

Candida Endocarditis Complicating Glucose Total Intravenous Nutrition

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A case of *Candida albicans* endocarditis is reported. The endocarditis occurred in a patient with a chronic illness who received intermittent glucose total intravenous nutrition for approximately 10 weeks. The patient developed severe aortic insufficiency with his valvular endocarditis and required emergency aortic valve replacement. Aggressive surgery and medical treatment appear to be the treatment of choice for these critically ill patients.

CANDIDA ENDOCARDITIS, although less common than bacterial endocarditis, carries a more serious prognosis. Medical treatment for this disease has not been satisfactory and mortality rates have remained high.⁴ Aggressive surgical treatment, on the other hand, has brought improved results over medical therapy.^{3,4} *Candida* endocarditis occurred in a patient following glucose total intravenous nutrition (TIN) and emergency aortic valve replacement was necessary to relieve heart failure.

Case Report

L.L., a 56-year-old male, was admitted 3-31-72, following treatment for perforated diverticulitis. Six weeks prior to admission the patient had developed left lower quadrant pain and was treated with a transverse colostomy and drainage of the perforation site. Postoperatively, a high output small bowel fistula developed through three separate suture tracts in the lower portion of the incision. On admission, the patient had a right subclavian catheter through which hypertonic glucose and an amino acid solution had been infused during the previous four weeks. Twenty-four hours following admission he was started on a low residue high nitrogen diet by mouth and the subclavian catheter was removed. During the next two weeks he continued to lose weight and drainage from the small bowel continued through the incision. On 4-18-72, a central venous catheter was positioned in the right atrium via the left basilic vein. Total intravenous nutri-

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tion was started using a solution of 25% glucose and 5% Travamin. The solution volume was serially increased to 3 liters per day.

On 4-30-72, he spiked a temperature to 102 F and this was associated with edema of the left arm and face. The central venous catheter was removed, intravenous penicillin started and enterococcus organisms were subsequently grown from the blood (Fig. 1). Three days later the temperature had returned to normal and glucose total intravenous nutrition was reinstated via a right subclavian catheter. During the subsequent period of infusion, he healed two of the three fistula sites, gained weight, and there was marked reduction in drainage from the remaining fistula site. On 5-20-72, he developed a shaking chill and spiked a temperature to 103 F. There was edema of the entire face and a catheter passed retrograde from the femoral vein revealed superior vena caval thrombosis on radiopaque injection (Fig. 2). The subclavian catheter was removed and the facial swelling subsided. On 5-30-72, the patient underwent sigmoid resection and resection of the small bowel fistula. Postoperatively, he developed a wound infection which resolved with open drainage. He continued to run a low grade temperature and was discharged on 6-16-72 on oral feedings.

On August 7, 1972, the patient was readmitted with pain, swelling, and coolness of the right hand. There was an axillary pulse but the remainder of the pulses distal to this region were absent. A grade 2 out of 6 diastolic murmur along the left sternal border was noted. A right subclavian arteriogram demonstrated an occlusion of the brachial artery (Fig. 3). Because of progressive symptoms, he underwent embolectomy of the brachial artery and improved inflow was established. No thrombotic material was recovered from the occlusion site. Postoperatively, the patient continued to have temperature elevations to 101 F each day. Repeated blood cultures did not grow any bacterial organisms, but one admission blood culture subsequently grew *Candida albicans*. This was considered a contaminant. Despite the negative blood cultures he was started on a ten-day course of intravenous Cloxacillin to treat a possible bacterial endocarditis. The daily temperature elevations remained despite therapy but the patient was not in overt heart failure, was ambulatory taking a regular diet, and in no distress. On 9-12-72, he underwent colostomy closure.

