The Development of Pericarditis Following Peripheral Blood Stem Cell Transplantation: A Case Report

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Mr. Z, a 45-year-old man with non-Hodgkin lymphoma, underwent six cycles of CHOP (cyclophosphamide, Adriamycin, vincristine, and prednisone) and rituximab, resulting in remission of his disease. However, plans for an autologous peripheral stem cell transplantation were delayed because of cellulitis in his left leg. Laboratory cultures revealed that methicillin-resistant Staphylococcus aureus (MRSA) was the cause, and he received a course of IV vancomycin and cefepime. After successful treatment, Mr. Z was evaluated for a stem cell transplantation. A chest computed tomography scan showed mild fullness around his mediastinum, and a multiple gated acquisition scan showed left ventricular ejection fraction of 62%. A level less than 50% may indicate cardiotoxicity or cardiac compromise. Mobilization chemotherapy of cytoxan and etoposide was administered, and peripheral blood stem cell collection was initiated after treatment.

During the interim between stem cell collection and readmission for high-dose chemotherapy, Mr. Z developed shortness of breath and a productive cough. He was diagnosed with pneumococcal pneumonia and admitted to a local hospital for a weeklong course of IV cefepime and tobramycin.

A chest computed tomography scan and x-ray revealed a pulmonary edema and small pleural effusions. A trans-thoracic echocardiogram showed concentric left ventricular hypertrophy with low-normal left ventricular systolic function, severe hypokinesia of the posterior basilar segment, and hypokinesia of the inferior basilar segment. A repeat multiple gated acquisition scan revealed left ventricular ejection fraction of 56%, lower than the previous measure. Mr. Z improved and was discharged with a weeklong supply of oral levofloxacin (750 mg).

Mr. Z was readmitted for stem cell transplantation. Cultures were obtained, and immunoglobulin G levels indicated that cytomegalovirus, varicella, and herpes simplex virus I and II were present. Prophylactic doses of acyclovir, levofloxacin, and fluconazole were started two days prior to the planned transplantation and continued throughout Mr. Z’s hospital stay.

Mr. Z was given high-dose cytoxan, carmustine, and etoposide for his myeloablative chemotherapy, followed by peripheral stem cell rescue. His white blood cell count after chemotherapy averaged 0.02 k/ul. Mr. Z’s recovery was normal until the fourth day after transplantation, when he complained of chest pain and described it as constant midsternal pressure. Mr. Z received 4 mg of IV morphine sulfate and 0.4 mg of sublingual nitroglycerin, which brought moderate relief. An electrocardiogram (EKG) demonstrated sinus rhythm and cardiac enzymes within normal limits (creatinine kinase < 20 ul; troponin 1 < 0.03 ng/ml). Increased midsternal pressure about five hours after the initial onset prompted additional morphine and nitroglycerin treatment. A second EKG showed diffuse ST elevation across the precordium, and a physical examination revealed a pericardial friction rub. The patient remained afebrile with stable vital signs. Repeat cardiac enzymes were again within normal limits; therefore, blood cultures were obtained and Mr. Z was started on IV vancomycin 1.5 g every 12 hours and IV cefepime 2 g every 8 hours for suspected bacterial pericarditis (Hughes et al., 2002). Mr. Z remained on vancomycin, cefepime, levofloxacin, fluconazole, and acyclovir for the remainder of his hospital stay, and his chest pain dissipated without complications.

Definition

The pericardium is a fluid-filled sac that surrounds the heart and serves as a protective barrier (see Figure 1). The pericardium is made up of two layers, separated by 15–20 ml of fluid: the parietal pericardium, which is a fibrous outer layer, and the visceral pericardium, which is the inner layer that lays directly over the epicardium of the heart (Marinella, 1998). Pericarditis occurs when the pericardium becomes inflamed, an adverse side effect of some cancer treatments (Ross & Grauer, 2004).
Pathophysiology

