Case Reports

Catheter-Related Thrombophlebitis of the Superior Vena Cava Caused by *Candida glabrata*

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ALTHOUGH FUNGEMIA occurs frequently in patients with central venous catheters, fungal thrombophlebitis of the superior vena cava and other great veins appears to be a rare complication. Only a few cases are reported in the medical literature, virtually all caused by *Candida*.[1-3] In this report we describe a case of catheter-associated fungal thrombophlebitis of the great central veins caused by *Candida glabrata* (formerly, *Torulopsis glabrata*). It emphasizes the role of computed tomography in diagnosis and, in this case, the success of medical therapy alone in its management.

Report of a Case

The patient, a 59-year-old man with steroid-dependent chronic obstructive pulmonary disease, entered the hospital because for three weeks he had had lower abdominal pain and symptoms of hyperglycemia. Although he had no history of diabetes mellitus, his blood glucose level at that time was 575 mg per dl. Following several diagnostic studies, the patient was taken to surgery where a large abscess adjacent to a perforated colonic diverticulum was found. He underwent drainage of the abscess, segmental colectomy and creation of an end-colostomy with a mucous fistula. Culture of specimens from the abscess yielded only *Escherichia coli*. The patient's management also included 11 days of subclavian vein catheterization for intravenous hyperalimentation, an intravenous insulin drip for several days and broad-spectrum antimicrobial therapy for 10 days. Before entering the hospital the patient had been taking 5 mg of prednisone twice a day. During this hospital stay he received 300 mg of hydrocortisone per day intravenously in the perioperative periods with rapid tapers back to maintenance levels (25 mg hydrocortisone per day or 5 mg prednisone per day) thereafter.

Following his first operation the patient progressed satisfactorily until the 24th hospital day, when abdominal pain recurred and an enterocutaneous fistula was detected. A subclavian vein catheter was placed for a second time and intravenous hyperalimentation was resumed. Computed tomography of the abdomen after the patient had several episodes of fever showed a left lower quadrant fluid collection. Broad-spectrum antimicrobial therapy was restarted and the patient had surgical drainage of a large pelvic abscess and repair of three associated perforations of the small bowel. Culture of specimens of the abscess yielded only *Klebsiella oxytoca*.

From the time of the second operation on hospital day 42 until day 59, the patient's course was characterized by daily spiking fevers and accompanying systemic toxicity. Culture of a specimen of blood that had been drawn on the 39th hospital day was reported positive for *Candida glabrata* in the immediate postoperative period. Fungemia persisted—cultures of 24 blood specimens drawn on 15 different days between hospital days 39 and 59 were positive for this organism. Four of these blood cultures were also positive for coagulase-negative staphylococci.

Management of the bloodstream infection consisted of administering antimicrobial agents, changing central venous catheters and repeatedly searching for other foci of infection; none were ever identified. *C glabrata* was cultured in a specimen of drainage from the abdominal wound or associated

