrombus (Figs. 1, 2). Four patients died: 2 of septicemia at about 1 year and 2.5 years; 1 of respiratory failure from chronic obstructive airway disease exacerbation at 20 months; and 1 from acute myocardial infarction at 17 weeks. None of the deaths was directly related to the previously diagnosed right atrial thrombosis, as each patient was free of atrial clot at the time of demise. Of the 5 living patients, 3 had successful kidney allograft transplantation procedures and 1 was switched to peritoneal dialysis. The remaining patient was still receiving hemodialysis 33 months after the diagnosis of RAT, using an AVF as dialysis access.

Discussion

Thrombosis is a common problem with tunneled cuffed catheters. The mean primary patency rate (time to first required therapeutic intervention) has been reported to range between 73 days and 84 days [8,9]. Catheter-associated thrombosis can be classified as extrinsic and intrinsic. Extrinsic thrombosis includes central venous thrombosis, the reported incidence of which varies from 2% to 63.5% in non dialysis central venous catheters such as the Hickman catheter used for chemotherapy and parenteral feeding [10,11]. Other extrinsic thromboses such as mural thrombosis or its variant,

TABLE I Demographic data and clinical presentation of the patients.

Patient	*Age*	*Race/sex*[a]	*Cause of ESRD*	*Chief complaint*	*Blood culture result*
1	46	A/F	Polycystic kidney disease	Dyspnea, cough	Negative
2	76	A/F	Diabetes mellitus	Poor blood flow	Not done
3	43	A/F	Glomerulonephritis	Fever	MRSA *Bacteroides* species
4	55	A/F	Diabetes mellitus	Poor blood flow	*Staphylococcus aureus* *Proteus mirabilis*
5	29	H/F	Diabetes mellitus	Dyspnea	Negative
6	38	C/F	Systemic lupus erythematosus	Poor blood flow	Not done
7	55	A/M	Sarcoidosis	Dyspnea	Negative
8	65	C/M	Diabetes mellitus	Poor blood flow	Not done
9	72	A/F	Renal vascular disease	Chest pain, fever	*Enterococcus* species
10	42	C/M	Renal vascular disease	Fevers	*S. aureus* Diphtheroid species

[a] A = African American; C = Caucasian; H = Hispanic; M = male; F = female.
ESRD = end-stage renal disease; MRSA = methicillin-resistant *Staphylococcus aureus.*

TABLE II Details of tunneled hemodialysis catheter (TC) and the characteristics of the thrombi.

Patient	*TC insertion (n)*	*Duration of TC (weeks)*	*2-D echo result*[a]	*Clot adherent to TC tip*	*Thrombus size (cm)*	*Urokinase*
1	5	1	Not done	Yes	2.0×1.0	Yes
2	8	3	Negative	Yes	2.5×1.0	No
3	3	6	Negative	No	2.7×1.2	No
4	6	2	Not done	Yes	0.3×1.0	No
5	0	21	Not done	No	3.5×2.7	No
6	2	29	Not done	Yes	2.2×2.0	No
7	0	4	Negative	Yes	3.0×3.0	Yes
8	3	16	Not done	Yes	1.0×1.0	Yes
9	4	35	Positive	Yes	0.3×1.0	No
10	N/A	N/A	Not done	No	2.0×2.0	No

[a] Four patients had 2-D echo.
N/A = not available.

TABLE III Result of chronic anticoagulation therapy and patient outcome.

Patient	*Repeat TEE showing negative clot (weeks)*	*Follow-up to 31/12/2000 (weeks)*	*Outcome*
1	Persistent clot	23	Died, surgical thrombectomy
2	12	118	Died, septicemia
3	15	49	Died, septicemia
4	61	85	Died, respiratory failure[a]
5	139	142	Alive, kidney transplant
6	60	97	Alive, kidney transplant
7	10	133	Alive, switched to PD
8	No repeat TEE	131	Alive on hemodialysis
9	No repeat TEE	17	Died, myocardial infarction[b]
10	No repeat TEE	134	Alive, kidney transplant

