Clinical Medicine

Catheter-Related Septic Central Venous Thrombosis—Current Therapeutic Options

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Central venous catheter-related infection and evidence for central venous thrombosis developed in five patients. On the basis of ongoing bacteremia after catheter removal and venographic confirmation, catheter-related septic central venous thrombosis (CR-SCVT) was confirmed. These patients were treated successfully with anticoagulation and antibiotics; none required surgical exploration or drainage.

CR-SCVT is a complication of modern venous access techniques and is easily confused with sepsis from other anatomic sites. Even when recognized antemortem, CR-SCVT carries an excessive morbidity and mortality. The therapy for this complication is not standardized, but catheter removal, anticoagulation and a prolonged course of antibiotics are appropriate initial therapy. Surgical vein ligation or excision are reserved for refractory sepsis or abscess formation.

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As complications of modern central venous access techniques, central venous thrombosis and catheter-related sepsis are individually well recognized.[1-5] The simultaneous occurrence of these two complications, catheter-related septic central venous thrombosis (CR-SCVT) is remarkably uncommon, with few well-documented cases in the literature and serious associated morbidity and mortality. Over a two-year period, we have treated five patients with proved CR-SCVT. In the present report we describe the peculiar problems associated with the diagnosis and treatment of this unusual disease.

Clinical Material

CR-SCVT is defined as the simultaneous occurrence of three findings: venographically proved thrombosis of the internal jugular, subclavian or brachiocephalic veins; central venous catheter infection, defined by positive catheter tip and peripheral blood cultures; ongoing bacteremia after catheter removal.[6]

Five patients considered to have CR-SCVT were treated by us between September 1983 and September 1985. Their clinical summaries are presented in Table 1. Catheter infection became evident 13.4 days after placement (mean; range 6 to 30 days). All patients had fever and leukocytosis. Signs of sepsis were described as moderate to severe in three patients, with tachycardia, mild hypotension and cardiac rhythm disturbances. Local signs of venous thrombosis (aspiration of thrombus from the catheter; ipsilateral neck, chest wall or upper extremity edema) were present in all cases, as was venographic confirmation of thrombosis. Cultures of peripheral blood and catheter tips yielded *Staphylococcus aureus* in all cases, and bacteremia continued after the catheter was removed. Endocarditis was excluded in all patients, based on the absence of new cardiac murmurs, the absence of evidence for peripheral microembolization or vasculitis and normal echocardiography.

Radiographic Signs

Venograms were abnormal in all instances, four with total venous thrombosis and one with a large nonocclusive mural thrombus in the subclavian vein (Figures 1 through 4). A perivenous phlegmon was shown by computed tomography at the level of thrombosis in two patients, one of whom also had mediastinal widening on a standard chest radiograph.

Treatment and Response

All patients received antibiotics intravenously and anticoagulation. Continuous heparin infusion was administered

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ABBREVIATIONS USED IN TEXT

CR-SCVT = catheter-related septic central venous thrombosis
CT = computed tomography
MLC = multiple-lumen [central venous] catheter

in a dosage sufficient to maintain the partial thromboplastin time twice control. Anticoagulation was continued for ten days in four cases, a time period during which there was clinical or radiographic evidence for cessation of active thrombosis. Nonocclusive thrombosis was present in one patient (case 3) with Wegener granulomatosis, renal failure and hemoptysis, an absolute contraindication to full continuous anticoagulation. He received thrice-a-week systemic anticoagulation with heparin during hemodialysis. All patients sur-

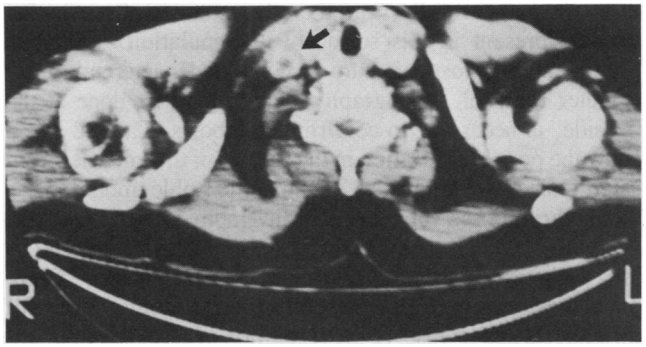

Figure 1.—An intraluminal thrombus in case 1: Computed tomography of the upper mediastinum, with radiographic contrast, shows thrombus **(arrow)** in the right internal jugular-brachiocephalic vein segment.

