[Abstract 38]

PARADOXICAL INCREASES IN SERUM IGM AND VISCOSITY LEVELS FOLLOWING RITUXIMAB IN WALDENSTROM'S MACROGLOBULINEMIA.

Andrew Branagan [1], Zachary Hunter [1], Daniel Ditzel Santos [1,2], Olivier Tournilhac [1,2], Robert Manning [1], and Steven P. Treon [1,2]. [1] Bing Program for Waldenstrom's Macroglobulinemia, Dana Farber Cancer Institute and [2] Harvard Medical School, Boston, MA, 02115, USA.

Background: The anti-CD20 monoclonal antibody rituximab is an important therapeutic in Waldenstrom's macroglobulinemia (WM), producing response rates of 30-50%. Responses, which are based on serum IgM levels, have typically been evaluated at 12 weeks. Paradoxically, we have observed that serum IgM levels can abruptly rise following rituximab therapy in patients with WM and can often lead to morbidity on the basis of hyperviscocity.

Methods: Eleven WM patients with CD20+ tumor cells who received rituximab at our Institution and had serum IgM levels measured within a 12 week period following start of therapy were evaluated. Therapy consisted of 4 weekly infusions of rituximab at 375mg/m2. Pre- and post-therapy serum IgM levels were determined by nephelometry, and corresponding serum viscosity levels were determined by viscometry.

Results: Ten of the 11 patients demonstrated an abrupt rise in serum IgM levels, with a >25% increase occurring in 8 (73%) patients. Mean serum IgM levels for all ten spiking patients rose from 4370 (range 655-7940) to a peak of 5865 (range 872-11,800) mg/dL (p=0.004), which occurred at a mean of 4 (range 1-8) weeks following initiation of therapy. Mean serum viscosity levels also increased from 3.5 to 5.6 CP (p=0.09) in 8 patients for whom pre- and post-therapy studies were obtained. A subdural hemorrhage occurred in one patient when serum IgM levels rose from 7,530 to 11,800 mg/dL, and serum viscosity increased from 3.9 to 10.1 CP. Two other spiking patients with pretherapy IgM levels of >5,000 mg/dL experienced worsening headaches and/or epistaxis attributed to increasing serum viscosity.

Conclusions: Abrupt increases in serum IgM levels commonly occur following rituximab therapy in WM. Careful clinical and laboratory monitoring is warranted, particularly if patients have pre-therapy serum IgM levels of >5,000 mg/dL. The mechanism of this effect is under active investigation, and may be related to signaling triggered by rituximab.