[a] Patient had longstanding chronic obstructive pulmonary disease.
[b] Patient had severe history of coronary artery and peripheral vascular disease.
TEE = trans-esophageal echocardiography; PD = peritoneal dialysis.

intra-atrial thrombus, may develop in association with a dialysis catheter and present as a mass within the right atrium. To date, no prospective study has established the incidence of dialysis catheter–related right atrial thrombus. The incidence of non dialysis central catheter–related intra-atrial thrombosis is reported to range between 12.5% and 17% [12,13]; most of the right atrial thrombi were seen in patients whose catheters were in use for more than 150 days [13]. However, a thrombus may form as early as 7 days post-insertion [12]. In our patients, the average length of time to thrombus development after catheter insertion was 13 weeks with a range of 1 – 35 weeks.

The tip of the catheter is frequently attached to the atrial thrombus, and when attachment occurs, the thrombus can interfere with catheter function. Most of the thrombi are not recognized unless catheter malfunction occurs. Trans-esophageal echocardiography is thought to be the best diagnostic tool [12,14]. In our study, trans-thoracic echocardiography was done in 4 patients prior to the TEE, and only in 1 patient was the RAT diagnosed by this means. No recommendation currently exists to screen all patients receiving dialysis through central venous catheters.

Thrombus formation is presumed to result from catheter tip movement that causes damage to the right atrial wall [14]. Gilon *et al.* [12] studied Hickman catheters in 48 patients undergoing bone marrow transplantation, and found that 46% of patients with the catheter tip in the RA have tip-associated thrombi within 1 week after placement of the catheter [12]. Hickman catheters with tips placed in the SVC or at the SVC/RA junction were not associated with any thrombus [12]. However, in our study, most of the dialysis catheter tips were at the SVC/RA junction. Of the thrombi in our patients, 70% were attached to the catheter instead of to the RA wall. The placement of the catheter tip external to the RA may not eliminate the risk of RAT formation. It should be noted that, to achieve the high blood flow necessary for high-efficiency hemodialysis, the current practice is to place the tip of the dialysis catheter in the right atrium. A large prospective study is needed to establish the incidence of this oft-missed complication, and to determine whether routine prophylactic anticoagulation is justified.

The optimal therapy of RAT has yet to be determined. Schwab *et al.* [15] suggested that removal of the catheter accompanied by three months of anticoagulation represents

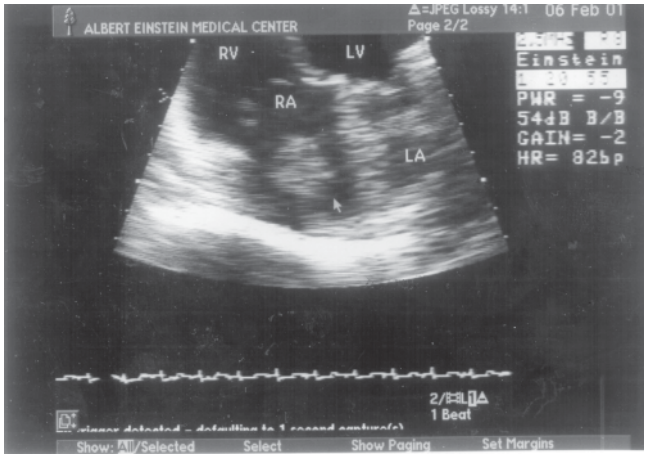

FIGURE 1 Trans-esophageal echocardiography showing the presence of thrombus in the right atrium of the heart (arrowhead). RA = right atrium; RV = right ventricle; LV = left ventricle; LA = left atrium.

