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Evaluation and Presentation of laboratory Results in Patients suspected of a monoclonal Gammopathy:

T*he value of free light Chains in Bence Jones Testing*

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Introduction

Patients suspected or presenting with a monoclonal gammopathy accumulate a lot of data (i.e. electrophoresis, immunofixation, immunoglobulin, etc). Since 1998 we present all relevant information in serum and urine including a colour-coded electrophoresis on a single cumulative page (Figure). The information on this page covers a time span up to 5 years.

This concept has several advantages, for instance:

- All relevant information, is, with little training, visible and self explanatory.
- Problems with a specific sample are evident. A low urinary creatinine concentration that indicates an invalid pre-analytical will be detected.
- Results for patient samples arriving on two different days in the laboratory (serum and urine) are both part of the cumulative report.
- Surveillance of long time patients, i.e. yearly check-up of renal transplant patients is simplified.

The measurement of free light chains could be integrated easily into this concept. The additional value of the test can be compared with existing laboratory measurements.

Intention of study

The standard method of detecting free light chains in urine (Bence Jones Protein, BJP), urinary immunofixation (IFE) is laborious and expensive. We evaluated free Kappa (FK) and Free Lambda Light Chains (FL) and the corresponding Kappa to Lambda (Fκ/Fλ) ratio as an alternative method.

Methods

Immunofixation in serum and corresponding urine immunofixation (Sebia), nephelometric free light chain determination (detection limit 5 mg/ l, New Scientific Company, Cormano (MI), Italy). Indecisive urinary immunofixation results were independently visually inspected by a second person and inconclusive samples rerun with different antibodies (Beckman-Coulter).

Study population

Routine urinary samples of the Kantonsspital Basel. Serum test results for immunofixation were available for all patients.

Two subgroups were evaluated:
One consisted of patient samples sent to the laboratory for the differentiation of proteinuria (n= 157). Most of these patients presented with elevated free light chains due to tubular dysfunction. This was the control group, as immunofixation in serum and urine was negative for a monoclonal gammopathy.

Samples of the second group were highly suspicious for BJP. It consisted of patients with a proven monoclonal gammopathy in serum (n= 147).
Both groups were classified according to the results of free light chain measurement (Classification).

Results

Most of the proteinuria samples showed elevated free light chains with a Fκ/Fλ ratio of 1.0 – 3.7. BJP patients presented either with a Fκ/Fλ ratio below 1.0 (Lambda monoclonal light chains) or above 3.7 (Kappa monoclonal light chains). The free Lambda concentration was below the detection limit for six samples and no ratio could be calculated.

Conclusion

In our study group, a fκ/fλ ratio below 1.0 or above 3.7 has a diagnostic sensitivity of 98% and a diagnostic specificity of 80% when compared with urinary immunofixation, provided that both free light chains are measurable. The patients are very likely to have BJP. IFE should serve as the confirmation method.

We also found free monoclonal light chains in six patients where the ratio could not be calculated as lambda was below the detection limit.

If BJP is clinically suspected, IFE is also indicated.

The detection limit of IFE (20 mg/l), however, is higher than that of nephelometry (5 mg/l) and cannot be considered a gold standard in these cases.

The most relevant finding is that BJP can be ruled out with 99% specificity in cases where the Fκ/Fλ Ratio is between 1.0–3.7.
Thus, a urinary immunofixation could have been avoided in 130 of 304 (42.7%) samples.

It must be emphasised, that a serum immunofixation is always required in patients to reliably diagnose or exclude a monoclonal gammopathy.

