Reviewer's report

Title: Colon biopsies for evaluation of Acute Graft-Versus-Host Disease (A-GVHD) in allogeneic bone marrow transplant patients.

Authors:

Dr Vinod Shidham (vshidham@mcw.edu)
Chung-Che Chang (icchang@mcw.edu)
Ganesh Shidham (gshidham@hotmail.com)
Farrukh Ghazala (meh407@aol.com)
Paul Lindholm (p-lindholm@northwestern.edu)
Bal Kampalath (bkampala@mcw.edu)
Varghese George (vgeorge@uab.edu)
Richard Komorowski (rkomor@mcw.edu)

Version: 1 Date: 11 Feb 2003

Reviewer: Lisbet Sviland

Level of interest: A paper of limited interest

Advice on publication: Unable to decide on acceptance or rejection until the authors have responded to the compulsory revisions

Discretionary revisions:
1. In the introduction the authors state that: "The incidence of intestinal A-GVHD after allogeneic BMT ranges from 30% to 60% and may be associated with or without clinical signs of skin and liver involvement". This is not entirely correct; the incidence of A-GVHD after allogeneic BMT ranges from 30% to 60% with the skin as the most commonly affected organ.

2. Under methods when the authors describe the negative control groups they state that "the histopathology was negative for diagnostic pathology..." Were these reported as normal?

3. I would like a comment on the design of the study. Was this a prospective or a retrospective study using archival biopsies?

4. Two negative control groups were included in the study and as the authors say it would have been desirable to have a control group from post BMT patients without GVHD. They state this was impractical due to "obvious ethical limitations". Other similar studies have managed to include autologous BMT recipients as a control group. Was this a possibility? The repopulation of lymphoid cells in the gut will be different in a BMT patient group (see below).

Compulsory revision:
1. I would like some more clinical information:
   - What kind of transplant did group A receive? Was it all bone marrow or did the group include patients who received peripheral stem cells or cord blood transplants?
   - There is no mention of what kind of conditioning the patients received. This is important in the differential diagnosis of A-GVHD in the gut. Although as the authors state most of the pathology caused by the conditioning regimen will have disappeared by day 21 it should be included in the clinical details.
   - What kind of GVHD prophylaxis did the patients receive?
   - Were the biopsies taken before any treatment for their GVHD was commenced?

2. It is important to exclude CMV infection as histological features of CMV can be identical to those
seen in A-GVHD. There is no mention in the paper how CMV infection was excluded. Serology for CMV is unreliable in the post-BMT setting. For that matter CMV may occur together with GVHD. Did they do immunohistochemistry for CMV on tissue sections and if not why not?

3. The authors state that plasme cells were more frequent in the negative control groups. They have in this context not discussed the difference in repopulation of lymphoid cells which occurs following a transplant. The control groups they have used are therefore not appropriate and the lack of a "chronic inflammatory response" would be expected in patients post BMT. They would have to include allogeneic BMT recipients with no GVHD or autologous transplant recipients to comment on this finding.

**Competing interests:**

None declared.