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Focus of this Presentation

This is an immunology case study. You will be presented with clinical and laboratory information and will be prompted with self-learning questions.
Credits

Images and case studies provided by the members of the IQMH Endocrinology and Immunology Scientific Committee, and the IQMH Consultant Technologist.
A 78-year-old male presents to the emergency department with symptoms of shortness of breath and lower back pain.

A CT scan reveals what appear to be osteolytic lesions in his vertebra.
## Laboratory Data – Hematology

<table>
<thead>
<tr>
<th>Test Parameter</th>
<th>Value</th>
<th>Reference Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocyte count</td>
<td>8.4</td>
<td>3.5 – 10.5 x 10^9L</td>
</tr>
<tr>
<td>Erythrocyte count</td>
<td>3.28</td>
<td>3.50 – 5.00 x 10^{12}L</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td>101</td>
<td>115 – 155 g/L</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>0.321</td>
<td>0.380 – 0.500 L/L</td>
</tr>
<tr>
<td>MCV</td>
<td>97.9</td>
<td>80.0 – 100.0 fL</td>
</tr>
<tr>
<td>MCH</td>
<td>30.8</td>
<td>25.0 – 34.0 pg</td>
</tr>
<tr>
<td>MCHC</td>
<td>315</td>
<td>315 – 355 g/L</td>
</tr>
<tr>
<td>RDW</td>
<td>16.4</td>
<td>11.5 – 15.5 %</td>
</tr>
<tr>
<td>Platelet Count</td>
<td>137</td>
<td>130 – 380 x 10^9L</td>
</tr>
<tr>
<td>MPV</td>
<td>11.3 fL</td>
<td>9.0 – 14.0 fL</td>
</tr>
<tr>
<td></td>
<td>Result</td>
<td>Reference Interval</td>
</tr>
<tr>
<td>----------------</td>
<td>--------</td>
<td>--------------------------</td>
</tr>
<tr>
<td>Calcium</td>
<td>2.64</td>
<td>2.12–2.52 mmol/L</td>
</tr>
<tr>
<td>Albumin</td>
<td>27</td>
<td>34–46 g/L</td>
</tr>
<tr>
<td>Protein Total</td>
<td>121</td>
<td>64–82 g/L</td>
</tr>
</tbody>
</table>
Based on the initial presentation, diagnostic imaging and laboratory results, click on which you think is the most likely cause of his elevated total protein.

a) **Dehydration due to decreased oral fluid intake**

b) **Chronic inflammation**

c) **Chronic Obstructive Pulmonary Disease (COPD)**

d) **Multiple myeloma**

e) **HIV infection**

Confidence. *Elevated.*
That’s Correct!

Multiple myeloma.

Continue e-Learn Module
That is not correct

Try Again!
What additional laboratory testing could be recommended?
Think about all that apply, and move to the next slide for the answer.

a) Ionized calcium  
b) Immunoglobulins (IgG, IgA, IgM)  
c) Liver enzymes (AST, ALT, GGT, ALP)  
d) Anti-nuclear antibodies (ANA)  
e) Serum Protein Electrophoresis  
f) Urine Protein Electrophoresis  
g) Beta-2 microglobulin  
h) Lactate dehydrogenase (LDH)  
i) Red cell morphology  
j) Serum free light chains  
k) Electrolytes (Na, K, Cl, CO₂, Anion Gap)  
l) Creatinine
Question 2 - Answer

- Immunoglobulins
- Serum Protein Electrophoresis
- Urine Protein Electrophoresis
- Beta-2 microglobulin
- Lactate dehydrogenase (LDH)
- Serum free light chains
- Creatinine
The International Myeloma Working Group (IMWG) in 2011 generated consensus recommendations for a standard investigative workup which include:

- CBC
- Calcium
- Creatinine
- Nephelometric quantification of serum immunoglobulins (IgG, IgA & IgM)
- Routine urinalysis
- 24h urine collection for urine protein electrophoresis and immunofixation, β2-microglobulin, lactate dehydrogenase (LDH), and serum free light chains.
The recommended initial investigation of suspected myeloma patients include testing to aid in the identification of a monoclonal protein but also include prognostic tests for determination of disease stage (e.g. monoclonal gammopathy of undetermined significance (MGUS) versus smoldering myeloma versus multiple myeloma).

The testing helps differentiate between MGUS or smoldering myeloma and multiple myeloma where there is the presence of end organ damage.
Discussion

• The presence of hypercalcemia, renal dysfunction and anemia are included in the CRAB criteria (hypercalcemia, renal disease, anemia and bone lesions) of multiple myeloma.

• Other biomarkers, such as LDH and $\beta_2$-microglobulin, are prognostic markers or are used in the international staging system for multiple myeloma.
If an anion gap was ordered on this patient, what would you expect the result to be? Think about all that apply, and move to the next slide for the answer.

- Low (below the reference interval)
- Low-Normal (within the reference interval)
- Mid-Normal (within the reference interval)
- High-Normal (within the reference interval)
- High (above the reference interval)
Question 3 - Answer

Low or Low-Normal.
Discussion

• Specimens with highly elevated protein concentrations can produce a low or negative anion gap.
• Calculation of the anion gap (AG) includes the major cations and anions but excludes minor contributions from molecules such as Ca\(^{2+}\), Mg\(^{2+}\), H\(_2\)PO\(_4\)\(^{-}\)/HPO\(_4\)\(^{2-}\) and plasma proteins. Serum or plasma cations and anions must remain at equal concentrations in order to maintain a charge balance (neutrality).
• Under normal conditions, the concentration of unmeasured anions exceeds that of unmeasured cations, and the AG is a positive value, i.e. \( \text{AG} = \text{measured cation(s)} - \text{measured anions} = \text{unmeasured anions} - \text{unmeasured cations} \).

• Therefore, the AG value represents the difference in the concentration of unmeasured anions and unmeasured cations present in the serum/plasma.

• The main source of unmeasured anions is plasma proteins, but includes \( \text{H}_2\text{PO}_4^-/\text{HPO}_4^{2-} \), \( \text{SO}_4^{2-} \) and organic anions.
Some monoclonal proteins, especially IgG, are cationic under physiologic pH, thereby increasing the concentration of unmeasured cations.\textsuperscript{2,3} Although of minor contributions on its own, hypoalbuminemia contributes to lower unmeasured anions and hypercalcemia contributes to unmeasured cations (both conditions are common in multiple myeloma), when present together contribute to a decreased anion gap.
Discussion

- The anion gap can be further decreased due to pseudohyponatremia if an indirect ISE is used to measure serum sodium.
- Therefore, a highly elevated concentration of monoclonal protein and/or the presence of hypercalcemia can disrupt the normal cation to anion ratio with a relative increase in unmeasured cations along with a decrease in unmeasured anions due to hypoalbuminemia, leading to a low or negative anion gap.
Take Away Messages

1. Laboratories should be aware of the potential issues associated with the analysis of specimens from patients with multiple myeloma.

2. Effective interpretation and communication of protein electrophoresis results to clinicians is imperative.
References


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Send an email to:
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