



Nursing Management of Sustained Rigors and Recurrent Fever as Symptoms of Filgrastim Hypersensitivity: A Case Report

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A 36-year-old man presented to an emergency room with fever, fatigue, and severe rectal pain. He was subsequently found to be pancytopenic with a perirectal abscess. A bone marrow examination revealed 58% blasts consistent with acute myeloid leukemia. The patient was initiated on clofarabine, idarubicin, and cytarabine therapy. The first cycle of therapy was complicated by neutropenic fever, bacteremia, and pneumonia. The second cycle was complicated by delayed platelet recovery. As a result, the patient was referred for possible stem cell transplantation. The patient was enrolled in a phase III trial using standard of care double umbilical cord blood transplantation with myeloblastic conditioning to include fludarabine and melphalan, with rabbit antithymocyte globulin. Filgrastim injections were initiated at 600 mcg daily.

The patient's post-transplantation phase was complicated by sustained rigors and recurrent febrile episodes. The patient experienced 1–6 episodes of rigors daily. During this period, the patient also reported severe lower back pain with a majority of the episodes of rigor. The patient then developed neutropenic fever on Day 17 with persistent fever daily ranging from 38.1°–39.5°C through Day 50, with only six days in which he was afebrile. Filgrastim injections were administered at 4 pm daily, and the febrile episodes were noted to occur primarily in the early to late evening hours, with rigors preceding the febrile events by about 30–60 minutes. By Day 30, the patient's engraftment had plateaued with a white blood cell count of 1.2 and an absolute neutrophil count of 0.89. As a result, the filgrastim dose was increased to 600 mcg twice daily.

Diagnostic Workup

Because of the ongoing symptoms associated with neutropenic fever, including rigors, and pain, an infectious disease consult was obtained on Day 8. Anticipating an infectious etiology corresponding with the neutropenic period, a complete infectious disease work-up was conducted (see Table 1). The patient developed diarrhea on Day 3 post-transplantation, which was positive for *Clostridium difficile*, and was resolved with metronidazole followed by oral vancomycin.

Diagnostic imaging studies including X-rays, and computed tomography (CT) scans of the chest, abdomen, and pelvis were negative. However, a positron-emission tomography (PET)/CT scan revealed multiple enlarged mediastinal and bilateral hilar lymph nodes. Flexible video bronchoscopy with endobronchial ultrasound and ultrasound-guided transbronchial fine needle aspiration (FNA) of the lymph node, as well as a bronchoalveolar lavage, were completed. Culture results were negative for a complete bacterial, viral, and fungal examination. Pathology revealed no malignant cells, no viral changes, fungal stains were negative, as was staining for pneumocystis. The FNA specimens also were negative. The patient's central venous catheter also was removed and the tip was sent for bacterial and fungal cultures, which returned negative for central line-associated bloodstream infection. Since the patient was not exhibiting symptoms of viral encephalitis or meningitis, lumbar puncture was not completed.

A bone marrow biopsy and aspiration was completed on Day 34 with no evidence of acute leukemia. All cultures,

including cytomegalovirus, human herpesvirus 8 (HHV8), herpes simplex virus, adenovirus, varicella zoster virus, parvovirus, fungal cultures, and bacterial cultures also were negative. HHV6 was positive in the peripheral blood on Day 29, as well as in the bone marrow study on Day 34 (less than 183 DNA copies/ml), but improved with foscarnet therapy. Despite improvement of HHV6 in the blood, the patient's symptoms persisted. An immunoglobulin-G level was obtained on Day 34, which returned low at 572 mg/dl and was replaced with IV immunoglobulin 50 g daily for four doses. Throughout the course of the rigors and febrile events, the patient received various IV and/or oral antimicrobial, antifungal, antiviral, and an aminoglycoside (amikacin) therapy with limited improvement in the frequency and severity of symptoms.

Identifying Hypersensitivity

As infectious sources were ruled out, the attending physician turned his attention to evaluating the potential for hypersensitivity to the pharmacologic regimen. Agents were systematically tapered to observe for changes in symptom severity. The patient also began to voice concerns regarding the filgrastim injections and, as a result of limited improvement in neutrophil recovery, it was decided to reduce the dose on Day 50. The following day, the patient's fever curve and symptoms of rigors and pain were reduced with the dose reduction of filgrastim. The medication was discontinued on Day 51, with no other febrile

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