State <10 in most cases), the laboratory values from the five AD patients with MG showed only mild abnormalities: three had albumin >30 g/L and two >27 g/L; four had transferrin >2.5 g/L and one had 1.9 g/L; thus the term undernutrition would have been more appropriate in our report.

We are aware that MG increase with age in various diseases (3), but we stress that the long period of observation of our patients allowed a reasonable accuracy in the diagnosis and ruling out of AD and certain other underlying diseases.

References

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Editor’s note: The results of Pirttila et al. and those of Berni et al. regarding monoclonal gammopathies (MG) may be less different than their Letters might suggest. The results are summarized below.

<table>
<thead>
<tr>
<th>MG</th>
<th>No MG</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Berni et al.</td>
<td>5</td>
<td>15</td>
</tr>
<tr>
<td>Pirttila</td>
<td>3</td>
<td>43</td>
</tr>
<tr>
<td>Total</td>
<td>8</td>
<td>58</td>
</tr>
</tbody>
</table>

By Fisher’s Exact Test, the two-tailed P-value is 0.0486; thus, such a difference as they report may be found 1 time in 20 by chance alone. Further studies will no doubt clarify the matter.

Kinetic Error on Kodak Ektachem: A Clue in Diagnosis of Myeloma

To the Editor:

Kinetic error flags (KE) on the Kodak Ektachem 700 (Eastman Kodak, Rochester, NY) are uncommon, but may occur on aspartate aminotransferase (AST) analyses in patients with multiple myeloma. Investigation of AST KEs can lead to the discovery of a monoclonal immunoglobulin in a previously undiagnosed patient.

KE flags are unique to the dry-aside technology used by Kodak instruments. They occur in assays based on reverse kinetic reactions, namely, AST, alanine aminotransferase (ALT), and lactate dehydrogenase (LDH). KEs alert the operator to an abnormality in the progression of the kinetic reaction, e.g., substrate depletion due to high analyte concentration or the presence of an interferent (Kodak Test Methodology Manual MP 2-7, March 1986). Pyruvate and lipemia are common LDH interferents. The interfering substances in AST and ALT measurements are usually immunoglobulins or other proteins (unpublished data; Robert F. Fricker, Eastman Kodak Clinical Products Div.). In our experience, almost all KEs are found on AST measurements.

KEs commonly indicate substrate depletion in patients with high AST concentrations. However, when they occur in patients with normal AST values, they are often due to high immunoglobulin concentrations, as are commonly found in myeloma patients. High concentrations of immunoglobulin or other proteins interfere with AST measurement by increasing the transit time for the sample to pass through the spreading layer. The delay in the initiation of the reaction leads to persistently high reflectance densitometric readings (personal communication; Paul Kildal-Brandt, Eastman Kodak Clinical Diagnostics Div.). The lack of progression of the reaction results in a KE flag.

Because of the frequent association of KE and myeloma proteins, we have established a protocol for investigating all samples with KEs, in an effort to detect undiagnosed myeloma. In our laboratory, all samples with KEs are repeated on dilution to eliminate KEs due to substrate depletion. Any sample with a normal AST that generates a KE is brought to the attention of a supervisor. The laboratory records are reviewed for documentation of a previously identified monoclonal immunoglobulin. If there is no previous diagnosis, a serum protein electrophoresis is performed. Any abnormal band is reported to the clinician and then further evaluated by immuno fixation.

In further investigation to elucidate the relationship between KE and monoclonal immunoglobulins, we measured AST in 31 patients’ samples with known monoclonal immunoglobulins. KEs were found in eight (26%) of the samples and were associated with all types of heavy chains (IgG, IgM, and IgA) and light chains. They were more common in patients with total proteins >80 g/L (range 67–145 g/L) and immunoglobulins >30 g/L (range 24–86 g/L). All myeloma patient samples with KEs had large amounts of monoclonal immunoglobulin.

Concentrates of human albumin and reconstituted lyophilized human immunoglobulin were added to 10 normal serum samples. The addition of human albumin did not yield KEs until the total protein concentration reached 120 g/L or greater. The addition of human immunoglobulin resulted in KEs at lower total protein concentrations (range 78–95 g/L, mean 86 g/L). Mann–Whitney comparison of all samples showed significantly higher total protein (P = 0.0001) and immunoglobulin levels (P = 0.0039) in samples with KE than in samples without KE. There was no correlation between the presence of KE and albumin concentration or concentration of proteins other than immunoglobulins (P = 0.33 and 0.54, respectively). These results suggest that immunoglobulin concentration is the major determinant of KE.

Our laboratory performs >45 000 AST measurements yearly. We estimate that KEs occur in 1 in 8000 patients’ samples. Many of these samples are from patients with known myeloma. Of the remainder, approximately one-half are due to previously unidentified monoclonal immunoglobulin; the rest are due to the polyclonal increases in immunoglobulins usually associated with cirrhosis. In our experience, AST kinetic error only occurs in 25% of patients with myeloma and cannot be used as a screening test. However, the investigation of KE can lead to the diagnosis of multiple myeloma. Over the past 5 years, we have identified at least seven cases of previously undiagnosed myeloma through investigation of AST KE. These patients had large quantities of monoclonal immunoglobulin and were subsequently diagnosed with myeloma. Several of these patients presented with nonspecific complaints or unexplained anemia, and laboratory investigation of the KE provided the first clue to establishing the diagnosis of myeloma.

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