Cardiovascular complications of parenteral nutrition

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Summary: During a 3 year period, 1987–1989, we encountered three major complications associated with parenteral nutrition leading to congestive cardiac failure – acute beriberi, right atrial and superior vena caval thrombosis, and fungal endocarditis. Unrecognized, these are invariably fatal. Persistent vomiting from intestinal obstruction led to the development of thiamine deficiency in the patient with beriberi. Recurrent catheter tip sepsis probably accounted for thrombosis and endocarditis in the second and third cases, respectively. These conditions are preventable with careful attention to nutritional replenishment and aseptic technique. In patients with catheter-related sepsis early, repeated blood culture is of diagnostic value. Patients with *Staphylococcus aureus* catheter-associated bacteraemia require at least 4 weeks of appropriate antibiotic therapy. Recurrent sepsis, especially when associated with pulmonary embolic phenomena, is an indication for echocardiography.

Introduction

Increasing use of parenteral nutrition in the critically ill is associated with its attendant risks of infection and metabolic derangement. Despite this however, serious cardiovascular complications have seldom been reported! During 1987–1989 we studied 20 patients who underwent parenteral nutrition for longer than one month and developed problems associated with line sepsis. All patients had routine culture of the catheter tip and blood cultures, and were referred for cardiac assessment and echocardiography. Three patients who had serious cardiovascular complications are described in the following report. During this period 600 patients received parenteral nutrition giving an incidence of 0.5% for serious cardiac complications. Though rare, these complications are preventable and amenable to therapy.

Case 1

A 25 year old female presented with a 3 month history of epigastric pain and vomiting followed by abdominal distension. Signs of sub-acute small bowel obstruction were confirmed on a barium meal study. Initial serum electrolyte estimation revealed a metabolic alkalosis. She received intravenous potassium replacement and a standard

regimen of parenteral nutrition (TPN) was administered in preparation for laparotomy.

The patient continued vomiting one litre of bile-stained fluid daily for the next 10 days. She received 2,000 calories per day and added fluids, vitamins, trace elements and potassium supplements. Weekly serum electrolyte estimation showed normal levels of sodium, potassium and bicarbonate. After one month of TPN she suddenly developed acute dyspnoea followed by hypotension and oliguria. Arterial blood gas analysis revealed a severe metabolic acidosis. After resuscitation with freeze-dried plasma, dopamine and 500 ml sodium bicarbonate (4%), she remained acidotic and hypotensive with persistent hypoglycaemia. Signs of right-sided heart failure (raised neck veins, right ventricular gallop, oedema and hepatomegaly) developed over the next 48 hours. Central venous pressure monitoring revealed elevated right atrial pressures. A ventilation-perfusion scan was normal. Echocardiography revealed normal ventricular function with mild dilatation of the right heart chambers. In the absence of pulmonary embolism, uraemia and septicæmic shock, acute thiamine deficiency was considered as a cause of severe metabolic acidosis with right heart failure. Parenteral thiamine (100 mg i.v.) produced a dramatic response: she immediately became alert and responsive and the systolic blood pressure rose to 110 mmHg. The acidosis improved steadily; 8 hours later it was fully corrected. Her urine output increased to 3–5 litres daily over the next 5 days. Upon recovery she was submitted to surgery. Laparotomy revealed three

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strictures of the small bowel which were 'plastied', Histology revealed non-caseating granulomata. She was discharged on anti-tuberculosis therapy and at follow-up showed steady improvement with weight gain.

This patient received 2.4 mg thiamine weekly. Thiamine status was determined by the red cell transketolase assay (anthrone method). Addition of thiamine *in vitro* produced a 24.4% increment in transketolase activity (normal 0–14%) indicating a thiamine-deficient state.

Case 2

A 46 year old male was admitted with a one week history of vomiting, colicky abdominal pain and abdominal distension. Examination revealed signs of peritonitis. At laparotomy a large intra-peritoneal abscess was drained. Despite adequate drainage and aggressive antibiotic therapy he developed an entero-cutaneous fistula at the site of the laparotomy incision 8 days post-operatively. Parenteral nutrition was commenced because the fistula output increased steadily reaching one litre daily.