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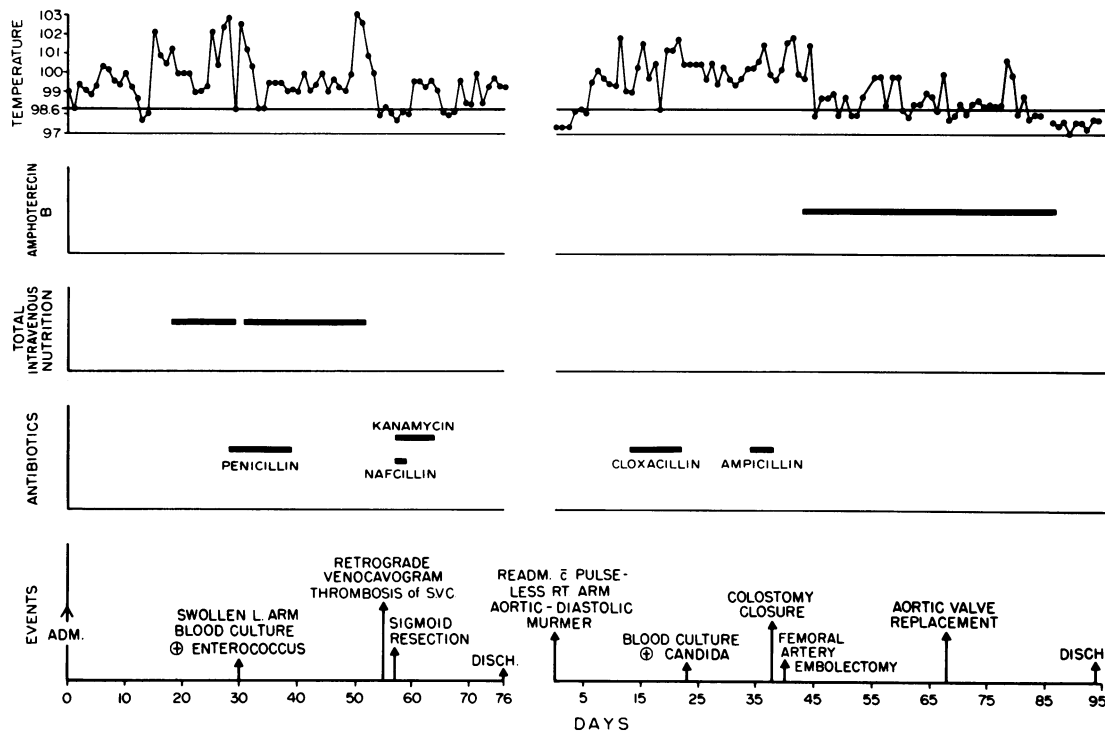


FIG. 1. The patient's temperature returned to normal after aortic valve replacement.

Two days later he sustained an embolus to his left femoral artery and underwent embolectomy. The emboli material grew *Candida albicans* and because of the return of two further positive blood cultures for *Candida albicans*, he was started on intravenous Amphotericin-B. Over an eight-day period the dose was gradually increased to 50 mg/day. Despite the Amphotericin therapy, he developed severe cardiac failure and an enlarging heart on chest x-ray. His aortic insufficiency murmur had become louder and it was felt that this was related to *Candida* endocarditis. Because of the obvious clinical diagnosis and the possibility of dislodging *Candida* vegetation, he did not undergo cardiac catheterization and on 10-13-72, his aortic valve was replaced with a model 1260 Starr-Edwards valve. At surgery, the entire left coronary artery leaflet had been destroyed with a heavy *Candida* overgrowth (Fig. 4). The area of the *Candida* infection was completely excised and there did not appear to be residual disease. The remaining heart valves were not explored. The ventricle was irrigated with an Amphotericin-B solution. Postoperatively, he was maintained on Amphotericin-B 50 mg/day for two weeks at which time therapy was discontinued. Subsequent blood cultures were negative and his temperature returned to normal. He was discharged on 11-8-72, and currently is asymptomatic eight months following aortic valve replacement.

Discussion

In a recent report from our institution, the most severe non-fatal complication in a series of patients treated with glucose TIN was aortic valve endocarditis.⁸ *Candida septicemia* has been a recurring complication in patients receiving hypertonic glucose solutions and the incidence in one series was as high as 16%.⁶ *Candida* endocarditis following glucose TIN to our knowledge, has not been reported. *Candida* septicemia occurs during glucose TIN probably because of contamination during the process

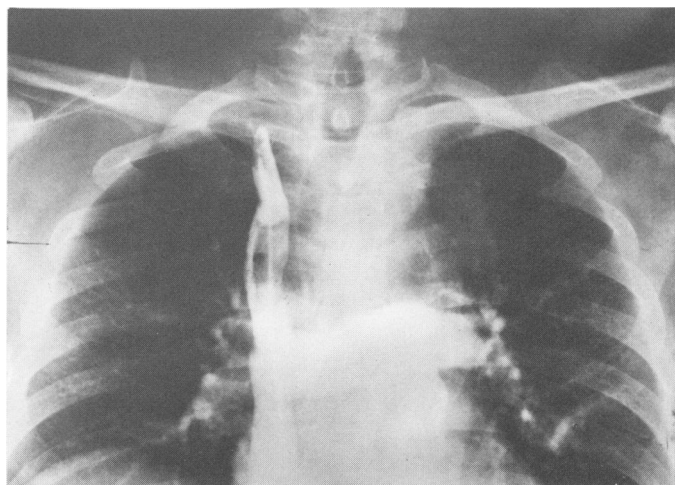


FIG. 2. Thrombus in the superior vena cava was demonstrated using a retrograde catheter.

