Re: Cancer Antigen 125 As a Biomarker in Peritoneal Dialysis: Mesothelial Cell Health or Death?

Editor:

I sincerely thank Dr. R.T. Krediet, a giant in the field of peritoneal physiology and pathophysiology, for responding to our opinion paper on cancer antigen 125 (CA125) (1).

Dr. Krediet was co-author of the paper by Koomen *et al.* (2) demonstrating that the CA125 in dialysis effluent must originate from within the peritoneal cavity, and correlating CA125 with the number of mesothelial cells *in vivo* and *in vitro*. However, in that paper, the authors quote another study from a decade earlier (3) that demonstrated that CA125-positive mesothelial cells are indeed located in the peritoneum, but especially in areas of inflammation and adhesions. They also note that CA125 levels are high in patients with malignant ascites and ascites associated with liver disease. So even in these early reports, it is not clear that effluent CA125 reflects a state in which all is well with the peritoneum.

Dr. Krediet further quotes the *in vitro* study by Zeillemaker *et al.* (4) that used human omentum [an approach that he cites as a weakness of the Breborowicz study (5)] and that found that tumor necrosis factor α , interleukin 1 β , and *Escherichia coli* lipopolysaccharide lead to increased CA125 secretion. Those results would be supportive of our own hypothesis that this biomarker might not necessarily reflect mesothelial health and mass, but instead might be a sign of intraperitoneal inflammation.

The hypothesis that a higher concentration of CA125 in peritoneal dialysis effluent may reflect an inflammatory state, such as peritonitis, is countered by Dr. Krediet's

alternative suggestion that elevated CA125 is the result of desquamation of dead or lysed mesothelial cells. However, that suggestion contradicts the statement in his own paper contending that CA125 in effluent cannot be explained by drained mesothelial cells. Indeed, his group states that it is "unlikely that more than 1% of the CA125 in the dialysate is produced by the mesothelial cells in the effluent" (2).

The final issue concerns pH-neutral, so-called "bio-compatible," peritoneal dialysis solutions. Dr. Krediet quotes his own animal studies finding a marked reduction in peritoneal microvessels when the animals received bicarbonate/lactate dialysate (6). It would be difficult to extrapolate that finding to the many human studies in which peritoneal permeability increases, rather than decreases, with the use of pH-neutral solutions. Indeed, in the recent Japanese study that Dr. Krediet cites, histology examination detected more angiogenesis and new vessel formation in patients using pH-neutral solution than in patients using conventional dialysate (7).

Clearly animals are animals, humans are humans, and many factors are at play in the response of the peritoneum to the onslaught of dialysis fluid. The purpose of our paper was to highlight the uncertainty surrounding this subject and to give pause to those who reflexively assume that an increase in effluent CA125 means only good things for the peritoneal membrane.

DISCLOSURES

JMB has been a consultant for Amgen and Baxter Healthcare, and is in the speakers' bureau for Amgen and DaVita Healthcare Partners.

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