

CONTRIBUTION OF THE QUANTITATION OF FREE LIGHT CHAINS IN 273 PATIENTS PRESENTING WITH A NEWLY DISCOVERED MONOCLONAL GAMMOPATHY

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INTRODUCTION

Quantitation of free light chains kappa and lambda (FLC) has become an important step in the diagnosis and follow up of patients with lymphoproliferative and plasma cells diseases. Between January 2002 and June 2004, 1160 patients attending a general hospital in Lyon (France) had their FLC quantitated. Of them, 273 presented with a newly discovered monoclonal gammopathy which was to be investigated. We report here our experience in the contribution of the quantitation of the serum FLC in patients with monoclonal gammopathies.

METHODS

273 sera issued from 151 males and 122 females were diagnosed in our laboratory as having a monoclonal gammopathy using capillary electrophoresis (Paragon CZE 2000[®], Beckman), a semi-automated electrophoresis-immunofixation (IFE) technique (SPIFE[®], Helena) and a modified technique of immunoelectrophoresis (IEP). FLC kappa and lambda were quantified by nephelometry (BN II[®], Dade Behring) using specific antibodies (The Binding Site). In 83 cases the serum was associated with a sample of a 24h-urine collection which after concentration was submitted to electrophoresis and IEP. Patients were then classified into 4 groups according to the concentration of FLC and to the value of κ/λ ratio. Comparisons taking into account the group and the clinical diagnoses were made.

RESULTS

Table 1 : Classification of 273 patients according to FLC quantitation, κ/λ ratio and the clinical diagnoses.

Clinical diagnoses	Group I	Group II	Group III	Group IV	Total
	3.3 mg/l < κ_1 < 19.4 mg/l 5.7 mg/l < λ_1 < 26.3 mg/l 0.26 < κ/λ_1 < 1.65	κ_1 > 19.4 mg/l and/or λ_1 > 26.3 mg/l 0.26 < κ/λ_1 < 1.65	κ_1 > 19.4 mg/l and/or λ_1 > 26.3 mg/l 0.26 > κ/λ_1 > 1.65	κ_1 < 19.4 mg/l λ_1 < 26.3 mg/l 0.26 > κ/λ_1 > 1.65	
MGUS	35 (35.4%)	24 (24.2%)	35 (35.4%)	5 (5%)	99
Myeloma	2	1	74 (93.7%)	2	79
Plasmacytoma		1	4		5
Waldenström macroglobulinaemia		2	6		8
Amyloidosis (AL)	1		2		3
Non-Hodgkin malignant lymphoma	1	1	2		4
B-cell chronic lymphocytic leukaemia		1	1		2
Plasma cell leukaemia			1		1
No diagnosis at the time of the study	22 (30.6%)	17 (23.6%)	29 (40.2%)	4 (5.6%)	72
	61 (22.4%)	47 (17.2%)	154 (56.4%)	11 (4%)	273

Table 2 : Classification of 201 patients according to κ/λ ratio and the clinical diagnoses.

Clinical diagnoses	Normal κ/λ ratio	Abnormal κ/λ ratio	Total
	Group I + II	Group III + IV	
MGUS	59	40 (40.4%)	99
Plasma cell dyscrasia	5	83 (94.3%)	88
Lymphoproliferative disorders	5	9 (64.2%)	14
	69	132	201

When clinical diagnoses were taken into account, a highly significant difference ($p < 10^{-4}$) appeared between patients with myeloma (79) and patients with monoclonal gammopathy of undetermined significance (MGUS) (99) : 74 patients with myeloma (93.7%) were in group III, while only 35 (35.4%) patients with MGUS were in this group.

FLC quantitation may detect monoclonal gammopathies liable to undergo a malignant evolution.

Table 3 : Serum κ/λ ratio in 22 patients with a normal β_2 fraction.

Clinical diagnoses	Normal κ/λ ratio	Abnormal κ/λ ratio
	Group I + II	Group III + IV
	4	18 (82%)
		8 Myeloma 3 MGUS 1 Amyloidosis (AL) 1 Lymphocytic leukaemia 1 Plasmacytoma 1 NHML 3 No diagnosis
Serum M. component	2 M. IgAk 2 M. IgAl	1 M. IgAl, + s.BJP 1 M. IgAl 7 s.BJP 9 s.BJPk

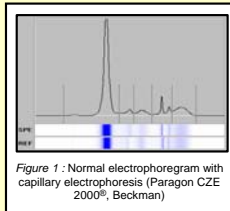


Figure 1 : Normal electrophoresis with capillary electrophoresis (Paragon CZE 2000[®], Beckman)

Quantitation of FLC may detect patients showing no evidence of monoclonal gammopathy on the electrophoresis.

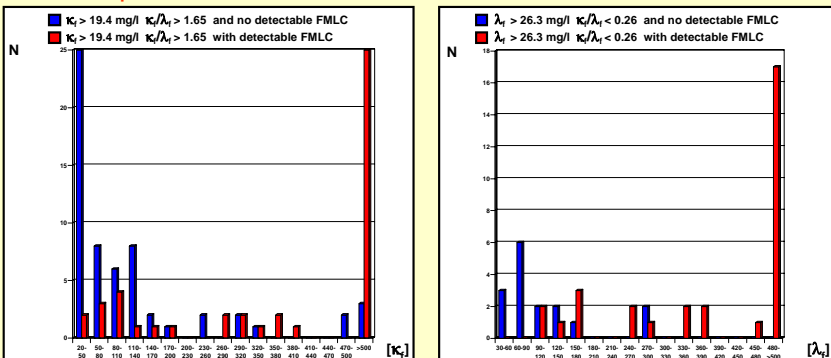
Table 4 : Serum κ/λ ratio in patients with and without a urinary BJP.

Bence Jones Proteinuria	Normal κ/λ ratio	Abnormal κ/λ ratio	Total
+	6 (9%)	61 (91%)	67
-	5	12	17
	11	73	84

6 patients (9%) had an unexpected normal κ/λ ratio, when it should have been abnormal : 1 had an amyloidosis (AL), 1 had a MGUS and 1 a myeloma with an IgA M. component. The 3 others had no diagnosis at the time of the study.

For metabolic reasons, serum should be preferred to urine for assessing FLC concentrations. But here, in 6 cases of 67, the ratio was within the reference range while there was a BJ proteinuria.

Figure 2 : Distribution of FLC according to the range of their concentration and the presence or absence of FLMC on conventional immunodetection tests.



a) The lowest concentration of κ_1 associated with a s. κ BJP was 28.7 mg/l. The highest one associated with no detectable s. κ BJP was 880 mg/l.

b) The lowest concentration of λ_1 associated with a s. λ BJP was 75.5 mg/l. The highest one associated with no detectable s. λ BJP was 293 mg/l.

Histograms showing that similar concentrations of κ_1 (or λ_1) and an abnormal ratio may or may not result in the occurrence of a s.BJP. In less than 50% samples (77/155), FLMC were correctly identified using IFE.



Figure 3 : IEP showing sera with M. components and BJP.

CONCLUSION

The preliminary results of this study confirm previous results obtained by others showing how valuable FLC quantitation may be, especially when there is no evidence of monoclonal gammopathies on the electrophoresis. Moreover, less than 50% samples with an elevated concentration of κ or λ FLC appeared to be positive for FLMC when using IFE. They also suggest that an abnormal κ/λ ratio and one or both FLC falling outwards the reference range might be the first sign of a malignant evolution for a MGUS.