Acute pericarditis in patients undergoing blood marrow transplantation for cancer has many causes. Radiation, as well as certain chemotherapies, may lead to cardiac toxicity (Lehmann, Isberg, Ljungman, & Paul, 2000). Cardiac arrhythmia is the most common cardiotoxic side effect of cancer chemotherapy, followed by congestive heart failure, pericarditis, and pulmonary edema. Chemotherapy regimens commonly associated with cardiotoxicity include cyclophosphamide, carmustine, cytarabine, and anthracyclines (Murdych & Weisdorf, 2001). Anthracyclines include doxorubicin, daunorubicin, idarubicin, and epirubicin (Lehmann et al.) (see Table 1). Adverse cardiac effects may occur days, weeks, or months after the initial chemotherapy or radiation. The incidence and extent of toxicity depend on the dose of the agent given (both cumulative and individual), the combination of drugs used, and the administration route of the antineoplastic medication (Yeh et al., 2004). Other factors that may cause toxicity are patient related, such as age, prior chest radiation therapy, a history of cardiovascular disease, or metabolic disorders (Yeh et al.). Cardiac toxicity may have played a role in Mr. Z’s pericarditis as he received cyclophosphamide and doxorubicin.

Infectious pericarditis (bacterial, viral, and fungal) is uncommon in patients undergoing blood marrow transplantation for cancer treatment; however, neutropenia is a predisposing factor (Ross & Grauer, 2004). Pericarditis from a bacterial infection is uncommon but treatable with antibiotics (Ross & Grauer). Infective pericarditis may take weeks to develop; staphylococcus, a gram-positive cocci, is the most common cause of bacterial pericarditis (Hancock, 2004). Mr. Z had MRSA before transplantation, which may have seeded the pericardium; however, blood cultures showed no growth after 24 hours. The etiology of his pericarditis remains unknown.

Pericarditis from fungal infections most often occurs in immunocompromised patients (Maisch & Ristic, 2003) but also may be found in patients who have undergone thoracic surgery or have chronic renal failure (Rabinovici, Szewczyk, Ovadia, Greenspan, & Sivalingam, 1997). Fungi that can cause pericarditis include candida, aspergillus, nocardia, actinomyces, and blastomyces species. Fungal infections are discovered by obtaining a sample of pericardial fluid for culture and gram stain (Maisch & Ristic). Serum samples containing fungal organisms also would reveal fungus as the cause of pericarditis.

Coxsackie and other enteroviruses are common causes of viral pericarditis, the most common infectious disease of the pericardium (Maisch & Ristic, 2003). Technical issues and the time constraints involved with viral cultures, however, create difficulty in assigning and diagnosing a causative organism (Ross & Grauer, 2004). Patients who have undergone stem cell transplantation and are immunocompromised also are at risk for Epstein-Barr virus reactivation (Aoyama et al., 2004). Other viruses may attack the pericardium, such as adenoviruses, cytomegalovirus, herpes simplex, influenza, and hepatitis C (Maisch & Ristic). Fortunately, viral pericarditis does not require specific treatment (Maisch & Ristic).

Signs and Symptoms

Restrosternal pain in patients with acute pericarditis is exacerbated when patients inhale or lie down. Symptoms generally improve when patients sit up and lean forward (Holcomb, 2004). Having the patient do this will aid in the auscultation of a pericardial friction rub, which is best heard along the left sternal border and is considered a hallmark sign of pericarditis (Holcomb). A pericardial friction rub can be heard at http://depts.washington.edu/physdx/heart/tech5.html.

Diagnostic Tests

Changes in an EKG are crucial for differentiating pericarditis from other possible diagnoses, including myocardial infarction, early repolarization, pneumothorax, and hyperkalemia, all of which have distinct EKG changes. Diffuse ST-segment elevation in all leads of the EKG is, however, indicative of pericarditis and is not normally present with other diagnoses (Snider, Pai, & Kusumoto, 2004). Mr. Z’s EKG showed diffuse ST elevation compared to earlier EKGs (see Figure 2). Other diagnostic EKG changes are biphasic T waves, PR segment deviation, and T wave inversion in later stages of pericarditis (Ross & Grauer, 2004; Snider et al.). The EKG changes can take months to resolve. The EKG may show atrial fibrillation or premature atrial beats if pericardial effusion is present. Low-voltage QRS complexes may be seen if cardiac tamponade is present (Holcomb, 2004).

