Author's response to reviews

Title: Chronic Diarrhea associated with Persistent Norovirus Excretion in Patients with Chronic Lymphocytic Leukemia: Report of Two Cases

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Version: 2 Date: 15 March 2011

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Response to Reviewer 1, T.W. Westhoff

1. **Overview of chronic norovirus infection**: a brief statement of expanded diagnoses was added to the discussion, with additional references and a recently reported case of a patient with chronic norovirus infection in the setting of AIDS.

2. **Acute presentation with nausea, vomiting and fever**: Both patients experienced this, and this has been clarified in the manuscript.

3. **Chronic shedding and isolation**: the patients had prolonged symptoms prior to diagnosis, but no family members contracted the ailment from them; case 2 actually developed her symptoms after a diarrheal illness affected her family members. No efforts at containment aside from hygiene were made. These points are clarified in the manuscript.

4. **Biopsies were obtained and no other diagnosis was found**: We could only speculate on which defect in these patient’s immune system correlated with norovirus persistence, aside from reporting the very low immune globulin levels that both patients experienced. While an exhaustive listing of immune defects in CLL patients is unlikely to add a great deal to the discussion, additional commentary is offered in the discussion, with supporting references. Reviewer’s manuscript made very interesting reading, and we appreciate that this was brought to our attention; however, given the limited clinical information available on the cases, we cannot comment further as (only) standard histologic evaluation was performed.

5. Both patients have now died, and this is clarified in the manuscript.

Response to Reviewer 2, Somashekar G Krishna

1. **Biopsies**: these are described in the manuscript as suggested. Photomicrographs could not be obtained prior to revision response date, but we feel these are not likely to add much to the point of the report, given the minor and unspecific findings.

2. **Association**: We do not believe that, aside from persistence of the diarrhea, evidence of persistent presence of norovirus in stool, the absence of another, tenable explanation based on biopsy, stool analysis or culture, and the description of other patients with chronic norovirus-associated diarrhea, a tighter association leading to causality can be drawn. That said, additional description of the testing conducted on each patient is provided, leaving norovirus persistence as the likely culprit. This is expanded upon in the discussion.

3. **Table of causative agents**: This is supplied, with accompanying references.

4. **Pathology and testing**: this is provided. Pathology is not completely normal, but findings were minor and non-specific, and is consistent with the consequence of severe diarrhea.

5. **Brief description of treatment options**: Provided in discussion. Very brief, regrettably.