



Canola flower fields, Western Cape, South Africa

PIC QUESTION OF THE WEEK: 3/22/10

Q: Is there any relationship between the administration of colony-stimulating factors and splenic rupture?

A: Filgrastim (granulocyte-colony stimulating factor; G-CSF; Neupogen), pegfilgrastim (Neulasta), and sargramostim (granulocyte-macrophage colony stimulating factor; GM-CSF; Leukine) are labeled for the treatment and prevention of chemotherapy-induced neutropenia as well the promotion of myeloid recovery in patients with hematologic malignancies following autologous stem cell transplantation (SCT). The drugs are also used to mobilize peripheral stem cells prior to apheresis in patients undergoing bone marrow ablation. Each of these agents can produce a number of significant adverse effects including leukocytosis, anaphylactoid reactions, bone pain, hyperuricemia, and respiratory distress syndrome. Splenomegaly and, rarely, splenic rupture are two unusual consequences of these CSFs. Product labeling for filgrastim cites the frequency of splenomegaly as 30% in patients treated for severe neutropenia and also acknowledges the possibility of fatal splenic rupture. Although not listed in the current product literature, splenic rupture has also been reported with sargramostim. These adverse events are thought to occur as a result of overt splenic distension from mass accumulation of various progenitor cells and immature granulocytes in the splenic sinuses. A recent study measured changes in spleen size during filgrastim treatment for peripheral progenitor cell mobilization in normal donors. In this report, 38% of the 303 subjects experienced a ≥ 2.0 -fold increase in spleen volume. Splenomegaly generally peaks within 4 to 6 days of therapy and subsides shortly after treatment is discontinued. Splenic rupture has been reported in patients receiving G-CSF for chemotherapy-induced neutropenia as well as in *healthy stem-cell donors*. Individuals receiving CSFs must be monitored closely and advised to notify the physician if left upper quadrant pain or tenderness occurs. Splenic rupture may also be accompanied by confusion and lightheadedness due to blood loss. During therapy, patients should be instructed to avoid physical activity that may result in trauma to the spleen. Patients who have suspected splenomegaly should be examined using abdominal ultrasound or CT. Splenectomy is usually indicated in the event of splenic rupture.

References

- Nuamah NM, Goker H, Kilic YA, et al. Spontaneous splenic rupture in a healthy allogeneic donor of peripheral-blood stem cell following the administration of granulocyte colony-stimulating factor (g-csf). A case report and review of the literature. *Haematologica* 2006;91:26-8.
- Stiff PJ, Bensinger W, Abidi MH, et al. Clinical and ultrasonic evaluation of spleen size during peripheral blood progenitor cell mobilization by filgrastim: results of an open-label trial in normal donors. *Biol Blood Marrow Transplant* 2009;15:827-34.
- Veerappan R, Morrison M, Williams S, et al. Splenic rupture in a patient with plasma cell myeloma following G-CSF/GM-CSF administration for stem cell transplantation and review of the literature. *Bone Marrow Transplant* 2007;40:361-4.

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