of mixing the solutions or as a result of mycelial growth in the infusion tubing or at the catheter entrance site.⁷ The general clinical status of the patient is also of consideration since those patients who are on immunosuppressive agents, steroids, or severely debilitated, have a greater chance of developing fungal infections than otherwise normal patients who are receiving glucose TIN. The most important factor in preventing this complication is the mixing of the solution with proper sterile technique under laminar flow hoods and daily changes of all infusion tubing and sterile dressings.⁷ There has been some discussion whether filters might actually increase the incidence of *Candida* septicemia but this question

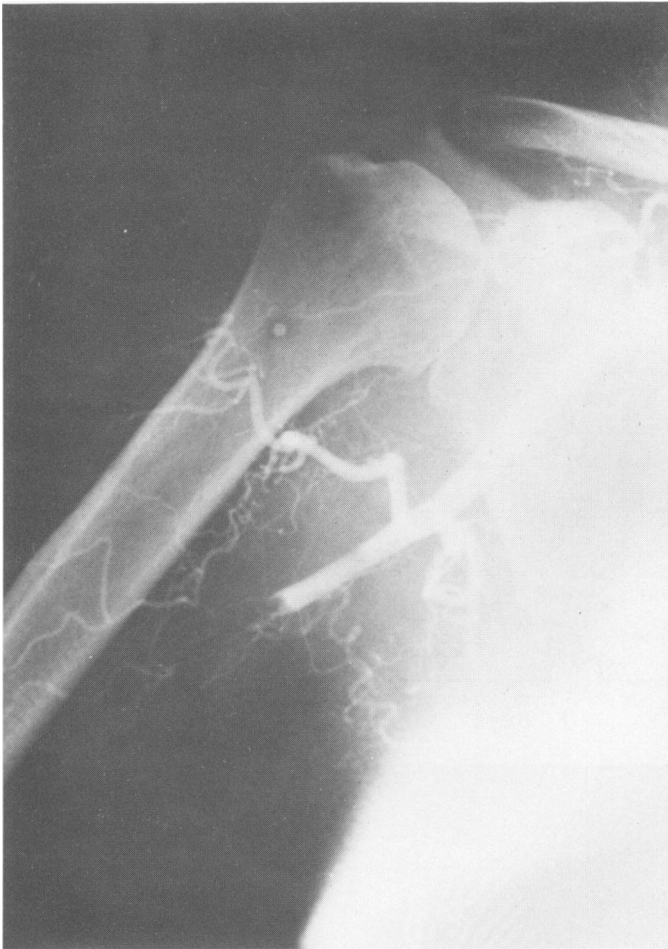


FIG. 3. Right subclavian arteriogram demonstrated an occlusion of the brachial artery.

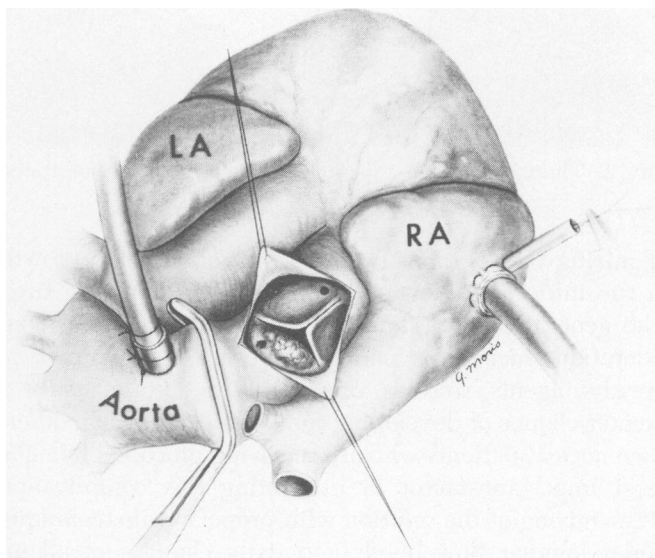


FIG. 4. The leaflet of the left coronary artery was completely destroyed by *Candida albicans*. A single cannula was used in the right atrium because of the previous caval thrombosis.

has not been resolved.¹ Others have recommended that Betadine or some iodine solution be used around the entrance site of the catheter through the skin, rather than topical antibiotic ointment, because iodine solutions are both bactericidal and fungicidal.⁷