After 20 days of TPN the patient became tachypnoeic and complained of pain at the tips of his fingers and toes. He had a low grade pyrexia, and 2 days later the temperature rose to 38.5°C when splinter haemorrhages and vasculitic lesions appeared at the finger tips and the right limb became cold. Precordial examination revealed a holosystolic murmur of mitral regurgitation and signs of biventricular failure. The central venous catheter was removed and blood cultures were taken. Echocardiography showed a stenotic mitral valve with a large vegetation attached to the anterior mitral leaflet, confirming the diagnosis of infective endocarditis for which he was treated with penicillin and amikacin. In the ensuing 48 hours the spleen became palpable, haemorrhages were observed in the fundi and the right radial and dorsalis pedis pulses were totally lost. Four positive blood cultures for candida (non-albicans) was subsequently obtained and amphotericin B was added to the therapeutic regimen. Shortly thereafter all pulses in the left lower limb became impalpable. Valve surgery was not contemplated because of the extremely poor anaesthetic risk. The patient remained critically ill and succumbed from severe pulmonary oedema and septicaemia. Autopsy confirmed the clinical findings.

Case 3

After extensive bowel resection in February 1987 a 30 year old female received parenteral nutrition for

one month at peripheral hospital. She then became pyrexial and *Staphylococcus aureus* was isolated from the catheter tip and blood cultures. She was treated with parenteral cloxacillin and then referred to us. A Vygon catheter was inserted into the right subclavian vein and parenteral nutrition was continued. Four weeks later she again became pyrexial and was referred for echocardiography. A large thrombus was identified in the right atrium and it appeared to prolapse through the tricuspid valve orifice (Figure 1). Because of her poor clinical state surgical thrombectomy was not contemplated. She received heparin and antibiotics, and because of difficulty in obtaining venous access, her catheter was changed over a guidewire. Repeat echocardiography did not show any thrombus in the right atrium and she made a steady, but slow recovery. She was readmitted in July 1987 with *S. aureus* septicaemia that again responded to antibiotic therapy. In February 1988 she again developed a pyrexial illness with rigors and *S. epidermidis* was isolated on repeated blood cultures. Again she was treated and responded to antibiotic therapy.

Early in March 1988 she experienced pleuritic chest pain but the chest radiograph and ventilation–perfusion were normal. In May she was again admitted with rigors and cyanotic attacks. Repeat echocardiography showed a thrombus on the atrial side of the tricuspid valve. Blood culture yielded *Proteus mirabilis* and culture from the central line yielded *Candida albicans*. TPN was discontinued and she was treated with miconazole. Repeated attempts at venous access via the subclavian vein failed and she was subjected to venography which revealed bilateral subclavian vein thrombosis (Figure 2). Tests for coagulation profile, anti-thrombin III deficiency and anticardiolipin antibody were normal. A 'Portocath' was inserted into the azygos system and TPN recommenced. On 21

Figure 1 Case 3: two-dimensional echo showing large free-floating thrombus (arrow) within the right atrium.

Figure 2 Case 3: left forearm venogram showing complete blockage of the left axillary, and subclavian vein with an extensive collateral circulation that communicates with the paracervical venous plexus (straight arrows) and enters the azygos venous system (curved arrows).

July she suddenly became dyspnoeic and died. Consent for autopsy was not obtained.

Discussion

Cardiac beriberi classically produces a high output state with preserved ventricular function. In the advanced stages heart failure, hypotension and severe metabolic acidosis typify the situation and may confound the clinician. The first patient developed severe metabolic acidosis with signs of right ventricular failure. Echocardiography showed normal left ventricular function and mild right ventricular dilatation that was not due to pulmonary hypertension. It also excluded pericardial tamponade as a cause of hypotension with distended neck veins, pointing to a metabolic cause for cardiovascular collapse.

Acute pernicious (Shoshin) beriberi has previously been reported in patients undergoing parenteral nutrition.¹⁻³ It has been described even during vitamin replacement therapy. Recently as many as 20% of patients receiving nutritional

support in an intensive care unit were shown to be thiamine deficient.⁴ Our patient's course explains the development of a thiamine-deficient state in such cases. She had depleted thiamine reserves because of poor intake and persistent vomiting. High bowel obstruction precluded absorption of what little vitamin was available. The hypercatabolic state associated with chronic infection, together with the caloric load of TPN (aggravated by dextrose administration for hypoglycaemia), increased the demand for thiamine.⁴ Thus, while the recommended daily allowance for thiamine is 0.5 mg/1000 kcal, requirements in parenterally fed patients will be much higher. We therefore recommend that an initial bolus of 100 mg be administered at the start of parenteral nutrition to replenish depleted stores, especially in alcoholic patients and those with a protracted history of gastrointestinal symptoms. The recommended maintenance dose is 3-5 mg daily in patients receiving parenteral nutrition.⁴ A deficiency state should be suspected and treated empirically in any patient who develops severe metabolic acidosis with hypotension and signs of heart failure during TPN.

