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# *Aspergillus* Pancarditis and Cardiac Arrest during Anesthesia

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Endocarditis, which may progress to myocardial and pericardial involvement (pancarditis), may be a slow, insidious disease with few clinical signs and symptoms. It may also be seen with clinical features that mimic other disease states, including renal failure. Clinical features common to endocarditis and renal failure include lassitude, anemia, embolic phenomena, heart murmurs, fever, and elevated white cell counts. We present a case of *Aspergillus* pancarditis associated with end stage nephrosclerosis, first, because it illustrates the difficulty in establishing the antemortem diagnosis of this type of endocarditis, and second, because repeated general anesthetics were associated with severe cardiovascular instability, including cardiac arrest. A relationship between intraanesthetic cardiovascular instability and mycotic pancarditis has not been previously reported.

## Case Report

A 43-year-old, 60.5-kg Puerto Rican man had been treated with hemodialysis for end stage nephrosclerosis for the past 4 years. Associated renal hypertension was treated with hydralazine, hydrochlorothiazide, methyldopa, propranolol, and clonidine, which maintained his blood pressure (BP) in the range of 160 to 212/90 torr. Electrocardiogram (ECG) at that time showed left ventricular hypertrophy with strain. Chest x-ray revealed cardiomegaly with clear lung fields. The only significant physical finding was a grade 2/6 systolic ejection murmur.

The patient was admitted 2 months before his death after sustaining a cardiac arrest possibly due to air or thrombotic emboli during hemodialysis. He regained consciousness after cardiopulmonary resuscitation.

The patient was readmitted 1 month later for cadaveric renal transplant. He had undergone hemodialysis uneventfully 2 days previously and preoperative hemoglobin was 10.9 g/100 ml, potassium 5.1 meq/L, and blood urea nitrogen 72 mg/100 ml. Blood pressure was 160/90 torr and heart rate (HR) and respirations were 100 beats per minute and 20 to 25/min, respectively, before induction of anesthesia with diazepam, meperidine, and thiopental. After succinylcholine was given to facilitate endotracheal intubation, BP and HR decreased to 100/40 torr and 40 beats per minute, respectively. Atropine and ephedrine had no effect on these vital signs. An arterial blood sample obtained during administration of 2 L/min of $O_2$ and 4 L/min of $N_2O$ revealed: $P_{O_2}$, 164 torr; $P_{CO_2}$, 50 torr; pH 7.13; base deficit (BD), 11.8 meq/L; sodium, 137 meq/L and potassium, 4.6 meq/L. Intravenous injection of sodium bicarbonate (88 meq) corrected the hypotension and bradycardia and improved the blood gas status. Anesthesia was maintained with meperidine, $N_2O$, and $O_2$ with *d*-tubocurarine (dTc) for relaxation. Azathioprine and methylprednisolone were given to decrease rejection of the kidney allograft. Reversal of residual neuromuscular blockade was accomplished with atropine and pyridostigmine; the patient was extubated and answered questions.

Approximately 10 minutes after extubation he suddenly became apneic and unresponsive with unobtainable BP and a sinus bradycardia of 40 beats per minute. Reintubation, ventilation with oxygen, and external cardiac massage were performed. Arterial blood gas tensions and serum electrolyte levels with an $F_{IO_2}$ of 1.0 were: $P_{O_2}$, 209 torr; $P_{CO_2}$, 51 torr; pH 7.14; BD, 11.5 meq/L; sodium, 146 meq/L; and potassium, 4.36 meq/L. Vital signs returned to normal after the intravenous administration of 88 meq of $NaHCO_3$. Mechanical ventilation was continued for the next several hours, during which time the patient gradually became more responsive. Following extubation arterial blood gas tensions and serum electrolyte levels with an $F_{IO_2}$ of 0.4 were: $P_{O_2}$, 130 torr; $P_{CO_2}$, 37 torr; pH 7.4; BD, 2 meq/L; sodium, 139 meq/L; and potassium, 3.7 meq/L.

During the next 19 postoperative days the patient remained cardiovascularly stable. He then underwent exploratory laparotomy because of ureteral obstruction with hydronephrosis. BP was 190/90 torr and HR was 80 beats per minute before anesthesia. Intravenous glycopyrrolate (0.2 mg) was given before induction of anesthesia with thiopental; endotracheal intubation was facilitated with dTc. Anesthesia was maintained with halothane in $N_2O$ and $O_2$. Reimplantation of an obstructed ureter into the bladder and a ureteronephrostomy were performed. The anesthetic course was uneventful. Postoperative vital signs were stable and the patient was awake and responsive.