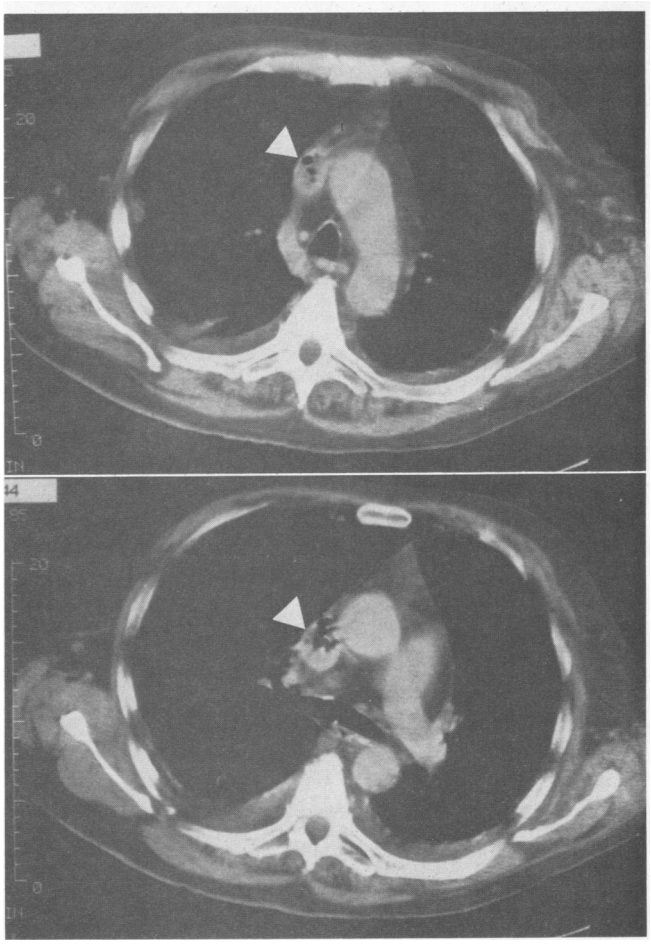

Figure 1.—Computed tomography done on the 59th hospital day, 50 seconds after contrast injection, shows, **top**, a low-density thrombus containing multiple gas bubbles in the superior vena cava **(arrow)** at the level of the aortic arch and, **bottom**, thrombus and extensive gas bubbles filling the lumen of the superior vena cava **(arrow)** at the level of the left pulmonary artery. (Other cuts revealed thrombus extending into the right atrium and subclavian veins.)

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drain sites on hospital days 24, 42, 48 and 58; these wounds were not infected at the time. The organism was not recovered from urine, sputum or abscess fluid. Amphotericin B therapy was begun on the 44th hospital day. The patient's systemic toxicity diminished somewhat, but fungemia persisted for another 15 days. Vancomycin therapy was initiated on the 49th hospital day and blood cultures rapidly became negative for staphylococci. Central lines, considered essential for hyperalimentation, were maintained in the left and right jugular veins throughout this period, though they were changed frequently and rotated from side to side in response to the continuing report of additional positive blood cultures. About half of the line changes were done over guide wires. Tips from the removed catheters were cultured three times during this period—on the 45th, 50th and 56th hospital days. The first culture was sterile, the second yielded more than 100 colonies of *C glabrata* alone and the third yielded more than 100 colonies of both *C glabrata* and coagulase-negative staphylococci.

On the 59th hospital day computed tomography of the thoracoabdominal region was carried out with contrast enhancement. This examination showed extensive thrombosis and associated gas formation extending from the entrance of the right atrium through the superior vena cava to both subclavian veins (Figure 1). Physical examination failed to disclose any signs of superior vena cava obstruction, but the radiologic findings, together with persistent fungemia, were interpreted as diagnostic for fungal thrombophlebitis of the great veins. Hyperalimentation was discontinued and all central venous catheters were removed permanently. Amphotericin B therapy, 50 mg every other day (about 0.3 mg per kg per day), was continued and heparin therapy was started. Echocardiography at this time did not show any vegetations on the patient's cardiac valves.

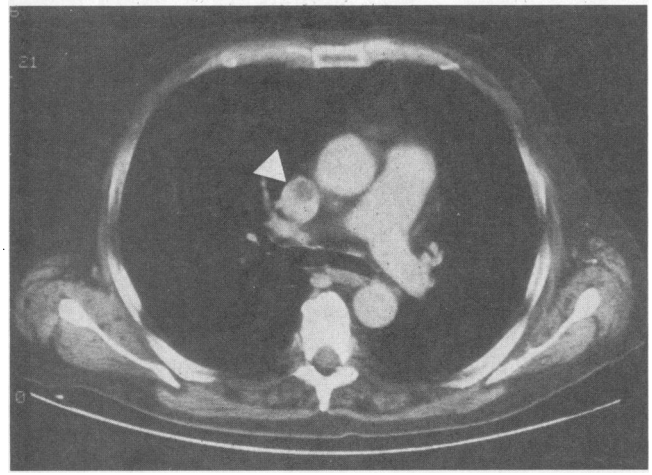

Figure 2.—Computed tomography with contrast enhancement done before discharge shows residual thrombus in the midportion of the superior vena cava **(arrow).** (The crescent-shaped low-density structure adjacent to the anterior wall of the ascending aorta is the superior pericardial recess.)