Our remaining two patients developed serious catheter-related complications against a background of persistent sepsis; they illustrate the importance of early, repeated blood culture in the management of catheter-related sepsis. In patients with central lines, the development of pyrexia, leucocytosis or local inflammation at the site of insertion is an indication for blood culture, one sample obtained from the catheter and another from a peripheral vein. Early detection of positive cultures will permit appropriate therapy and avert the development of endocarditis with valve disruption and its sequelae. A prospective study has shown that 8-9% of patients with *S. aureus* catheter association bacteraemia will develop endocarditis or metastatic abscess after intravenous antibiotic treatment for 2 weeks.⁵ A further 2 weeks of antibiotic therapy has therefore been recommended to help avoid these dreaded complications. The presence of prolonged bacteraemia, suppurative thrombophlebitis at the catheter site, serious underlying systemic disease or the development of signs of infective endocarditis dictate continuation of intravenous medication for a full 4-6 week period.

Although endocarditis is a recognized complication of right heart catheterization⁶ it has only rarely been reported with permanent indwelling catheters,⁷ probably due to insertion under ideal, aseptic conditions. The usual clinical picture⁸ is infection confined to the tricuspid valve, characterized by recurrent pulmonary embolic episodes which manifest as reappearing lung infiltrates with/without pleural effusion. Cardiac murmurs are

either unremarkable or even absent and signs of right heart failure occur only late in the illness. Recently^{9,10} three cases of endocarditis were described which involved both the tricuspid and aortic valves, all with a fatal outcome. In our patient the mitral valve was the site of infection, probably due to previous valvular damage from rheumatic heart disease. The fungal infection was also probably related to catheter sepsis. The incidence of catheter sepsis due to fungal infection has declined in recent years.¹¹ Systemic infection is rare^{12,13} and responds poorly to therapy; candidal lung abscess¹⁴ and endophthalmitis¹⁵ have also been reported in patients on TPN. Our second patient is probably the first reported case of endocarditis due to this organism developing in an adult patient on parenteral nutrition.

In the third patient echocardiography revealed an intracardiac thrombus shortly after she developed staphylococcal septicaemia. Thereafter she had repeated episodes of sepsis with the subsequent development of subclavian vein and superior vena caval thrombosis, a complication that has hitherto been described in infants receiving TPN.¹⁶ Intracardiac thrombi have also been reported with the use of central venous catheters in paediatric patients.¹⁷⁻¹⁹ More recently, two cases have been reported in adults,¹⁰ one of whom presented with a pulmonary embolus. It has been said that routine screening of patients undergoing TPN may yield a greater number of patients developing right atrial thrombi.¹⁰ While this is probably true it is not clear whether all such patients should be offered surgery or any form of treatment at all. In our patient thrombus formation and propagation seems to have occurred in a setting of long-standing and inadequately treated sepsis. The isolated reports to date suggest that these complications are rare and echocardiography is of value only when persistent complications prevail.

In patients with suspected catheter tip thrombosis right atrial thrombi should be excluded by

echocardiography prior to removal of the catheter. Centrally placed catheters should not be replaced using a guidewire. Not only may this introduce sepsis but thrombi may become dislodged leading to embolic phenomena during replacement. The management of intracardiac thrombi presents a dilemma since resolution of the thrombus has been achieved with anticoagulant or thrombolytic therapy; even spontaneous resolution has been documented.⁹ The role of surgery is less clear. Prompt antibiotic therapy and fibrinolytic agents currently seem to be the most practical and effective form of therapy. The catheter should be removed unless it is attached to the thrombus. Surgical removal is required in cases which fail to respond to medical therapy or for large masses at risk of embolism, or occlusion of the tricuspid valve orifice. Small, stable thrombi should probably be left alone. In patients with right-sided endocarditis persistent sepsis, despite adequate antibiotic therapy, constitutes an indication for surgery.⁸

In conclusion, we have described three patients who developed heart failure or different aetiologies while receiving TPN. Echocardiography is of value in elucidating the cause for heart failure. In the setting of metabolic acidosis, empirical treatment with thiamine is mandatory. Close observation and early, repeated blood culture are the mainstay in the diagnosis and management of catheter-related sepsis. In uncomplicated *S. aureus* catheter-associated bacteraemia appropriate antibiotic therapy should be administered intravenously for 2 weeks followed by a further 2 weeks of oral medication. Our limited experience indicates that two-dimensional echocardiography should be performed in patients receiving TPN when catheter sepsis is recurrent, or when infection cannot be eradicated. It is clearly indicated when catheter sepsis is associated with cardiorespiratory phenomena such as the development of a new murmur or pulmonary infiltrates, even in the absence of signs of heart failure.

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