Three hours after surgery his blood pressure decreased

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to 90/60 torr but responded to intravenous administration of plasma protein fraction. Ten hours after surgery, reexploration was necessary because his abdominal incisions were draining urine, with minimal drainage from the Foley catheter and nephrostomy tube. Before anesthesia for this procedure the patient was lethargic. This finding was attributed to meperidine and phenergan given for management of postoperative pain. Glycopyrrolate and 3 mg of dTc were given intravenously before induction of anesthesia with thiopental; endotracheal intubation was facilitated with succinylcholine. No other muscle relaxants were used during the procedure and anesthesia was maintained with $N_2O$ and $O_2$. The transplanted kidney was removed because of unrepairable leakage around the nephrostomy site. Approximately 40 minutes after the skin incision had been made (15 minutes after nephrectomy) the patient had a sudden unexplained decrease in BP to 60/30 torr with a decrease in HR (sinus bradycardia) to 40 beats per minute followed within a few seconds by asystole. Cardiopulmonary resuscitation and atropine, 0.6 mg, restored the BP to 190/120 torr and HR to 100 beats per minute. No sodium bicarbonate was administered at this time. After resuscitation arterial blood gas tensions with an $F_{IO_2}$ of 1.0 were: $P_{O_2}$, 114 torr; $P_{CO_2}$, 40 torr; pH 7.25; and BD, 9 meq/L. Over the next 6 hours mechanical ventilation was continued. He gradually recovered consciousness and was extubated. Arterial blood gas tensions following extubation with an $F_{IO_2}$ of 0.4 were: $P_{O_2}$, 136 torr; $P_{CO_2}$, 34 torr; pH 7.35; and BD, 6 meq/L.

Azathioprine was discontinued and the amount of steroids administered was gradually decreased. Leukocytosis that had been present since the transplantation gradually decreased. In the days following nephrectomy the patient developed intermittent elevations of temperature to 38.3 C, decreases in BP from 170 to 200/100 to 110 to 110 to 120/70 torr without associated bradycardia, and increasing lethargy. On the 3rd day after nephrectomy, ticarcillin and oxacillin were started because of a *Pseudomonas* wound infection and a right upper lobe infiltrate. On the 4th day after nephrectomy-diminished heart sounds suggested the possibility of pericarditis with pericardial effusion. At this point massive melena caused the hematocrit level to decrease to 11%. Duodenoscopy revealed a bleeding peptic ulcer.

The patient was brought to the operating room for exploratory laparotomy with a BP of 140/90 torr and HR of 90 beats per minute. After preoxygenation and pretreatment with dTc, anesthesia was induced with thiopental; succinylcholine was used to facilitate endotracheal intubation. Anesthesia was maintained with $N_2O$ and $O_2$. About 5 minutes after the skin incision had been made, hypotension to 80/50 torr and bradycardia to 30 beats per minute that was unresponsive to atropine developed. Ephedrine and sodium bicarbonate intravenously, together with compression of the abdominal aorta, increased BP to 120/80 torr and HR to 100 beats per minute. Hypovolemia was presumed to be the cause of this episode and packed red blood cells were rapidly transfused while the bleeding from the ulcer was controlled. Vital signs remained stable for the next 30 minutes when suddenly another episode of hypotension to 60/30 torr and sinus bradycardia to 30 beats per minute occurred which was unresponsive to atropine and ephedrine. An intravenous infusion of dopamine and the intravenous administration of sodium bicarbonate restored the BP to 160/100 torr and HR to 90 to 110 beats per minute. An arterial blood sample at a time when the $F_{IO_2}$ was 1.0 showed the following: $P_{O_2}$, 55 torr; $P_{CO_2}$, 49 torr; pH 7.28; and BD, 3.6 meq/L. The dopamine was gradually discontinued over the next 20 minutes. Subsequent arterial blood samples showed gradual improvement in $Pa_{O_2}$ and $Pa_{CO_2}$. Vagotomy and pyloroplasty were performed and a bleeding duodenal ulcer ligated.

After surgery, with mechanical ventilation and an $F_{IO_2}$ of 0.3, arterial blood gas tensions were: $P_{O_2}$, 73 torr; $P_{CO_2}$, 41 torr; pH 7.39; and BD, 0 meq/L. He was extubated a few hours later and remained alert with stable BP and HR and a postoperative hematocrit level of 37%. Arterial blood gas tensions with an $F_{IO_2}$ of 0.35 by face tent were: $P_{O_2}$, 64 torr; $P_{CO_2}$, 36 torr; pH 7.51; and BD, 1 meq/L. There was now a three-component pericardial friction rub which obscured the previously noted murmur; inspiratory wheezes and diffuse rhonchi were also present. A diagnosis was made of uremic pericarditis exacerbated by withdrawal of steroids.

