Management of Septic Thrombosis of the Inferior Vena Cava Caused by *Candida*

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- Septic thrombosis of central veins is rarely diagnosed during life and nearly always proves fatal. We have recently successfully treated a patient with a 75% body surface burn in whom septic thrombosis of the inferior vena cava developed associated with high-grade candidemia as a complication of parenteral nutrition. Signs of venous thrombosis and candidemia persisted after catheter removal. Prompt and intensive therapy with amphotericin B, monitored by fungicidal assays of serum, resulted in cure. Generous hydration and directed supplementation of sodium bicarbonate permitted us to administer a large total dose of amphotericin over a relatively brief period of time with no nephrotoxic effect whatsoever. Septic central venous thrombosis mandates a pharmacologic approach to therapy similar to that used for infective endocarditis, with the addition of anticoagulation. Should sepsis prove refractory to this program of if pulmonary embolization occurs, operative intervention is indicated despite the high risks involved.

(Arch Surg 113:637-638, 1978)

**REPORT OF A CASE**

A 27-year-old man was admitted to the Burn Center of the University of Wisconsin (Madison) Hospitals after sustaining 75% second- and third-degree burns of the back, neck, trunk, and upper extremities that involved 75% body surface area. Initial fluid resuscitation was uneventful and the burns were treated with daily sucralfate and sulfadiazine silver cream. Total parenteral nutrition was initiated because of prolonged ileus and a persistent high caloric requirement.

Twenty-eight days after admission, he became septic from an intravenous line cannulating the left femoral vein and *Staphylococcus aureus* or *Enterococcus* grew from seven blood cultures. His temperature returned to normal after catheter removal and treatment with intravenous antibiotics (Fig 1).

Because the groin was among the few unburned areas, intravenous access was reestablished by percutaneous puncture of the opposite femoral vein, and total parenteral nutrition was resumed. Three days later, the patient again became febrile, with a WBC count elevation to 36,000/mm³. Over the succeeding days *C albicans* grew from eight blood cultures, the right groin became tender, and the right lower extremity became edematous (Fig 1). Seven days after insertion the caval catheter was removed and a fibrin clot was found tenaciously adherent to its tip. A Gram stain of this material (Fig 2) revealed sheets of blastospores and pseudohyphae consistent with *Candida*, and a heavy growth of *C albicans* grew from semiquantitative culture of the catheter tip. A serum test for *Candida* precipitins was negative but became strongly positive (1:32) during the next three weeks. Immediately after removal of the right femoral vein catheter, attempts to reestablish central venous access percutaneously via the left femoral vein were unsuccessful due to the inability to advance the catheter into the inferior vena cava (Fig 3).

Despite catheter removal, the candidemia continued as did high fever, rigors, and leukocytosis (Fig 1). Extensive clinical, microbiological, and roentgenologic studies for other sources of fungal or bacterial infection were unrevealing, and therapy with amphotericin...
Fig 1.—Clinical course of case of septic thrombosis of inferior vena cava caused by Candida albicans.

Fig 2.—Candida blastospores and pseudohyphae seen on Gram-stained smear of fibrin adherent to tip of vena caval catheter (× 400)

Fig 3.—Plain abdominal x-ray film showing inability to advance percutaneously inserted intravenous catheter into inferior vena cava because of mechanical obstruction.

Icin B was begun in low dosage (5 mg/day) but was rapidly increased to a maintenance dosage of 75 mg daily. The patient was at all times kept sufficiently hydrated to ensure a urine output of at least 4,000 ml/day and whenever drug-induced renal tubular acidosis or hypokalemia became evident, supplemental sodium bicarbonate or potassium chloride was provided. Anticoagulation was not used because of persistent occult blood in the stool.

Continued evaluation did not reveal any evidence of CNS or cardiac sources of infection. Two lung scans were normal for pulmonary emboli. The patient's fever gradually subsided and he regained his baseline mental status. Amphotericin therapy was discontinued after 30 days (total dosage, 1.6 gm) because of fever thought to be in part drug related. The serum creatinine level at this time was 0.9 mg/100 ml.