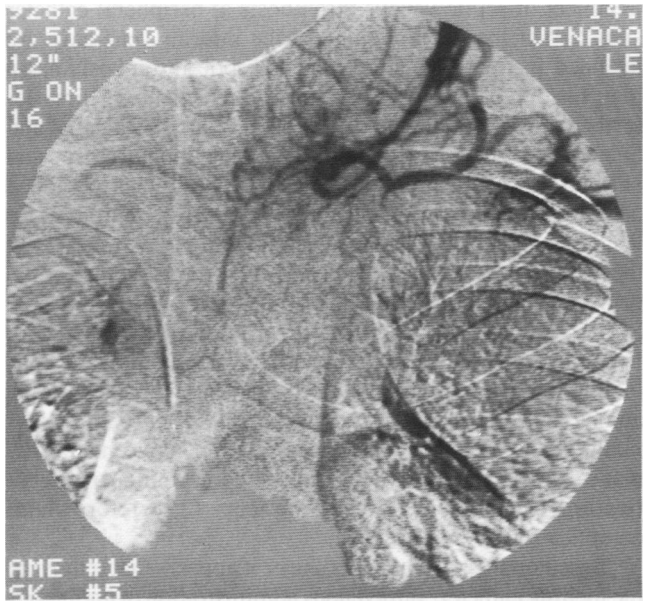

Figure 2.—Total venous occlusion in case 2: A digital subtraction venogram shows left subclavian, jugular and brachiocephalic venous occlusion.

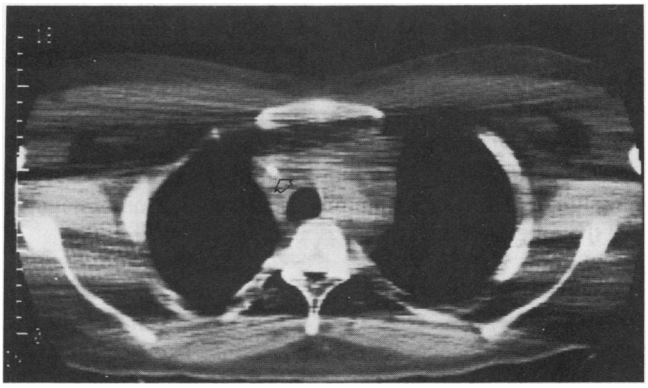

Figure 3.—A mediastinal phlegmon in case 2: Computed tomography of the upper mediastinum shows the mediastinal widening and effacement of structural borders typical of a mediastinal phlegmon from catheter-related septic central venous thrombosis. The arrow marks the position of a right internal jugular central venous catheter. Bony artifact is present.