On the 3rd postoperative day the patient was pyrexic and during hemodialysis suddenly became confused, tachypneic, and hypotensive. Endotracheal intubation was followed by ventricular tachycardia. Defibrillation and atropine resulted in a BP of 120/80 torr and in sinus tachycardia. Serum electrolyte levels, hematocrit, and arterial blood gas tensions during mechanical ventilation with an $F_{IO_2}$ of 0.3 were unremarkable. ECG showed decreased voltage in all leads. Approximately 10 hours later the patient's systolic BP suddenly decreased to 70 torr, followed by episodes of ventricular fibrillation and tachycardia recalcitrant both to numerous attempts at defibrillation and to antiarrhythmic drugs. Pericardiocentesis was attempted during resuscitation without success before the patient was declared dead.

Postmortem examination revealed pancarditis with myocardial and pulmonary abscesses which on culture grew out *Aspergillus fumigatus*. The Figures show the myocardial involvement by this organism.

## Discussion

Infective endocarditis can cause cardiac dysrhythmias and arrests (1–4). Mycotic endocarditis as a cause of cardiac dysrhythmias and arrest in association with anesthesia has, however, not been previously reported.

Although mycotic endocarditis has been reported in drug addicts (5–7) and in patients without predisposing causes (8), it is perhaps most frequently observed in patients receiving antibiotics and/or steroids, in patients undergoing open heart surgery, and

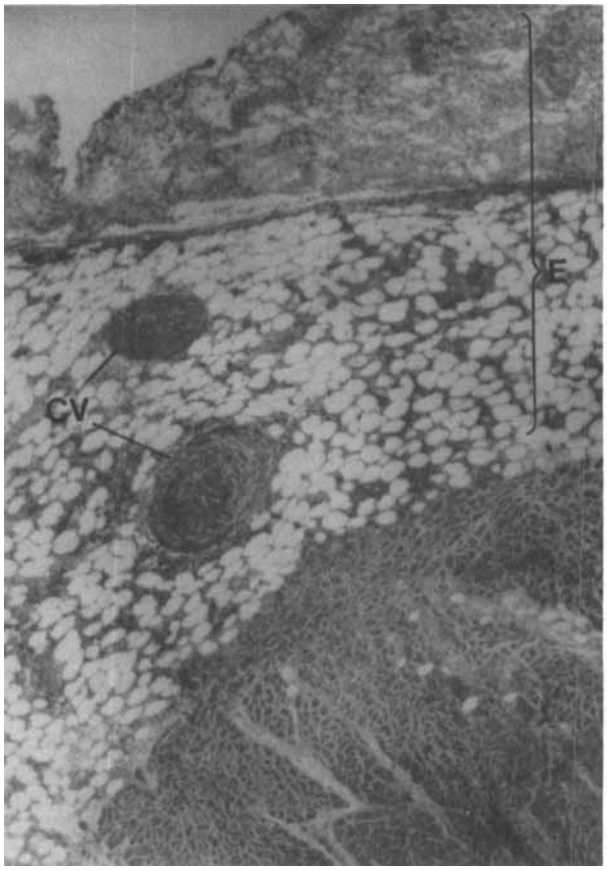


FIG 1. Section showing fibrinous purulent inflammatory reaction and two thrombosed coronary vessels (CV) in epicardium (E) of patient described in case presentation (100×).

