Osmotic Fragility of Erythrocytes and Secondary Hyperparathyroidism in Chronic Renal Failure

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Dear Sir,

The letter of Massry and Akmal, published in Nephron 43:10 (1986) [1], attacks harshly our previous papers [2,3] on the relation, if any, between red blood cell (RBC) osmotic fragility and secondary hyperparathyroidism (HPT) in chronic renal failure. We would like to have had a reply printed simultaneously; nevertheless, let us make some comments now.

Firstly, Massry and Akmal [1] state that in the study of Bogin et al. [4] amounts of parathyroid hormone (PTH) only ½ to 1 times higher than normal were found to induce the maximum increase in the osmotic fragility of human RBC in vitro. Thus, since all our patients had exceedingly high blood levels of PTH, the lack of correlation between RBC osmotic fragility and serum PTH in these patients may be not unexpected. It is apparent that an important fact escaped these authors. We agree that the mean serum PTH concentration in our patients was 7–14 times more than normal, as stressed by Massry and Akmal [1]. Yet, as can be inferred by the wide standard deviation, a considerable range in the individual values was observed. The patients studied indeed had serum PTH levels by between 1.4 and 50.7 ng/ml (i.e., 0.56–56.6 times higher than normal). It is in such patients that we failed to find a significant correlation between RBC osmotic fragility and serum PTH [2,3]. Parenthetically, Massry and Akmal [1] are quite uncritical as to what exactly the different PTH assays used in the different studies measure [5]. Secondly, Massry and Akmal [1] state that we claim that treatment with 1,25-(OH)₂D₃ was effective in controlling blood levels of PTH in our patients. Again, this observation reflects undue haste in the reading of our papers. On the contrary, as clearly stated in the 'Results' sections [2, 3], we found that the fall in the mean serum

PTH concentration after treatment did not achieve statistical significance because of the wide variation in the individual changes in the patients. Yet, according to Massry et al. [6], we think that such a treatment was all the same effective in controlling secondary HPT in our patients in view of the normalization or near normalization of serum alkaline phosphatase levels in them. Moreover, it should be remarked that in such patients the individual changes in RBC osmotic fragility in response to treatment with 1,25-(OH)₂D₃ did not correlate with the respective changes in serum PTH [2,3] and that no improvement in RBC osmotic fragility was observed in 2 patients after parathyroidectomy in the face of the substantial decrease in serum PTH in both [2].

In our opinion, these findings speak strongly against at least the third and fourth criteria recommended by Massry himself [7] to consider a substance responsible for a given uremic

manifestation. All things considered, our data can allow the conclusion that secondary HPT is probably not a 'major' factor influencing RBC osmotic fragility in chronic renal failure. Lastly, we know very well the studies [8, 9] cited by Massry and Akmal [1]; we agree that they provide important findings in support of the theorized hemolytic effect of PTH in chronic renal failure. Yet, we found it difficult to quote such studies in our papers merely because they had not yet been published at that time. Vice versa, had Massry and Akmal read the 'previous' literature carefully, our papers included, they would have been more prudent in the conclusions they drew [9]. We think that the role of PTH as uremic toxin is still quite a debatable issue in view of the increasing bulk of contradictory data that come from institutes other than the Division of Nephrology of the University of Southern California.

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