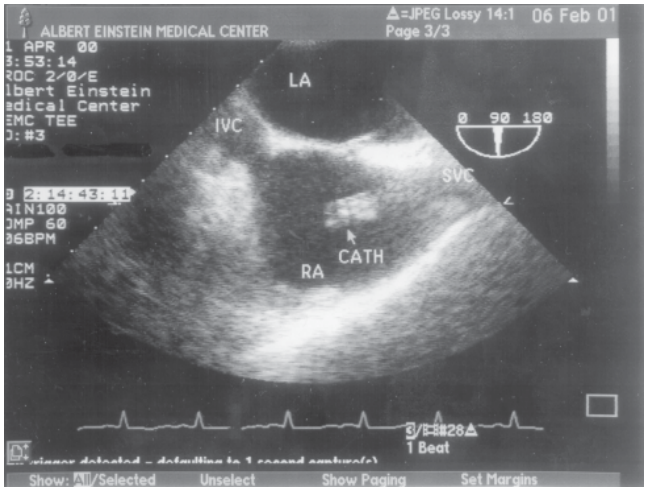

FIGURE 2 Trans-esophageal echocardiography of the patient in Fig. 1 after 8 weeks of anticoagulation; the tip of the dialysis catheter is visible in the right atrium, which is free of thrombus. RA = right atrium; LA = left atrium; IVC = inferior vena cava; SVC = superior vena cava; CATH = tip of dialysis catheter.

adequate treatment. Case reports exist of successful chemical thrombolysis using urokinase and streptokinase in central venous catheter–related RAT in children receiving chemotherapy [16,17] and in pacemaker wire–related RAT in adults [18]. A case report of successful treatment of catheter-related right atrial and ventricular thrombus with tissue plasminogen activator [19] also exists. In early 1998, we attempted to dissolve RATs in 3 patients by using urokinase, but these attempts were unsuccessful. After failing urokinase, 1 patient had an attempted surgical thrombectomy. The patient died during the procedure. Domoto *et al.* [20] reported 2 cases of recurrent catheter tip thrombosis associated with permanent internal jugular vein hemodialysis catheters and concluded that anticoagulation did not prevent the recurrence of thrombosis. Kingdon *et al.* [5] reported that 4 of 5 patients had persistent atrial clot despite chronic anticoagulation. Our experience found that, with adequate anticoagulation, the thrombi dissolved and, once the catheters were removed, the patients remained free of clots (Fig. 2). The duration of anticoagulation and the need for prophylactic anticoagulation in all patients are uncertain. Whether all patients receiving dialysis via a tunneled catheter as permanent means of access need to be anticoagulated prophylactically is controversial.

Reed *et al.* [13] published autopsy findings that showed 17% of children with leukemia had catheter-related right atrial thrombi, but none of the deaths were related to the thrombi and no pulmonary emboli discovered. No large study reports the incidence of pulmonary embolism in patients with tunneled cuff dialysis catheters. However, Kingdon *et al.* [5] found that 60% of their dialysis patients ($n = 3$) with catheter-related right atrial thrombi suffered multiple episodes of pulmonary emboli and died from them, as late as 3 years after the diagnosis. This finding does not reflect our experience, where none of the patents had pulmonary embolism at the time of diagnosis and none of the patients had pulmonary embolism during the follow-up period.

The incidence of infection with septicemia associated with the tunneled cuff dialysis catheter varies between 0.25 infections and 1.0 infections per patient–year [21]. Catheter-related thrombosis and sepsis are closely associated. In a prospective study of patients in an intensive care unit with central venous catheters, Timsit *et al.* [22] found that the risk of sepsis is increased 2.6-fold when catheter-related thrombosis was present. In our report, 40% of the patients had documented bacteremia. The infection is easily treated with antibiotics. It is noteworthy that 2 patients ultimately died of septicemia at 49 and 118 weeks. Both patients were still receiving hemodialysis via the TC; however, neither patient had any residual atrial thrombus at the time of death.

Conclusion

Tunneled cuff dialysis catheter–associated right atrial thrombus is a recognized complication. No large study has established the incidence of this complication (as has occurred for indwelling central venous catheters used for parenteral feeding and chemotherapy, for example). At present, no accepted recommendation exists regarding diagnosis and treatment of the complication.

We found that TEE is the best diagnostic tool. Placement of the catheter tip external to the right atrium did not prevent RAT, as most of the clot originated in the SVC. The incidence of pulmonary embolism is not increased in association with RAT. Chronic anticoagulation successfully treated 90% of our patients, who then had no recurrence. Further large

studies are needed to establish the incidence of RAT, the need for screening, and the optimal form of treatment and prophylaxis.

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