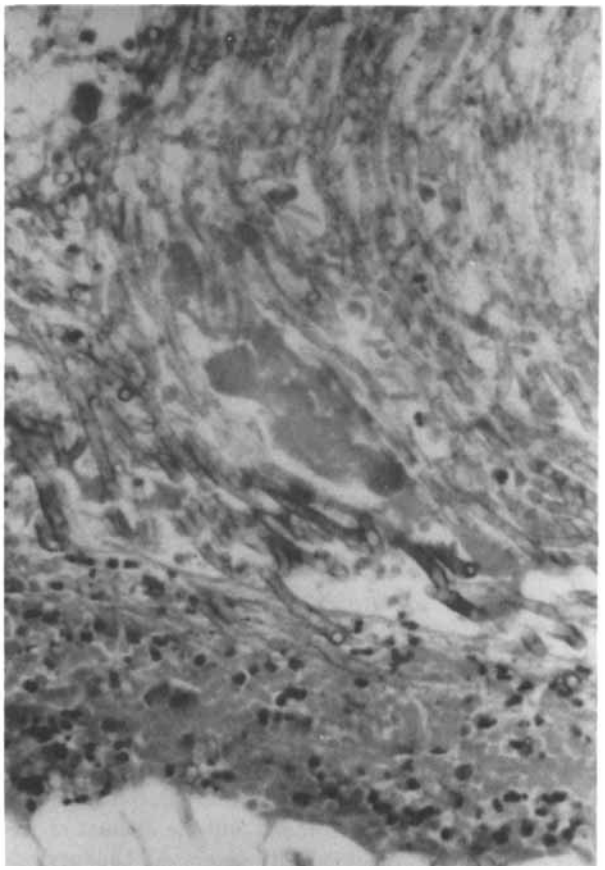

FIG 2. High power view of epicardium of Fig 1 showing extensive septated mycelia typical of *Aspergillus* and generalized inflammatory response (400×).

in debilitated patients. Bacterial, but not fungal, endocarditis has been reported as an infrequent complication (9) in patients undergoing hemodialysis.

Endocarditis may have an insidious onset. The few symptoms and signs that may develop can mimic those of other disease states. This is especially true with patients in renal failure (9). Findings common to endocarditis and renal failure include anemia, fever, heart murmurs, fatigue, malaise, anorexia, and headaches. Neurologic changes and peripheral vascular embolization may result from endocardial vegetations.

*Aspergillus* infection is rare but increasing in incidence (10). Myocardial involvement has been reported by Young et al (11) and by Walsh and Hutchins (12). These authors described patients who manifested a variety of clinical signs and symptoms, including: congestive heart failure; peripheral edema; ECG changes consistent with pericarditis, myocardial infarction, and nonspecific ST segment and T wave changes; debility; leukocytosis; fever; pulmonary infiltrates; and renal failure. Associated factors included long-term and multiple antibiotic therapy, cytotoxic drug therapy, steroid therapy, uremia, and numerous surgical procedures. Necropsy findings included widespread myocardial and pulmonary lesions containing the *Aspergillus* organisms. The classic findings of endocarditis (changing murmur, Osler nodes, Roth spots, splinter hemorrhages, petechiae, or Janeway lesions) are characteristically absent. Although all patients with *Aspergillus* endocarditis had blood cultures taken, none was positive antemortem for *Aspergillus*. *Aspergillus* pneumonia in one patient and widespread dissemination in another patient were the immediate causes of death. Immediate causes of death in the other cases included Gram-negative sepsis, gastrointestinal hemorrhage, pulmonary hemorrhage, and congestive heart failure.

Findings common to our patient and those reported in the above patients include the nonspecific ST segment and T wave changes, renal failure, high dose steroid and immunosuppressive drugs, uremia, nu-

