## Urinary proteins in multiple myeloma: strong correlation with the indices of tumor burden

Urinary α1 microglobulin (α1M), IgG and albumin (alb) are more sensitive parameters of renal dysfunction, than creatininemia and uremia. We report the history of two multiple myeloma patients in whom variations of urinary proteins strictly correlate with those of tumor burden indices, suggesting a possible new role for these proteins.

GL, a 54-year old white man, with a previous history of monoclonal gammopathy of unknown significance (MGUS) IgGκ, came to our attention in February 2000 because of progression of his disease into plasma cell leukemia. Laboratory tests showed: bone marrow plasmocytosis (BMPC) of 70%, monoclonal component (MC) of 4.8 g/dL, serum $\beta_2$ microglobulin ($\beta_2$M) of 7,570 mg/dL, and alteration of urinary proteins (Figure 1). He underwent chemotherapy with 2 cycles of pulse-VAD and two DCEP (dexamethasone, cyclophosphamide, etoposide, and cisplatin), without response. In fact, disease parameters worsened ($\beta_2$M 8,139 mg/dL, BMPC 90%, MC 6.1 g/dL), and contemporaneously a worsening of urinary protein values was recorded (Figure 1). He started thalidomide and, after three months, his performance status improved with an amelioration of disease parameters ($\beta_2$2M 2534 mg/dL, BMPC 4%, MC 3.4 g/dL) and urinary proteins (Figure 1).

PL, a 50-year old white man, was referred to us because of multiple myeloma IgGκ at clinical stage IIA, which had progressed from a MGUS lasting ten years. He received a high dose protocol of chemotherapy and an autologous transplantation, conditioned with high dose melphalan, and obtained a very good partial response. Seventeen months after transplantation his disease progressed. Laboratory examinations showed BMPC 50%, MC 3.4 g/dL, $\beta_2$M 3,900 mg/dL, and high values of urinary markers (Figure 2). After two months of chemotherapy the disease parameters had improved (BMPC 20%, MC 2.7 g/dL, $\beta_2$M 3,160 mg/dL), and so had the urinary proteins (Figure 2). The response was maintained under treatment for five months after which the disease progressed ($\beta_2$M 4,043 mg/dL, MC 4.5 g/dL, BMPC 70%), with a parallel worsening of urinary proteins (Figure 2).

Renal involvement in multiple myeloma is usually evaluated and monitored with serum parameters which do, however, have a low sensitivity and are consequently inadequate for identifying initial renal damage. Several previous reports have demonstrated an important role of urinary proteins in better definition of renal damage, and in identifying those patients who deserve more accurate examination (renal biopsy).[1-4]

The cases described here shed new light on a possible further use of urinary parameters as markers of disease progression. In fact, both patients showed a parallel behavior of disease parameters ($\beta_2$M, MC, BMPC), and urinary markers of renal function ($\alpha_1$M, IgG, albumin). On the basis of this close correlation, it may be hypothesized that urinary proteins are not only reliable indicators of renal involvement, but also indices of disease. In that case, they could be used, together with $\beta_2$M, MC, and BMPC, for the staging and the monitoring of multiple myeloma.[5,6]

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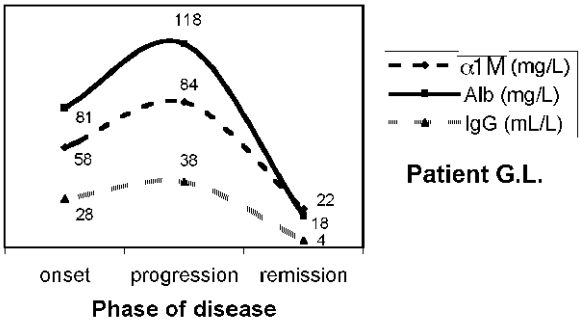


**Figure 1. Modifications of urinary protein values in relation to the clinical course of the disease in patient G.L.**

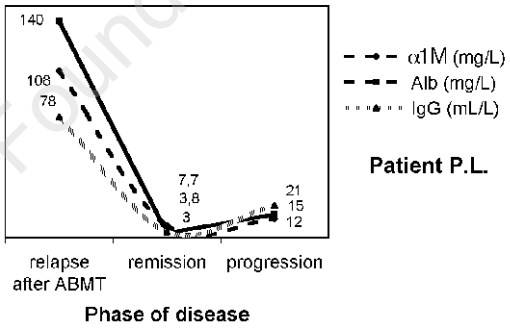


**Figure 2. Modifications of urinary protein values in relation to the clinical course of the disease in patient P.L.**



## References

1. Yu H, Yanagisawa Y, Forbes MA, Cooper EH, Crockson RA, MacLennan IC. α1-microglobulin: an indicator protein for renal tubular function. J Clin Pathol 1983; 36:253-9.
2. Cooper EH, Forbes MA, Crockson RA, MacLennan IC. Proximal renal tubular function in myelomatosis: observations in the fourth Medical Research Council Trial. J Clin Pathol 1984; 37:852-8.
3. Honkanen E, Pettersson T, Teppo AM. Urinary α1- and β2-microglobulin in light chain proteinuria. Clin Nephrol 1995; 44:22-7.
4. Corso A, Serricchio G, Zappasodi P, et al. Assessment of renal function in patients with multiple myeloma: the role of urinary proteins. Ann Hematol 1999; 78:371-5.
5. San Miguel JF, Blade Creixenti J, Garcia-Sanz R. Treatment of multiple myeloma. Haematologica1999; 84:36-58.
6. Harousseau JL. Optimizing peripheral blood progenitor cell autologous transplantation in multiple myeloma. Haematologica 1999; 84:548-53.