Figure 1

Kantonsspital Basel
Universitätskliniken
Dep. Zentrallaboratorium

Proteinelektrophorese und Immunfixation

Chemielabor
Petersgraben 4, CH-4031 Basel
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Zellersatzambulatorium

Pat. **B..... M.....**
Geb./Geschl. **00.00.1900 / W**

Fall-Nr. **00000000000000**
Pat.-Nr. **01111111111**

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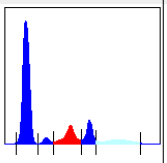
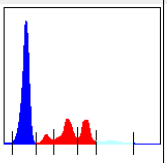
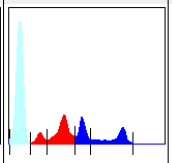
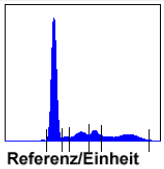
Auftrag-Nr. 5132337 **Labor-Nr.** PR000035 / 20.09.01 **Entnahme** 20.09.01 12:24

Diagnose/Fragestellung

11.06.2001	09.07.2001	17.07.2001	20.09.2001	20.09.2001	Serum		
							
					Analyse	**Referenz/Einheit**	
60.0 -		50.0 -	57.0 -		**Totalprotein**	62-80g/l	
37.4 62.4%		29.0 57.9%	29.7 52.1% -		**Albumin**	34.7-56.0g/l	56.0-70.0%
1.9 3.2%		2.5 4.9% +	2.9 5.0% +		**Alpha-1**	1.0-2.9g/l	1.6-3.6%
8.5 14.1% +		9.1 18.1% +	11.1 + 19.5% +		**Alpha-2**	5.0-10.4g/l	8.0-13.0%
6.8 11.4%		7.2 14.3% +	6.2 10.9%		**Beta**	5.0-11.2g/l	8.0-14.0%
5.3 - 8.9% -		2.4 - 4.8% -	7.1 12.4%		**Gamma**	6.2-14.4g/l	10.0-18.0%
		negativ	IgG Kappa 2.90		**Leichtketten- Nachweis** **M Gradient**	g/l	
0.63 -		0.13 -	1.43		**IgA**	0.70-3.80g/l	
4.11 -		2.01 -	6.93		**IgG**	6.50-15.00g/l	
0.66		0.10 -	0.36 -		**IgM**	0.50-2.60g/l	
		keine Ang.		2.Morg.U.	**Urin**		
	ka 2.48 -	ka 1.39 -		ka 2.83 -	**Urinvolumen**	-2000ml	
		0.06		<0.04	**Kreatinin**	7.00-18.00mmol/l	
					Totalprotein	<0.07g/l	
	negativ	negativ		negativ	**Leichtketten- Nachweis**		
	4.0 1.6 +	6.0 + 4.3 +		8.0 + 2.8 +	**Kappa, frei**	5mg/l	<0.57mg/mmol
	<4	<4		<4	**Lambda, frei**	5mg/l	

Beurteilung

Unterschrift Dr.med. A. Regeniter

Legende: - erniedrigt, + erhöht, nb nicht bestimmbar, nbr nicht berechenbar

Table 1 - Classification

		Proteinuria N = 157	BJP Suspicious N = 147	
Group	**Free Light Chains**	**(Control)**	**No BJP**	**with BJP**
A	FK and FL < 5 mg/l	10	34	0
B	FK between 5-25 mg/l , FL <5 mg/l	37	23	6
C	Fκ/Fλ Ratio > 3.7	1	1	29
D	Fκ/Fλ Ratio < 1.0	8	3	22
E	Fκ/Fλ Ratio between 1.0 and 3.7	101	28	*1
* Patient with a bi-clonal gammopathy and simultaneous excretion of FK and FL chains				

Table 2

Group	Combined Collectives (N = 304)	Total Number	with BJP
A	FK and FL < 5 mg /l	44	0
B	FK between 5-25 mg/l , FL <5 mg/l	66	6
C	Fκ/Fλ ratio > 3.7	31	29
D	Fκ/Fλ ratio < 1.0	33	22
E	Fκ/Fλ ratio (KL 1.0- 3.7)	130	*1
* Patient with a bi-clonal gammopathy and simultaneous excretion of FK and FL chains			