Rheumatoid Factor in serum from patients with monoclonal proteins.
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Introduction

Rheumatoid factor (RF) is one of the most commonly requested tests in rheumatology, and it is also used to classify cryoglobulins.

RF refers to antibodies directed against antigenic determinants on the Fc fragment of IgG (1). RF can be any isotype, though most commonly IgM. The immune complexes formed by RF binding to IgG can be detected and used to determine the RF concentration e.g. by rate nephelometry.

Cryoproteins are associated with B cell malignancy, vasculitic disease, and infectious disease, particularly hepatitis C, and can be classified as Type I, II or III (2-4). Positive RF is an important characteristic of Type II and Type III cryoglobulins. However, samples that have type I cryoglobulins (i.e. the cryoprecipitate consists entirely of a monoclonal immunoglobulin) can also have positive rheumatoid factor, and this can cause confusion when typing cryoproplets.

The aim of this study was to determine the prevalence of rheumatoid factor in non-cryoprecipitating monoclonal proteins, as this is not well documented.

Methods

108 patient samples with a monoclonal protein >10g/L were identified from samples received in the Protein Reference Unit in a two week period. There were 65 IgG paraproteins (43 IgGk and 22 IgGλ), 21 IgA paraproteins (14 IgAκ and 7 IgAλ) and 22 IgM paraproteins (19 IgMκ and 3 IgMλ). The mean paraprotein concentrations were IgG mean=21 g/L (range 10 - 97 g/L); IgA mean =22 g/L (range 10-73 g/L); IgM mean=18 g/L (range 10-33 g/L).

RF was measured in all samples by rate nephelometry (Beckman Immage 800 analyser; calibration traceable to WHO International reference material, NIBSC 64/2).

Results

Figure 2. RF results for all patients
The number of patients with (solid) or without (striped) RF activity is shown by paraprotein type. IgG (blue), IgA (red), IgM (yellow).

Figure 3. Percentage of patients with positive RF for IgG, IgA and IgM

<table>
<thead>
<tr>
<th>Protein</th>
<th>Percentage of RF positive patients (%)</th>
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<tbody>
<tr>
<td>IgG</td>
<td>11</td>
</tr>
<tr>
<td>IgA</td>
<td>10</td>
</tr>
<tr>
<td>IgM</td>
<td>10</td>
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1. RF activity was found in 10% of the samples tested: in 7/65 (11 %) IgG, 2/21 (10%) IgA, and 2/21 (10%) IgM paraproteins.
2. The mean RF concentration for the eleven positive samples was 194 IU/ml (range 20 IU/ml - 767 IU/ml).
3. The RF concentration did not correlate with the paraprotein concentration.

Conclusion

10% of patients with monoclonal proteins had high levels of RF activity.

Discussion

- Our data show that RF activity is seen in 10% of patient samples containing non-cryoprecipitating monoclonal proteins with a concentration over 10g/L.
- It is important to recognise that samples containing monoclonal proteins can have RF activity and that RF activity can be seen in the absence of cryoproteins. This is of importance when interpreting cryoprotein results.
- Similar results have been seen in another study where patients with an IgM non-cryoprecipitating monoclonal protein had high levels of RF (5).
- Due to the lack of awareness about this finding, this has not been well documented. Further studies should be done to support this conclusion.

References