Macroglobulinemia Associated with IgA Gammopathy in a Patient with Different Light-Chain Specificity and No Associated Clinical Findings, V. T. Innanen, E. Maalihnan, T. Lipo, N. Korogyi, and F. Recknagel (Div. of Clin. Biochem., Women's College Hosp., Toronto, Ontario; and Dept. of Clin. Biochem. (V.T.I.), Univ. of Toronto, Toronto, Ontario, Canada)

We describe an unusual case of macroglobulinemia—myeloma with light chains of differing specificity in a 96-year-old man. The patient presented for investigation of lower back pain secondary to a fall. Positive clinical findings included a small compression fracture involving L1, attributed to the fall, and mild congestive heart failure treated with digoxin. The concentrations of albumin, electrolytes, creatinine, urea, calcium, erythrocytes, and leukocytes in serum were within normal limits. On immunoelectrophoresis we found the bicalonal gammopathy shown in Figure 1, confirmed by immunofixation (not shown). IgM, on immunquantification, was 7.51 g/L (normal, 0.45–2.50 g/L). IgG and IgA were within normal limits. A bone-marrow sample from the iliac crest was normal.

This case is unusual in several respects. Only one previous report of a macroglobulinemia associated with IgA myeloma with differing light chains has been reported (1). That case, however, differed from ours in that it was associated with a lymphocytic lymphoma. Recently, Weinstein et al. (2) reported a case of IgM(κ), IgA(κ) double

![Fig. 1. Agarose immunoelectrophoresis of the patient's serum](image)

We used Conring Universal agarose electrophoresis film (Conring, Palo Alto, CA), barbitral buffer (50 mmol/L, pH 8.6) containing 0.35 g of EDTA per liter, antisera from Kallestad Laboratories, Inc., Austin, TX, and Amido Black to stain the gels. The gels were run for 35 min at 20 V. The extraneous IgM arc (arrow 2) shifts on reduction (arrow 4) with 2-mercaptoethanol to occupy a slightly more anodic position (arrow 4); this corresponds to the distortion in the kappa line brought about by the reduction (arrow 5). The extraneous IgA arc (arrow 1) in the β region corresponds to the lambda arc (arrow 2).

![Graph](image)

Fig. 1. Linear comparison between measured (abscissa) and predicted by Widmark curve (ordinate) equilibrated plasma concentrations of ethanol above 3 mmol/L after intravenous injection in dogs

Measured Ethanol Concentrations (mmol/L)

<table>
<thead>
<tr>
<th>Predicted Ethanol Concentrations (mmol/L)</th>
<th>Measured Ethanol Concentrations (mmol/L)</th>
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<tbody>
<tr>
<td>3</td>
<td>1</td>
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<tr>
<td>9</td>
<td>2</td>
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<tr>
<td>15</td>
<td>3</td>
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<tr>
<td>21</td>
<td>4</td>
</tr>
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\[
y = 0.2 + 0.99x \\
r = 0.992 \ (p < 0.01)
\]

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gammopathy, but light-chain specificity was identical for both. They suggested that this would provide evidence for the origin of both lines of gammopathy in a common stem cell. The reverse would seem to be the case in our situation, where the light chains are not identical. A suitable characterization would therefore appear to be benign bicalonal gammopathy, "benign" because several standard criteria used to distinguish benign monoclonal gammopathies—such as negative clinical findings, normal albumin, paraprotein <30 g/L, no suppression of alternative immunoglobulin, normocelia, and normal bone marrow—were present in the patient. In addition, about a year after initial investigation, the IgA, IgM, IgG values have shown no significant change.

Macroglobulinemia—myeloma double gammopathy in itself is an extremely rare finding (1, 3), and this case further illustrates the heterogeneity of clinical presentation in these patients first described by Pruzanski et al. (3). Most patients with macroglobulinemia—myeloma present with manifestations unrelated to either gammopathy. This diversity can range from various lymphomas (1, 3) to von Recklinghausen's neurofibromatosis (4, 5). This bicalonal gammopathy, detected incidental to the investigation of back pain, further illustrates that the clinician will place heavy reliance on the laboratory to detect double gammopathies, which remain extremely variable in their clinical presentation.

References


Several kits for quantifying lipase (EC 3.1.1.3) in serum are commercially available. In one, the "Delta Test Assay" by Princeton Biomed (division of Electronucleonics, Inc., Fairfield, NJ), a turbid suspension of olive oil (triglycerides, 84% oleic acid) is hydrolyzed by the enzyme, diminishing turbidity (1).

We find this method easily adapted to centrifugal analyzers, with concomitant savings in time and money. Specifically, with the CentrifChem 500 (Baker Instruments, Allentown, PA), the following advantages were realized: (a) The size of a batch (specimens and controls) is increased from seven in the manual assay to 29, with a corresponding decrease in analysis time for 28 samples from 1.5 to 0.5 h. (b) The volume of serum is reduced from 100 µL to 20 µL and the working substrate required from 3 mL to 350 µL per test, an 8.6-fold decrease in reagent use. (c) With the manual assay, some specimens showed a paradoxical increase in turbidity, for reasons not well understood; these same specimens showed either no change or a decrease in turbidity in the automated method. Additionally, whether manual or automated, this assay requires no calibrator, again with a cost savings.

Various operating settings and characteristics have been defined. By dilution studies, we have found that the useful technical range of the assay extends to 450 U/L.

The normal reference interval, as established from the middle 95% of lipase values from patients presenting at Erie County Medical Center for one-day surgery is 13 to 72 U/L, with a positive skew to the distribution. This range is narrower than that quoted by Princeton Biomedix and many other manufacturers.

We have found it useful and necessary to predetermine the concentration factor of the lipid emulsion (using a molar turbidity constant analogous to an absorbivity value) in a preliminary run to take advantage of the instrument's calculation capability. This also is necessary because of the variability between preparations of substrate and within the same preparation on successive days of use. We have also found it necessary to use an assay temperature of 37 °C, there being insufficient activity over the assay time interval at lower temperatures.

Evidence (2) suggests that lipase may be a more specific assay for pancreatic conditions than that for amylase, or perhaps even amylase isoenzymes, and is a simpler assay than the latter.

References

Measurement of Serum Estradiol: Comparison of Three "Direct" Radioimmunoassays and Effects of Organic Solvent Extraction, C. M. G. Thomas, R. J. van den Berg, and M. F. G. Segers (Dept. of Obstet. & Gynecol., Sint Radboud Hosp., Catholic Univ., 6525 GA Nijmegen, The Netherlands)

Immunochromatographic techniques for estradiol measurement in serum include either extraction of serum with organic solvent ("extraction assays"), or the serum sample is applied without any pretreatment ("direct assays"). Direct assays are much easier to perform and faster, but results are affected by the presence of steroid-binding proteins (e.g., albumin, sex-hormone binding globulin), thereby (a) decreasing the amount of free estradiol available to bind the assay's antibody, and (b) interfering in this reaction and so affecting the immunochromatographic reaction kinetics. Thus direct assays may lead to lower results for estradiol concentrations than do extraction assays. To study this possibility, we compared three direct estradiol kits ("Spectra" (Spe; Farmos, Turku, Finland), the "Coat-A-Count" no extraction RIA (Diagnostics Products Corp. (DPC), Los Angeles, CA), and the "125I-Estradiol" direct (ER 156) and extraction (ER 150) RAs (Clinical Assays, Cambridge, MA).