Laboratory results that may corroborate a pericarditis diagnosis include an increase in erythrocyte sediment rate, C-reactive protein, and leukocyte count. Creatine kinase muscle/brain (MB) type and troponin I also may be elevated; however, elevations in cardiac enzymes would point more toward acute myocardial infarction (Yeh et al., 2004). Mr. Z’s creatine kinase MB and troponin I remained normal.

Pericarditis occasionally is accompanied by pericardial effusion or cardiac tamponade, which can compress the heart and obstruct venous blood flow. Physical examinations that may help to diagnose cardiac tamponade include increased jugular vein distension, decreased heart tones, decreased pulse pressure, and increased heart rate (Itano & Taoka, 2005; Otto, 2004). Cardiac tamponade is life threatening and requires immediate treatment with pericardiocentesis (Holcomb, 2004; Itano & Taoka; Otto). An echocardiogram may be performed to evaluate for pericardial effusion with or without tamponade. The echocardiogram helps
to identify the amount of fluid present in the pericardial space and whether diastolic compression of the right and left atria is occurring (Holcomb; Itano & Taoka; Otto). A chest x-ray will reveal an enlarged cardiac silhouette that resembles the shape of a water bottle when pericardial fluid reaches approximately 250 ml (Holcomb) (see Figure 3). Mr. Z’s echocardiogram and physical examination did not demonstrate a large pericardial effusion or cardiac tamponade.

### Table 1. Agents Used in Stem Cell Transplantation

<table>
<thead>
<tr>
<th>DRUG</th>
<th>PHARMACOLOGIC CLASS</th>
<th>INDICATION</th>
<th>DOSE</th>
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</thead>
<tbody>
<tr>
<td>Cyclophosphamide&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Alkylating agent</td>
<td>Non-Hodgkin lymphoma; chronic lymphocytic leukemia; chronic myelocytic leukemia; acute lymphocytic leukemia; multiple myeloma; Hodgkin disease; breast, head and neck, prostate, lung, and ovarian cancers; neuroblastoma; retinoblastoma; sarcoma; and mycosis fungoides</td>
<td>400 mg/m² via IV for five days; 100 mg/m² orally for 14 days; or 500–1,500 mg/m² via IV ever three to four weeks. Blood marrow transplantation: 1.8–7 g/m²</td>
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<tr>
<td>Daunorubicin&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Antibiotic (anthracycline)</td>
<td>Acute myelogenous, monocytic, and erythroid leukemia and acute lymphocytic leukemia</td>
<td>30–60 mg/m² per day via IV for three consecutive days</td>
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<tr>
<td>Doxorubicin&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Antibiotic (anthracycline)</td>
<td>Hodgkin disease; acute lymphocytic leukemia; acute myelocytic leukemia; bladder, breast, lung, ovarian, gastrointestinal, testicular, and thyroid cancers; Wilm tumor; neuroblastoma; lymphoma; and sarcoma</td>
<td>30–75 mg/m² every three to four weeks; 20–45 mg/m² via IV for three consecutive days; 3–60 mg/m² for bladder instillation, 40 mg in 2 L dextrose for intraperitoneal instillation</td>
</tr>
<tr>
<td>Carmustine&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Alkylating agent; nitrosurea</td>
<td>Non-Hodgkin lymphoma, Hodgkin disease, multiple myeloma, brain tumors, recurrent glioblastoma multiforme, and metastatic brain tumors</td>
<td>75–100 mg/m² via IV per day for two days; 200–225 mg/m² every six weeks; and 40 mg/m² per day for five consecutive days, repeating cycle every six to eight weeks. Blood marrow transplantation: 450–600 mg/m² IV</td>
</tr>
<tr>
<td>Cytarabine&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Antimetabolite</td>
<td>Acute nonlymphocytic leukemia, acute lymphocytic leukemia, blast phase of chronic myelocytic leukemia, and leptomeningeal leukemia</td>
<td>Leukemias: 100 mg/m² per day via IV infusion for 5–10 days; 100 mg/m² every 12 hours for one to three weeks either IV or subcutaneously. High dose: 2–3 g/m² via IV every 12 hours for 4–12 doses to treat refractory acute leukemia; intrathecal: 20–30 mg/m²</td>
</tr>
<tr>
<td>Epirubicin&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Anthracycline, antitumor antibiotic analog</td>
<td>Adjuvant therapy in patients with evidence of node involvement following resection of primary breast cancer</td>
<td>100–120 mg/m² via IV every three to four weeks</td>
</tr>
<tr>
<td>Etoposide&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Plant alkaloid; derivative of the mandrake</td>
<td>Testicular and small cell lung cancers</td>
<td>Testicular: 50–100 mg/m² via IV every day for five days every three to four weeks. Small cell lung cancer: 75–200 mg/m² via IV every day for three days every three to four weeks. Blood marrow transplantation: 750–2,400 mg/m² via IV or 10–60 mg/kg over one to four hours per day</td>
</tr>
<tr>
<td>Idarubicin&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Antitumor antibiotic</td>
<td>Acute myelocytic leukemia</td>
<td>12 mg/m² every day for three days with cytarabine 100 mg/m² continuous infusion for seven days or in combination with cytarabine 25 mg/m² IV followed by cytarabine 200 mg/m² infusion every day for five days, 8–15 mg/m² via IV every three weeks has been studied.</td>
</tr>
<tr>
<td>Vincristine&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Plant alkaloid extracted from periwinkle</td>
<td>Acute lymphocytic leukemia and other leukemias, non-Hodgkin lymphoma, Hodgkin disease, neuroblastoma, rhabdomyosarcoma, and Wilm tumor</td>
<td>0.4–1.4 mg/m² via IV every three weeks</td>
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<tr>
<td>Rituximab</td>
<td>Monoclonal antibody</td>
<td>Low-grade or follicular CD20-positive and B-cell non-Hodgkin lymphoma that is relapsed or refractory to other treatment</td>
<td>375 mg/m² IV every week for four weeks (days 1, 8, 15, 22)</td>
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<tr>
<td>Prednisone</td>
<td>Hormones</td>
<td>Lymphatic leukemia, myeloma, and malignant lymphoma</td>
<td>5 mg orally</td>
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<sup>a</sup> Considered part of the therapeutic class of antineoplastics