Candida endocarditis was first described by Friedman in 1939. Kay *et al.*⁴ pointed out that the mortality rate for this disease based on reports from the literature up to 1968 were over 80% despite the advent of Amphotericin-B. Kay *et al.* also reported the first successful surgical treatment of this disease and later two other successful cases. Harris *et al.*³ recently reported five cases of *Candida* endocarditis with survival in four patients. Both Kay and Harris have emphasized the need for aggressive excision of all foci of the *Candida* organism during the open heart procedure. This has been carried to the extent of excising portions of the ventricular septum and producing heart block.³ Including our case, ten patients with *Candida* endocarditis treated with combined surgical and medical management have been reported, and eight of ten patients have survived and are free of residual disease.

The patients reported by Kay developed *Candida* endocarditis following treatment for bacterial endocarditis. In Harris' series, all the patients were heroin addicts who had developed combined bacterial and *Candida* endocarditis. In our patient, bacterial endocarditis did not seem to be a precursor to the development of fungal endocarditis. The patient had one positive bacterial blood culture during his first admission following a central venous catheter related septicemia. He was treated with a short course of antibiotics and subsequent blood cultures were negative. The pathological tissue excised at the time of surgery revealed evidence only of mycelial organisms and no smoldering or quiescent underlying bacterial endocarditis. Harris has emphasized the need for careful follow-up studies in these patients because recurrence can occur. He feels that the *Candida* precipitans test may be a more reliable means of following these patients than with blood cultures.

In our patient, the leaflet underlying the left coronary artery ostia had been entirely destroyed by a heavy overgrowth of *Candida* organisms. Because the patient had two previous systemic emboli, it was elected not to catheterize his heart for fear of dislodging further vegetations. Systemic emboli are a frequent manifestation of *Candida* endocarditis and should help in making the diagnosis.⁴ Our patient had two embolic episodes before the diagnosis was made. The thrombotic material obtained from the second embolectomy grew *Candida* organisms and this conclusively made the diagnosis. Harris has emphasized that these patients should not undergo cardiac catheterization prior to surgery. He recommends exploring all three valves at the time of

surgery to be sure that there are no residual vegetative foci involving either the mitral or tricuspid valves.

In terms of the prosthetic valve, we choose to use the Starr-Edwards Series 1260 valve which has a silastic ball and steel struts. Theoretically, the interstices in the cloth covered struts might act as potential sites for residual mycelia to lodge and propagate producing obstruction to the ball. The prosthesis itself was soaked in Amphotericin-B before insertion and the left ventricle was thoroughly irrigated with the same solution. Post-operatively, the patient should be maintained on therapy for a minimum of two to four weeks and followed closely for recurrence.

References

1. Brennan, M. F., Goldman, M. H., O'Connell, R. C., Kunds, R. B. and Moore, F. D.: Prolonged Parenteral Alimentation: Candida Growth and the Prevention of Candidemia by Amphotericin Instillation. *Ann. Surg.*, **176**:271, 1972.
2. Friedman, N. B. and Donaldson, L.: Chicago Pathological Society: Systemic Mycosis with Mycotic Endocarditis. *Arch. Path.*, **27**:394, 1939.
3. Harris, P. D., Yeoh, C. B., Breault, J., Meltzer, J. and Katz, S.: Fungal Endocarditis Secondary to Drug Addiction: Recent Concepts in Diagnosis and Therapy. *J. Thorac. Cardiovasc. Surg.*, **63**:980, 1972.
4. Kay, J. H., Bernstein, S., Tsuji, H. K., Redington, J. V., Milgram, M. and Brem, T.: Surgical Treatment of Candida Endocarditis. *JAMA*, **203**:621, 1968.
5. Kay, J. H., *et al.*: Surgical Cure of Candida Albicans Endocarditis with Open-heart Surgery. *N. Engl. J. Med.*, **264**:907, 1961.
6. Quie, P. G. and Curry, C. R.: Fungal Septicemia in Patients Receiving Parenteral Hyperalimentation. *N. Engl. J. Med.*, **285**:1221, 1971.
7. Symposium on Total Parenteral Nutrition. American Medical Association, Nashville, Tennessee. January 17-19, 1972, page 125.
8. Yeo, M. T., Gazzaniga, A. B., Bartlett, R. H. and Shobe, J. B.: Total Intravenous Nutrition: Experience with Fat Emulsions and Hypertonic Glucose. *Arch. Surg.*, **106**:792, 1973.