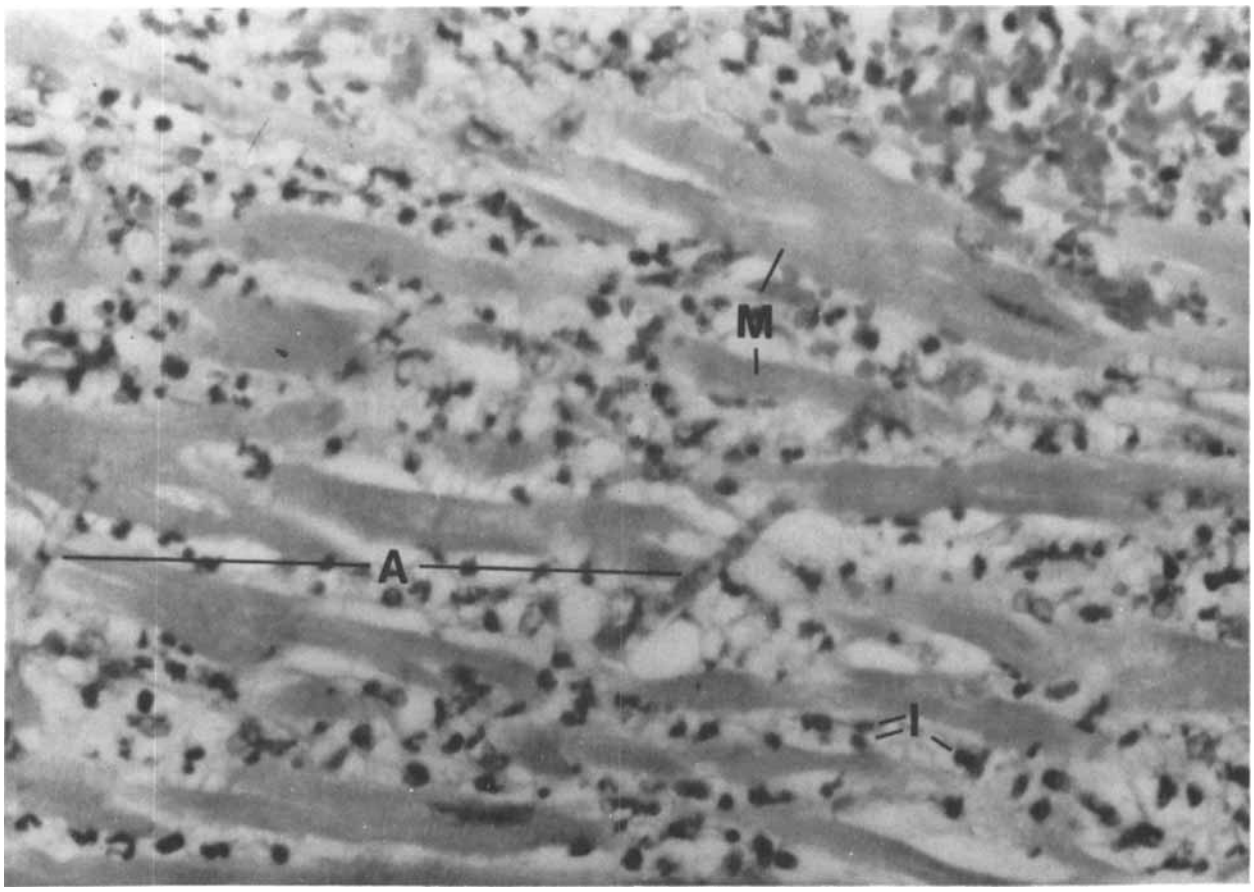


FIG 3. High power view of myocardium showing necrotic myocardial fibers (M), severe polymorphonuclear cell inflammatory response (I), and two well defined septated mycelia (A) (400×).

merous surgical procedures, lack of classic findings of endocarditis, gastrointestinal bleeding, and myocardial and pulmonary abscesses at the time of postmortem examination. Differences between our case and those reported above include lack of chest x-ray findings until the last few days before death, conduction abnormalities as the immediate cause of death, leukocytosis present only while the cadaveric kidney was in place, and lack of fever except, occasionally, a few days before death, and a striking cardiovascular instability associated with general anesthesia, including cardiac arrest.

The diagnosis of *Aspergillus* mycotic endocarditis in the present case was, as in previously reported cases, made only at the time of postmortem examination due to the insidiousness of the disease and the masking of its symptoms and signs by associated renal disease. Consequently the circumstances surrounding each arrest or unstable period led to explanations and diagnoses other than mycotic endocarditis, even when a changing murmur and pericardial rub were heard in the last few days of the patient's life. For example, without the postmortem examination the first episode of cardiorespiratory insufficiency that occurred outside the operating room might still be attributed to pulmonary embolus. The cardiac arrests, hypotension, and bradycardia during anesthesia might also still be attributed to vagal stimulatory and/or vagomimetic effects of succinylcholine, to the cardiovascular effects of laryngoscopy and intubation, to myocardial depression produced by the anesthetic agents, to hypovolemia, to recurarization, and to preoperative medication.

The changes in the level of consciousness observed in our patient were, in retrospect, probably due to decreased cerebral blood flow. Embolic phenomenon (5, 12) from vegetations seems unlikely because of the lack of permanent neurologic findings or vascular compromise at other sites. The acidosis found in association with the episodes of cardiovascular instability could be attributed to decreased peripheral perfusion. The metabolic acidosis would have further

decreased myocardial function, and could account for the improvements that occurred with sodium bicarbonate treatment. The large alveolar-arterial $P_{O_2}$ gradient no doubt resulted from abnormalities of pulmonary ventilation and perfusion due to decreased cardiac output and to pulmonary abscesses noted on postmortem examination.

As, in our case, there was no premortem evidence of *Aspergillus* pancarditis, no causal relationship between it and intra-anesthetic cardiovascular instability can be established. However, over the last several years our institution has averaged 38 renal transplants per year and this is the only patient who had multiple episodes of cardiovascular instability with no apparent cause other than the *Aspergillus* infection found postmortem.

In summary, a case of *Aspergillus* pancarditis is presented. This infection could have accounted for many of the unexpected episodes of cardiovascular instability associated with general anesthesia. The infection is difficult to diagnose antemortem as it generally occurs in the debilitated patient with many drugs and predisposing factors. Although usually not an immediate cause of patient's death, *Aspergillus* pancarditis should be considered in the chronically ill, uremic patient with pronounced cardiovascular instability during anesthesia.

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