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Detection of a monoclonal gammopathy by lipemia-index measurement

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Introduction

Monoclonal gammopathy is defined by the presence of monoclonal immunoglobulins in serum or urine. It is caused by the proliferation of a single clone of plasma cells and is visible in serum electrophoresis as a single, sharply defined band. The monoclonal immunoglobulin is also called paraprotein or M-protein and can occur in human serum in extremely high concentrations (1). A single M-protein is homogeneous in terms of its structure and specificity. It consists of either complete immunoglobulin molecules or fragments, which may form polymers. This can influence the solubility and binding ability in a non-predictable way (2, 3). M-proteins in clinical chemistry assays are attracting increasing attention. When it occurs in very high concentrations, it may cause significant interference in clinical chemistry assays (4, 5). Serum indices are calculations of absorbance measurements that provide a semi-quantitative representation of levels of icterus, hemolysis, or lipemia that are present in patient samples. These indices can be easily measured on a Modular P analyzer by spectrophotometry. Here, we report a case in which a monoclonal gammopathy was detected by measurement of the serum lipemia-index on a Modular Analytics P module.

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Methods

A 50 year old female patient was admitted to the hospital for loss of consciousness and a resulting wound on her head. Upon admission a plasma sample was drawn and serum indices, creatinine, urea nitrogen, electrolytes, glucose, total protein, CRP, and liver enzymes were measured on a Modular P analyzer (Roche Diagnostics, Manheim, Germany) according to the manufacturer's manual.

For serum index measurement 8 µl of sample is mixed with 200 µl of saline and the bichromatic wavelength pairs at 480 and 505, 570 and 600, and 660 and 700 nm are measured. Based on these absorbances semi-quantitative values are calculated for the degree of lipemia, hemolysis and icterus present in the sample.

Table 1. Immunoglobulin and serum index results in the patient's sample at 18.04.08. Results outside the reference range are bold. * Later a M-protein of type IgM-λ was confirmed.

		Sample	Ref. range	
IgM*		**26**	0.4-2.3	g/l
IgG		7.6	7.0-16.0	g/l
IgA		**0.62**	0.70-4.0	g/l
κ		1.40	0.38-3.75	g/l
λ		**3.18**	0.93-2.42	g/l
κ/λ ratio		**0.44**	1.17-2.93	
Serum index	L	**4000**	<1000	
	H	32	<300	
	I	0	-	

The degree of lipemia can be more precisely described as the degree of turbidity in the sample. The lipemia-index is more or less equivalent to the Intralipid concentration up to the linearity limit of 10 g/l.
Screening and quantification of M-protein was performed on a Sebia Capillarys (Sebia, Lisses, France). Immunoglobulins, Kappa and Lambda bound and free light chains were determined on a Modular P analyzer.

Results

The lipemia (turbidity) index showed a value of 4000 although the sample itself was perfectly clear. The other results were abnormal or suspected to be either false or not plausible, e.g. a negative glucose, a very high creatinine (726 µmol/l) and urea (12.9 mmol/l) levels were measured. Later, values of creatinine up to 1286 µmol/L were found. The thought of a gammopathy crossed our minds but was quickly dismissed, because of a total protein level in the sample that was below the upper limit of 80 g/l. The possibility of medication interference was also considered, but additional experiments could not confirm interaction between the drugs the patient took and our tests.
Since no satisfactory explanation could be found further investigations were initiated including the measurement of immunoglobulins. The results and corresponding reference ranges are shown in table 1. The sample contained a very high concentration of IgM (26 g/l) which is indicative for the presence of a monoclonal gammopathy. Therefore, the concentrations of Kappa and Lambda bound and free light chains were determined. These showed a ratio that was below the normal range. Further investigations showed that the patient has a monoclonal gammopathy of the type IgM-lambda caused by a morbus Waldenström as confirmed by bone marrow investigation, which was not known. The M-protein most probably was responsible for the formation of turbidity upon dilution with saline. In the meantime, the patient sample was send to another hospital where creatinine was determined by the Jaffé method (instead of the enzymatic method), which yielded a normal value of 70.4 µmol/L. Urea was also measured and was within the reference range (4.9 mmol/L).

Conclusion

This case nicely supports the fact, that the behaviour of M-proteins is highly unpredictable. In most cases samples containing a M-protein can be easily diluted with saline without precipitation. However, in this case the M-protein precipitated upon dilution with saline, resulting in turbidity and an elevated lipemia-index. More importantly, the previously unknown monoclonal gammopathy was hereby detected.
Therefore, we would like to stress that when a sample has a high lipemia-index but is not visibly lipemic, one should consider the presence of a M-protein and the appropriate reflex test should be performed.

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