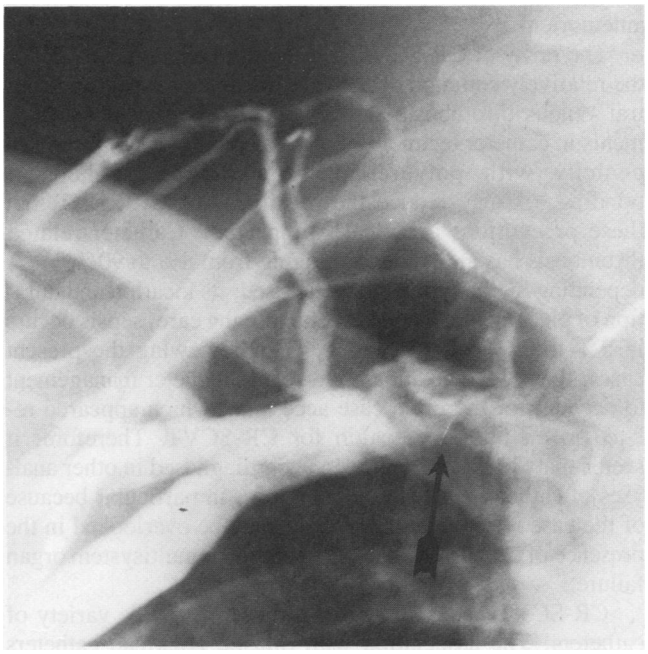

Figure 4.—A sleeve thrombus in case 3: A right upper extremity venogram shows a sleeve thrombus **(arrow)** at the junction of the subclavian and internal jugular veins.

TABLE 1.—*Confirmed Cases of Catheter-Related Septic Central Venous Thrombosis—Present Series*

Patient	*Age*	*Sex*	*Underlying Disease*	*Type of Catheter*	*Interval: Placement to Infection, Days*
1	72	F	Pancreatitis	Pulmonary artery, introducer sheath, internal jugular	6
2	26	M	Testicular carcinoma	Hickman Silastic subclavian	30
3	34	M	Wegener granulomatosis	Subclavian dialysis catheter	14
4	20	M	Multiple trauma	Single lumen subclavian	11
5	34	F	AIDS	Multiple-lumen internal jugular	6

AIDS = acquired immunodeficiency syndrome

vived without residual symptoms of thrombosis. Although pulmonary angiograms or lung scans were not done, there was no clinical evidence of pulmonary embolism in any patient. After the acute thrombosis resolved, there were no late sequelae due to venous hypertension in any patient.

Antistaphylococcal agents were selected on the basis of sensitivity testing and were administered for four to six weeks. In case 1, a two-week course of nafcillin given without anticoagulation was followed by recurrent bacteremia and clinically active thrombosis with tenderness, erythema and edema in the neck ipsilateral to the site of catheterization. Although antibiotic therapy was restarted at the recurrence of fever, it was only after the addition of heparin that the process abated.

Discussion

Strictly defined, CR-SCVT is proved thrombosis of the jugular, subclavian or innominate veins, catheter infection and continued bacteremia after catheter removal.[6] CR-SCVT must be differentiated from simple catheter contamination without thrombosis, exit-site sepsis, skin tunnel infection and infusion fluid sepsis. In an exhaustive analysis of reported catheter complications, including all types of central venous catheters currently available, we have been able to find only 32 confirmed and 5 probable cases of CR-SCVT diagnosed antemortem.[1-3,6-13]

The rarity of CR-SCVT is difficult to explain, in view of the relatively common occurrence of catheter sepsis and central venous thrombosis alone. Some of the recent developments in catheter technology, such as reductions in thrombogenicity with polyurethane construction or heparin bonding,[6,14] may reduce the possibility of CR-SCVT, but these precautions are clearly imperfect. Catheter-related thrombosis has an incidence ranging from 8% to 90%,[2,15-18] depending on the type of catheter used, its location and duration of placement. Despite careful nursing care, sepsis occurs in 3% to 21% of catheters.[4,5,19] In reviewing the present cases, there were no apparent errors in catheter management to account for the rapid case accession, which appeared related to an intensive search for CR-SCVT. Therefore, it seems that CR-SCVT has been underdiagnosed in other analyses of catheter-related complications, in particular because of the ease with which CR-SCVT may be overlooked in the presence of concurrent sources of sepsis or multisystem organ failure.

CR-SCVT occurred during the use of a wide variety of catheters. The association with Silastic Hickman catheters (case 2) has been described previously.[6] The associations with a subclavian dialysis catheter, a pulmonary artery catheter introducer sheath and a multiple-lumen central venous catheter (MLC) have not been previously described, and each catheter has peculiar risk factors for CR-SCVT. Introducer sheaths[20] are often left in place for long periods and, due to their bulkiness and the presence of a side-arm infusion port, are difficult to maintain with sterile dressings. They have rubber diaphragm partition mechanisms that may fail, allowing bacterial entry. Because early formation of a fibrin sheath around pulmonary artery catheters is well defined,[14] sheath thrombosis may be common, but no study has examined its incidence. Subclavian dialysis catheters are likewise stiff and difficult to maintain with a sterile technique when used in an outpatient setting.[21] Sepsis has been reported in as many as 14% of these catheters[22,23] and thrombosis in at least 2%.[21-23] CR-SCVT was not a complication in the one MLC series reported to date.[24] The risk factors for CR-SCVT in association with MLC include use in an intensive care unit, the wide variety of infusions administered and the duration of catheterization.[12]