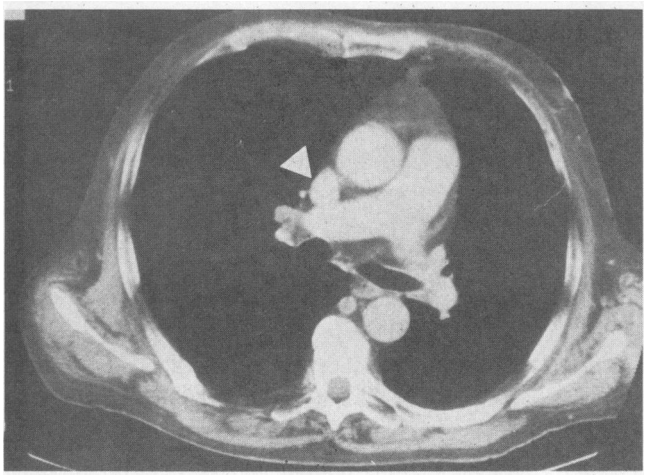

Figure 3.—Computed tomography with contrast enhancement done three months after discharge shows normal superior vena cava **(arrow)** at the level of the right pulmonary artery.

Following the changes made on the 59th hospital day, the patient's condition began to improve. His fever remitted, systemic toxicity resolved, blood cultures became negative and convalescence proceeded without complication. Amphotericin B therapy was continued until the 105th hospital day, for a total course of 1,675 mg (19.4 mg per kg). Anticoagulation was maintained with a regimen of warfarin sodium, which was ultimately administered for about six months. Computed tomography done before the patient's discharge on the 106th hospital day showed considerable improvement in the superior vena cava, though some clot remained (Figure 2).

The patient continued to do well after discharge and, in what is now six months of outpatient follow-up, he has shown no evidence of lingering or metastatic infection. Repeated examinations have failed to disclose any signs of endophthalmitis. A computed tomographic examination of his chest done about five months after the original one showed complete resolution of disease in the superior vena cava and other great veins (Figure 3).

Discussion

Serious nosocomial infections caused by *Candida glabrata* have occurred with increasing frequency in recent years. This yeast, which is smaller than other species of *Candida* and lacks mycelial forms,[4-6] inhabits a variety of environmental niches in addition to the stool, skin, oral cavity and vagina of healthy persons.[7] Although once considered relatively avirulent, during the past 15 years *C glabrata* has been recognized as an opportunistic pathogen in immunocompromised and debilitated patients. Our patient showed several risk factors associated with *C glabrata* infections: diabetes mellitus, corticosteroid therapy, a major operation, broad-spectrum antibiotic therapy, hyperalimentation and central venous catheterization. Other recognized risk factors include malignancy, transplantations, profound neutropenia, alcoholism and immunosuppressive or antineoplastic chemotherapy.[4,8] *C glabrata* may have entered the bloodstream of our patient through the bowel, by absorption or by traumatic injury related to a surgical procedure and perforations or through the skin at the site of one or more intravenous lines. These portals of entry and the urinary tract have received most attention in reported cases of fungemia.[9] Our patient had no evidence of urinary tract involvement, transient or otherwise.

Diagnosing fungal septic thrombosis is difficult, especially in the absence of endophthalmitis or localized edema indicating venous obstruction. Serologic tests, indium-labeled leukocyte scans and even blood or urine cultures are not reliable indicators of infected clot.[1] The presence of the previously mentioned risk factors, a persistent low-grade fever despite removal of intravenous lines and a deteriorating clin-

ical state are associated with serious *C glabrata* infections in contrast to transient catheter-related fungemia.[8]