No intra-abdominal sources of infection were evident at the time an emergency subtotal gastrectomy was performed for a bleeding gastric ulcer. He was discharged after 4½ months of hospitalization and successful coverage of the wound by split-thickness skin grafts. Eighteen months later he shows no evidence of residual Candida infection or venous insufficiency of the lower extremities.

**COMMENT**

*Candida sepsis* is being seen increasingly in critically ill patients, most often in association with total parenteral nutrition through central venous catheters during treatment with broad-spectrum antibiotics and corticosteroids, and with cachexia, or prematurity. Popp and his co-workers described 26 severely burned children given total parenteral nutrition and found that 16 of 19 episodes of septicemia, half caused by *Candida* or other fungi, were traced to central venous catheters. Five children with fatal catheter-related candidiasis had septic thrombosis of the superior vena cava and endocarditis. All had extensive full-thickness burns that involved both subclavian areas and...
necessitated cannulation of the central circulation through peripheral veins or the burn wound.

Our patient had high-grade candidemia traced to septic thrombosis of the right femoral vein and inferior vena cava. Clinical signs of sepsis and positive blood cultures persisted despite removal of the implicated catheter. Attempts to re cannulate the inferior vena cava through the opposite groin were unsuccessful due to mechanical obstruction by caval thrombus. Since detectable pulmonary embolization had not occurred and it was thought that operative caval interruption would be very hazardous in a patient with sepsis who had a 75% burn, we elected a course of management similar to that used with infective endocarditis; ie, intensive, prolonged, microbicidal therapy.19 Intravenous amphotericin B was increased over a ten-day period to provide a daily dosage of 1.0 mg/kg/day and the drug was continued until a total dosage of 1.6 gm was attained. Sodium bicarbonate was given to enable the administration of so substantial a total dose over relatively brief period of time (39 days) with no decline whatsoever in his renal function. The work of Burgess and Birchall15 suggests that early therapy of reversible, drug-induced renal tubular acidosis can prevent progression of renal injury and reduction in the glomerular filtration rate. Fungicidal activity > 1:4 on all occasions tested confirmed an adequate antibiotic dosage.20 Venography was not initially performed since it would not have altered our decision to pursue nonoperative management. If septic pulmonary emboli had occurred, necessitating caval interruption, venography would then have been performed before operation.

Warden and his co-workers' recently reported 25 instances of septic thrombosis of the central veins in 129 burn patients that involved the superior vena cava (three cases) or the subclavian (nine cases) or the iliofemoral veins (13 cases), all associated with indwelling plastic catheters used for total parenteral nutrition, central venous pressure monitoring, or for conventional intravenous therapy. With the exception of two cases of septic subclavian vein thrombosis diagnosed antemortem, all were discovered only at autopsy. Septic pulmonary emboli occurred in one third of the cases in addition to the expected clinical picture of refractory sepsis typically seen in septic thrombophlebitis of peripheral veins.16-19

Septic thrombosis of the iliofemoral, distal subclavian veins, or the inferior vena cava below the renal veins can be successfully managed by antibiotics given for systemic effect and anticoagulation11 and if necessary, by surgical ligation and debridement of the clot.5,8 Surgery is indicated for septic pulmonary emboli or refractory sepsis occurring despite optimal medical therapy. Involvement of the proximal subclavian vein, superior vena cava, or proximal inferior vena cava usually must be managed with anticoagulants and high-dosage antibiotics alone. Surgical debridement of the infected clot might be considered as a last resort in individual cases, but no published experience exists to support or guide its use.

In view of the high mortality from Candida sepsis and particularly septic thrombosis of central veins, restricted use of plastic catheters is imperative. When they must be used, avoiding cannulation of lower extremity vessels, stringent attention to local asepsis, and limiting the duration of venous cannulation < 72 hours seem to be the most important measures to reduce the incidence of catheter-related sepsis in burn patients.23,26 Septic thrombosis of a central vein must always be considered when signs of sepsis persist after removal of a culture-positive central venous catheter, especially if signs of venous obstruction or pulmonary embolism are also present. We found in this case and have shown in a prospective study that semiquantitative culturing of catheter segments can provide further objective data establishing the presence of catheter-related infection, and possibly septic thrombophlebitis.

Nonproprietary Names and Trademarks of Drugs

Amphotericin B—Fungizone.
Sulfadiazine silver—Silverdine.

References