**Case Study**

**A 57-YEAR-OLD WOMAN WITH UNSTABLE ANGINA**

Stephen J. Noga, MD, PhD*

**History**

The patient is a 57-year-old woman with a history of hypertension and exertional angina. A positive exercise stress test in December 2001 showed a small area of ischemia in the lateral inferior wall of the heart near the apex. She had undergone coronary artery bypass surgery about 5 years previously.

The patient presented to the emergency room in mid-January 2002 with chest pain characterized by sudden onset at rest and accompanied by nausea, palpatations, diaphoresis, and dizziness, but no shortness of breath. The electrocardiogram was indicative of lateral-wall ischemia, but myocardial infarction was ruled out by cardiac enzyme studies. Her chest pain was relieved by nitroglycerin.

**Physical Examination**

On physical examination, the patient appeared pale and had a resting heart rate of 100 beats per minute, respiratory rate of 20 breaths per minute, blood pressure of 130/70 mm Hg, core temperature of 37.2°C, and an oxygen saturation of 96% on room air by pulse oximetry. She had jugular venous distention of 6 cm. The remainder of her examination was significant for a 2/6 systolic ejection murmur, best heard at the lower left sternal border, and 1+ pitting pedal edema.

**Laboratory Results**

Laboratory evaluation revealed the following: white blood cell count of 19 000/µL with a left shift, many young myeloid forms, and 10 nucleated red blood cells/100 white blood cells; hematocrit of 16%; hemoglobin level of 5 g/dL; and platelet count of 34 000/µL. Bone marrow aspiration and biopsy revealed nests of metastatic poorly differentiated adenocarcinoma and fibrous tissue.

Over the next 2 weeks, computed tomography (CT) scans of the chest, abdomen, and pelvis; a whole-body positron emission tomography scan; magnetic resonance imaging of the lumbar spine; and a bone scan failed to identify a primary source of the patient's malignancy, although approximately 20 low-density liver lesions and splenomegaly were apparent on CT. Liver function tests were elevated (total bilirubin, 1.4 mg/dL; alkaline phosphatase, 286 U/L; aspartate aminotransferase, 79 U/L; alanine aminotransferase, 70 U/L; and gamma-glutamyltransferase, 286 U/L) as was the carcinoembryonic antigen level (44 ng/mL). The final pathologic and clinical diagnosis was adenocarcinoma with an unknown primary source of malignancy.

**Intervention**

During the initial hospitalization, the patient received 5 units of packed red blood cells, which
CASE STUDY

restored the hematocrit to approximately 28%. During 2 weeks of diagnostic workup, the patient had several episodes of angina after her hematocrit dropped below 25%. She was admitted twice to the hospital for transfusion of red blood cells. Chemotherapy with gemcitabine (1000 mg/m² weekly) was attempted, but the patient had worsening thrombocytopenia, anemia, and angina. Docetaxel chemotherapy was then initiated at a dosage of 30 mg/m² weekly (on days 1, 8, and 15).

At that time, the patient’s hemoglobin level was 8 g/dL, and her hematocrit was 25%. In preparation for therapy with long-acting recombinant erythropoietin, the patient’s iron status was evaluated, revealing a normal serum iron level (50 µg/dL); low iron saturation (20%); and low ferritin levels (25 µg/mL). She was treated with parenteral iron gluconate.

The patient began taking darbepoetin alfa once weekly, 4.5 µg/kg by subcutaneous injection. After 2 weeks, her hemoglobin level was 9.5 g/dL, and her hematocrit was 29%. At 4 weeks, the hemoglobin level had risen to 11 g/dL, and the hematocrit had risen to 34%, at which time the schedule for administering darbepoetin was changed to every 2 weeks at the same dosage. After 6 additional weeks of therapy, the patient’s hemoglobin level and hematocrit reached a plateau at 12.5 g/dL and 39%, respectively, which permitted a further reduction in dosing frequency to every 3 weeks. With this dosing regimen, the patient’s hematocrit has remained at the target level for the past 3 months. She has had no other episodes of myocardial ischemia or angina. After 3 cycles of docetaxel, the patient’s white blood cell count returned to 6000/µL, with a normal differential. The platelet count rose to 206 000/µL.

DISCUSSION

The patient’s elevated white blood cell count was initially suggestive of myeloid leukemia. In reality, it resulted from the replacement of bone marrow with tumor and a shift of hematopoiesis to the spleen. Bone marrow replacement also markedly reduced the ability to produce red blood cells and platelets.

The goal of chemotherapy was to clear a large amount of the tumor from the bone marrow and allow normal reconstitution. The patient was already moderately anemic, however, and use of the chemotherapeutic agent docetaxel would be expected to cause the hematocrit level to decrease even further. A further reduction in the hematocrit level was particularly risky in this patient because of her severe myocardial ischemia and unstable angina.

Continued transfusion of large quantities of blood was contraindicated for several reasons, eg, the patient’s poor cardiac function. She was unable to tolerate intravenous infusion of even moderate quantities of fluid and tended to develop congestive heart failure during transfusion. Other reasons for avoiding repeated transfusions included the desire to avoid such risks as transfusion reactions, transmission of infectious disease, and iron overload.

It was important for the patient’s iron status to be evaluated before the initiation of erythropoietin therapy. The potential for iron overload was not a concern in this patient, as she had not received a large number of blood transfusions. Failing to replete iron stores before starting erythropoietin is a common error, resulting in a suboptimal response to erythropoietin therapy.

This patient required a substantial amount of outpatient care. Streamlining this process as much as possible was particularly important, as her median life expectancy was about 6 months. The ability to limit injections of darbepoetin to 1 time per week and, subsequently, to 1 time every 2 weeks to 3 weeks, represented an important therapeutic benefit. If the patient had continued to receive blood transfusions, she would have spent much more time in the outpatient clinic, and may have required hospitalization for transfusion-related complications.