In the absence of biopsy specimens from the superior vena cava or other involved veins, a diagnosis of fungal thrombophlebitis in our patient remains somewhat conjectural. From a clinical standpoint, however, the evidence for this diagnosis is compelling. First, our patient had persistently positive blood cultures for *C glabrata* over a period of 20 days despite more than two weeks of intravenous antifungal therapy and numerous replacements of his central venous catheters. These data strongly suggest the presence of a fixed intravascular focus of infection. No extravascular focus or evidence of endocarditis was ever detected. Second, the appearance of the superior vena cava and other great veins on computed tomography attested not only to the presence of extensive thrombosis but also to the likelihood of infection within the clot itself—microbial growth in the clot matrix is the most likely explanation for the observed gas bubbles. *C glabrata* metabolizes glucose to produce gas, and gas was observed throughout the entire length of clot. Schmitz and co-workers have reported a case of septic thrombophlebitis of the inferior vena cava due to toothpick perforation, with gas bubbles in the thrombotic material.[2] Finally, our patient's course paralleled that of other reported cases in which the evidence for fungal thrombophlebitis of the great veins was more direct.[1]

In reported cases the diagnosis of thrombophlebitis involving the superior vena cava and other great veins has usually been established by contrast venography.[1,10] Computed tomography with contrast can also be used to establish this diagnosis. This technique has been used to diagnose venous diseases in other vascular beds: inferior vena cava,[2] portal venous system[11] and jugular venous system.[12] Characteristic findings of thrombotic disease include enlargement of the vessel lumen, the demonstration of collateral vessels, enhancement of the vessel wall and the presence of a nonenhancing filling defect within the vessel lumen.[11,12] Ring enhancement, which is sometimes observed, is due to dilation of the vasa vasorum. Our patient's initial scan showed many of these findings plus gas bubbles in the clot, a finding probably due to microbial metabolism. Because computed tomography is much less invasive than venography, it may prove to be more useful for the initial evaluation of patients with possible thrombophlebitis of their great central veins. As our experience indicates, computed tomography can also be used to follow the course of the disease and the response to therapy even in the absence of clinical manifestations of venous obstruction.

The therapy for thrombophlebitis involving the great veins differs radically from that for thrombophlebitis of peripheral veins—surgical excision of the affected vein is considered mandatory in the latter condition,[13] especially when fungi are involved.[14] As our case shows, however, medical therapy alone may suffice for patients with infection of the great central veins,[10] even when fungal disease is present.[1] Prolonged courses of antimicrobial agents with or without concurrent anticoagulation therapy have been used successfully in most reported cases regardless of the cause. Removal of the venous catheter has also figured prominently in management.

Our patient's case resembles those of the eight patients with *Candida* thrombophlebitis of the great central veins associated with central catheters reported by Strinden and colleagues.[1] Our patient's risk factors and disease manifestations were similar, and, like six of their eight patients, he was cured with intensive medical therapy alone. This case report brings a unique species of *Candida* into the spectrum of causes of thrombophlebitis of the great central veins. Most important, it shows the value of computed tomography in diagnosis. This case also suggests that permanent catheter removal and anticoagulant therapy are needed in addition to antifungal therapy to cure this type of infection.

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Wound Botulism

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WOUND BOTULISM is a rare disease. During the past 11 years (1976 through 1986), 19 cases have been reported to the Centers for Disease Control (CDC) through their botulism surveillance program and requests for botulism antitoxin. These 19 cases of wound botulism occurred in 9 states: 8 in California, 3 in Washington, 2 in Texas and 1 each in Maryland, Pennsylvania, New York, Tennessee, Arizona and Wyoming (MacDonald and co-workers[1] and an oral communication January 16, 1987, with Andrew T. Pavia MD, CDC, Atlanta). Before 1976 (1943 to 1945), 15 cases of wound botulism had been reported, all associated with traumatic extremity injuries.[2] We report a case of wound botulism (Wyoming, 1986) that occurred in a young man after he sustained a puncture wound to his foot associated with a retained foreign body (wood splinter).

Report of a Case

The patient, a 21-year-old man with alcoholism and a history of intravenous (IV) abuse of cocaine, was brought to

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