A suspicion of CR-SCVT necessitates a departure from the ordinary management of catheter sepsis. Because the treatment of CR-SCVT is prolonged and costly, it should be differentiated carefully from the other sources of sepsis that may be present in this seriously ill population. The most prominent diagnostic feature is continued bacteremia after catheter removal. Venography, which may be done at the bedside, is necessary to confirm thrombosis. Cases 2 and 3 show the possible variation in the pattern of thrombosis, from a large sleeve thrombus to a mediastinal phlegmon about a totally thrombosed vein. Echocardiography is used to exclude a valvular lesion from endocarditis, which may be induced by long catheters on the tricuspid or pulmonary valves.[25] Computed tomography (CT) is a useful adjunct to define regions of thrombosis and to observe the resolution of associated inflammation.[10,26] CT is diagnostic for the development of an abscess in an area of mediastinal phlegmon.

Treatment of CR-SCVT is not standardized, in contrast to the generally accepted use of excision and antibiotics in the treatment of septic venous thrombosis at peripheral catheter sites.[27,28] If the pelvic veins and the inferior vena cava are included in review, central venous septic thrombosis has a long history of evolving treatment. Trendelenburg first described the use of vein ligation in 1906.[29] In 1947 Neuhof and Seley noted the effectiveness of local phlegmon drainage and antibiotics.[30] Mitre and Rotheran later described the added need for anticoagulation to achieve control of central septic venous thrombosis.[31] More recent attention has returned to the use of vein ligation, excision or thrombectomy as the primary treatment.[7] Only 13 of the 37 case reports of CR-SCVT noted above included a description of the treatment: five with antibiotics alone, six with anticoagulation and antibiotics and two with ligation or thrombectomy. The outcome among 22 determinant cases was 14 survivors (63%) and 8 fatalities (37%). There was no correlation between a particular treatment and survival. Notably, septic pulmonary embolization occurred in 4 of 16 patients (25%) for whom complications were described.

Based on the present experience, it appears that removing the inciting catheter, intravenous administration of antibiotics and anticoagulation are appropriate initial therapy. Heparin is important in halting the extension of septic thrombus and in preventing pulmonary embolization, which has been reported in as many as 32% of patients with central venous thrombosis.[1] Heparin should be given at full doses for a period long enough to achieve clinical resolution of the thrombotic process.[32] In the four cases in which thrombosis was associated with clinical signs, this resolution occurred over a one-week period. The choice of antibiotics is based on specific organism sensitivity testing. Because the organizing thrombus may be a privileged endovascular site with potentially reduced drug levels,[12] antibiotics should be administered in a quantity and for a duration similar to those for endocarditis. Insufficient antibiotic therapy may lead to recurrent bacter-

emia, as occurred in case 1. Surgical therapy is indicated after failure of an adequate course of antibiotics and anticoagulation. The presence of a phlegmon alone at the site of thrombosis is not an indication for exploration. Drainage is indicated after clinically unmistakable mediastinal abscess develops. Ligation and transcervical or transthoracic excision of central veins should be only rarely indicated, primarily in the presence of recurrent bacteremia and when a phlegmon fails to resolve.[7]

Catheter-related central septic venous thrombosis is a disorder that deserves increased attention in the modern era of invasive monitoring and intravenous therapy. Any patient with a catheter-related infection and persistent bacteremia after catheter removal should receive a full evaluation for CR-SCVT, including venography. If CR-SCVT is defined, anticoagulation and a prolonged course of antibiotics given intravenously are the preferred initial treatment.

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