

BENCE JONES PROTEIN IN PRIMARY SYSTEMIC AMYLOIDOSIS

To the Editor:

The recent population-based study by Kyle et al,¹ which was the first to provide precise epidemiologic information about primary systemic amyloidosis, reported the demonstration of a monoclonal (M)-protein in the serum or urine from 16 of 21 patients (76%) with amyloid of unequivocal Ig origin (AL).

However, the number of patients in whom free monoclonal Ig light chain (ie, Bence Jones [BJ] protein) represented the sole detectable M-protein was apparently lower than I would have expected to find in this disease. The frequency with which BJ proteinuria occurred in association with an intact M-protein in the serum is somewhat difficult to evaluate from the separate presentation of the results of the serum and urine investigations. All but one patient had the serum protein pattern analyzed by at least electrophoresis, with an M-protein band being recognizable in 18 (90%), whereas in only 2 (12%) of the 17 patients who had their serum further investigated by immunoelectrophoresis or immunofixation did the M-protein consist of free λ light chain. The search for BJ protein by immunoelectrophoresis or immunofixation was negative in the urine from one-third of the 15 patients and 3 others had a normal urine electrophoretic pattern. Thus, negative results were obtained in 44% of the 18 patients who had their urine studied by at least electrophoresis. These figures most likely reflect the necessary inclusion in such a retrospective study of patients who had their serum and urine examined by using less sensitive techniques than those available at present. The same reason might also account in part for the 11% to 14% frequency of "nonsecretory" AL reported in other large series,^{2,4} from which the occurrence of BJ protein alone can be inferred to be as much as 43%.^{3,4}

Over a 10-year period since 1980, when our laboratory introduced immunofixation in combination with a high-resolution agarose gel electrophoresis⁵ for the routine investigation of M-proteins in the serum and concentrated urine, 18 patients (9 males and 9 females from 47 to 79 years of age; median, 68 years) were recognized as having systemic deposition of AL without evidence of coexistent

multiple myeloma or any other B-lymphoproliferative disease. BJ protein was demonstrated in the urine from 89% of the patients, being the only M-protein in 61% of the cases (Table 1). BJ protein bands were also evident on serum electrophoresis of 5 patients, 4 of whom presented with serum creatinine levels greater than 177 $\mu\text{mol/L}$ and with greater than 3 g of BJ protein excretion per day. Although most patients without an intact serum M-protein excreted BJ protein at amounts detectable by electrophoresis and immunofixation of unconcentrated or 100-fold concentrated urine, BJ protein would have been missed in almost one-third of the series by using such a degree of urine concentration.

These findings agree with our laboratory's experience in demonstrating that the results of screening for BJ protein depend not only on the application of immunofixation itself but also on the sensitivity of the electrophoretic method used, as well as the degree of urine concentration.⁶⁻⁹ In a series of 152 patients with IgG and IgA myeloma,⁶ BJ protein was detected in 78% of the urines concentrated up to 300-fold, whereas an overall incidence of 96% was obtained by using higher degrees of urine concentration. The finding of 85% of cases with an immunocytic malignancy, including multiple myeloma and amyloidosis, among 33 patients who excreted less than 0.2 g/d of BJ protein without any intact M-protein detectable in their serum⁸ further stresses the clinical interest of demonstrating BJ proteinuria even when it occurs at such small concentrations that are likely to remain undetected by the routine procedures used in most hospital clinical chemistry laboratories.

The ability to confidently detect small amounts of urine BJ protein would be of even more interest for the clinician in primary systemic amyloidosis, as the discovery of such an M-protein abnormality does often suggest appropriate investigation and diagnosis.^{2,3}

ENZO PASCALI
*Institute of General Clinical Medicine
 University of Trieste
 Trieste, Italy*

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Table 1. Serum and Urine M-Proteins in 18 Patients With Primary Systemic Amyloidosis

M-Protein	No. of Patients (%)	Serum BJ Protein No.	BJ Proteinuria			
			Total No.	Excretion (g/d)		
			<0.2	0.2-0.99	≥1	
Intact M-protein						
IgG κ	1 (6)	0	1	0	1	0
IgG λ	4 (22)	0	2	2	0	0
IgA λ	2 (11)	0	2	1	1	0
Total	7 (39)*	0	5	3	2	0
BJ protein only						
κ	4 (22)	1	4	2	0	2
λ	7 (39)	4	7	0	2	5
Total	11 (61)	5†	11	2	2	7
All M-proteins	18 (100)	5	16‡	5	4	7

* Serum M-protein concentration (median, 1.4 g/dL; range, 0.5 to 3.5 g/dL).

† Serum BJ protein concentration (median, 0.37 g/dL; range, 0.1 to 0.9 g/dL).

‡ Urinary BJ protein excretion (median, 0.92 g/d; range, 0.17 to 16.6 g/d).

RESPONSE

Dr Pascali has correctly emphasized the importance of finding a monoclonal protein in the serum and urine of patients with primary amyloidosis (AL). As he pointed out, our study began in 1950, when immunoelectrophoresis and immunofixation were not available.

We found that 85% of the 710 AL patients we examined at the Mayo Clinic from 1982 through 1991 had a monoclonal protein in the serum or urine. When we examined the bone marrow for a monoclonal excess of plasma cells in patients without a monoclonal protein in the serum or urine, we found that 98% of patients with AL will have either a monoclonal protein in the serum or urine or a monoclonal excess of bone marrow plasma cells.¹ Immunohisto-

chemical staining of the amyloid is necessary in the remaining patients to differentiate AL from hereditary or senile systemic amyloidosis.

ROBERT A. KYLE
Hematology and Internal Medicine
Mayo Clinic
Rochester, MN

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