*Note.* Based on information from Wilkes et al., 2003.
Pharmacologic Treatment

Outpatient therapy is possible if the patient is hemodynamically stable. If cardiac tamponade is present or suspected, the patient would be admitted to the hospital for observation (Holcomb, 2004). Treatment should focus on the underlying etiology of the pericarditis (Maisch & Ristic, 2003). Amphotericin B is the preferred treatment of fungal pericarditis (Rabinovici et al., 1997). Antibiotics for bacterial pericarditis include broad-spectrum antistaphylococci (beta-lactams) and aminoglycosides until cultures from the drainage can identify a specific organism (Holcomb). If tuberculosis pericarditis is found, the healthcare team should prescribe 9–12 months of tuberculostatic drugs. These can be given in conjunction with prednisone (1 mg/kg) for five to seven days before tapering the patient off steroids over six to eight weeks (Maisch & Ristic; Schifferdecker & Spodick, 2003) (see Table 2).

Nonsteroidal anti-inflammatory drugs (NSAIDs) remain the mainstay of treatment for pericarditis (Maisch & Ristic, 2003; Schifferdecker & Spodick, 2003). Ibuprofen has minimal side effects and is the preferred NSAID; however, peptic ulcer disease and renal insufficiency can be exacerbated with the use of NSAIDs. Ibuprofen 400 mg every eight hours is the common initial dose, with titration according to symptomatic relief up to 800 mg every six hours (Schifferdecker & Spodick). The patient should be evaluated within weeks of starting therapy to determine treatment effectiveness (Schifferdecker & Spodick). Colchicine also is effective in the treatment of pericarditis, both as monotherapy or in conjunction with ibuprofen (Maisch & Ristic). Bed rest may be helpful in more severe cases because activity may exacerbate pericarditis (Ross & Grauer, 2004).

Nonpharmacologic Treatment

Pericardiocentesis and pericardiectomy may be necessary when a large pericardial effusion or cardiac tamponade is present (O’Brien & Nunnemaker, 2002). Pericardiocentesis also may be used for symptomatic patients who suffer from neoplastic pericarditis (Maisch & Ristic, 2003). Pericardiocentesis is useful in relieving cardiac tamponade, draining large effusions, and diagnosing the cause of the infection; however, relief may be temporary and pericardiectomy still may be needed (Rabinovici et al., 1997). Draining and irrigating the pericardial cavity can provide a culture specimen. Once the cause is determined, antibiotics or antifungal medications can be administered (Holcomb, 2004). Neutropenia, however, is a relative contraindication to pericardiocentesis and pericardiectomy. Mr. Z did not require either intervention when his pericarditis resolved without treatment.

Nursing Implications

Because nurses play an integral role in the emotional and physical support of patients, they must be aware of the side effects of chemotherapy (Otto, 2004). Early pericarditis detection can lead to effective treatment and fewer complications; therefore, nurses and advanced nurse practitioners must be aware of the diagnostic criteria and available treatment options. Mr. Z’s pericarditis was caught early and antibiotic treatment was started, possibly contributing to his full recovery.

Conclusion

Pericarditis is a rare cardiac disease that can be a side effect of cancer treatment. Although pericarditis has been known to resolve without treatment, patients with a compromised immune system should be treated as though the pericarditis is caused by an infection until laboratory results can identify the cause. Early pericarditis diagnosis and...
Table 2. Pertinent Antimicrobial Agents

<table>
<thead>
<tr>
<th>DRUG</th>
<th>THERAPEUTIC CLASS</th>
<th>PHARMACOLOGIC CLASS</th>
<th>INDICATION</th>
<th>DOSE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin</td>
<td>Antibiotic</td>
<td>Glycopeptide</td>
<td>Staphylococcal infections</td>
<td>1 g via IV every 12 hours</td>
</tr>
<tr>
<td>Cefepime</td>
<td>Antibiotic</td>
<td>Third-generation cephalosporin</td>
<td>Lung, soft tissue, bone, joint, urinary and respiratory tract, blood, and abdominal and heart infections. More active against gram-negative than first- and second-generation cephalosporins</td>
<td>2 g via IV every 8 hours</td>
</tr>
<tr>
<td>Tobramycin</td>
<td>Antibiotic</td>
<td>Aminoglycoside</td>
<td>Certain infections caused by sensitive strains of <em>Citrobacter</em>, <em>Enterobacter</em>, <em>Escherichia coli</em>, <em>Klebsiella</em>, <em>Proteus</em>, <em>Providencia</em>, <em>Pseudomonas</em>, <em>Serratia</em>, and <em>Staphylococcus aureus</em></td>
<td>500 mg orally or via IV daily</td>
</tr>
<tr>
<td>Levofloxacin</td>
<td>Broad-spectrum antibiotic</td>
<td>Fluoroquinolone</td>
<td>Mild to moderate skin and skin structure infections; also acts as a prophylaxis for afebrile neutropenic patients</td>
<td>500 mg orally or via IV daily</td>
</tr>
<tr>
<td>Acyclovir</td>
<td>Antiviral</td>
<td>Synthetic purine nucleotide</td>
<td>Initial and recurrent episodes of mucocutaneous herpes simplex virus infections</td>
<td>5 mg/kg dose every 8 hours</td>
</tr>
<tr>
<td>Fluconazole</td>
<td>Antifungal</td>
<td>Bitriazole derivative</td>
<td>Prevention of candidiasis in bone marrow transplantation</td>
<td>400 mg orally or via IV daily</td>
</tr>
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</table>

Note. Based on information from Hughes et al., 2002; Kanda et al., 2001; Segal et al., 2007; Weingarten, 2002.

## References


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treatment improve patient outcomes by decreasing morbidity and mortality.

Long-term low-dose acyclovir against varicella-zoster virus reactivation after allogeneic hematopoietic stem cell transplantation. *Bone Marrow Transplantation,* 28(7), 689–692.


