Owen Seddon
University Hospital of Wales, Cardiff

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<tr>
<th>Speaker Name</th>
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<th>Date</th>
<th>April 2016</th>
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Are laboratory specialties recommending HIV testing for suggestive results, and is anyone listening?

Seddon O, Froude S, Freedman AR. Infectious Diseases and Microbiology, Cardiff
Routine laboratory tests

HAEMATOLOGY

- BHIVA testing guidelines recommend HIV testing in any unexplained haematological dyscrasia including thrombocytopenia, leucopenia or anaemia
Routine laboratory tests

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IMMUNOLOGY
• HIV associated with polyclonal rise in IgG
• Represents B Cell activation by virus
• Visible as rise in globulin on routine biochemistry
• Limited prevalence studies
• Not mentioned in BHIVA testing guidelines

March 15, 2004; Blood: 103 (6)
Mechanisms of hypergammaglobulinemia and impaired antigen-specific humoral immunity in HIV-1 infection
Angelo De Milito, Anna Nilsson et al
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*Mechanisms of hypergammaglobulinemia and impaired antigen-specific humoral immunity in HIV-1 infection*
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Retrospective cohort study of 148 patients with polyclonal gammopathy.

Dispenzieri A, Gertz MA, Therneau TM, Kyle RA.
Raised globulin fraction noted on LFTs. Sample referred to immunology

Serum Protein Electrophoresis

Monoclonal (paraprotein), investigate for MGUS/Myeloma

Polyclonal IgG

Raised CRP? Abnormal LFTs Clinical details?

May comment “Polyclonal rise in IgG can be seen in retroviral infection”
Raised globulin fraction noted on LFTs. Sample referred to immunology

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Abnormal LFTs
Clinical details?

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Serum Protein Electrophoresis 

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Raised CRP? Abnormal LFTs 

Clinical details?

Test Undertaken: Electrophoresis (IEPH) Sample Type: [BMM - 23.07.10 16:49] 

Ser.Electrophoresis  ? Faint compact band in Gamma

Test Undertaken: IgG, IgA & IgM (IGAM) Sample Type: [BMM - 23.07.10 16:49] 

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<tr>
<th>Test</th>
<th>Value</th>
<th>Reference Range</th>
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<tr>
<td>Serum IgG</td>
<td>31.90 g/l</td>
<td>6.00-15.50</td>
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<tr>
<td>Serum IgA</td>
<td>5.07 g/l</td>
<td>0.90-3.40</td>
</tr>
<tr>
<td>Serum IgM</td>
<td>2.96 g/l</td>
<td>0.48-1.90</td>
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Polyclonal rise in serum [IgG] can occur in retroviral infection.
Are laboratories suggesting HIV testing?

- 97 new diagnoses of HIV in University Hospital of Wales, Cardiff 2012-2015
- Results at diagnosis and historical results reviewed for unexplained haematological dyscrasias and raised globulin/polyclonal rise in IgG
97 patients

- Abnormality present pre-diagnosis but no comment added: 31
- No laboratory abnormality: 30
- Abnormality present but patient diagnosed at first presentation: 23
- Abnormality present pre-diagnosis and comment added: 13
97 patients

31 with laboratory abnormalities preceding diagnosis
97 patients

- 7 with polyclonal rise in IgG
- 9 haematological abnormalities (1 anaemia, 5 leucopenia, 7 thrombocytopenia)
- 15 both

31 with laboratory abnormalities preceding diagnosis
Time from blood test abnormality to diagnosis in 31 patients where no comment was added

- Uncommented abnormalities preceded diagnosis by median 9 months
- Range few days to >6 years
97 patients

31 with laboratory abnormalities preceding diagnosis

13 with laboratory abnormalities and subsequent comment
97 patients

31 with laboratory abnormalities preceding diagnosis

13 with laboratory abnormalities and subsequent comment

8 with polyclonal rise in IgG

3 Haematological dyscrasia
   (2 leucopenia, 1 thrombocytopenia)

2 combination
Timing of first appearance of abnormality and lab comment being added for 13 individual patients

- Abnormality present
- Test suggested

Years preceding diagnosis

Diagnosis with HIV

-10 -9 -8 -7 -6 -5 -4 -3 -2 -1 0
Timing of first appearance of abnormality and lab comment being added for 13 individual patients

- Median time from abnormality to lab comment 1.8 years
- Median time to diagnosis from lab comment 1 month
- No statistically significant improvement in time from abnormality to diagnosis when comment made
Conclusions – Are laboratories recommending testing?

- Laboratory comment suggesting testing potentially prompted diagnosis in up to 13%
- Inconsistency in comments being added to results – discussion with laboratory confirms no SOP
- Opportunity to recommend HIV testing in further 32%
- In some cases a comment had the potential to hasten diagnosis by 6 years
Conclusions – Is anyone listening?

• Evidence that comments are not being seen/acted upon

• However median time to testing from diagnosis suggest many are

• How do we ensure results are seen?
Limitations

- Small group – patient diagnosed whilst in hospital, will expand to collect data from community diagnoses
- Whether tests were seen and not acted on or not seen, no audit trail
- Workload involved from laboratory side – how many cases of polyclonal gammopathy are laboratory authorising? – data collection ongoing
- Other centres experience?
Recommendations

• Standard operating procedure for immunology and haematology to add comments to polyclonal gammopathy or unexplained dyscrasias

• Rewording of suggested comment
  “Amongst other possible causes, this pattern of abnormalities can be seen in HIV, which should be excluded by testing”

• Should polyclonal IgG rise be mentioned within BHIVA testing guidelines?

• Look back exercises should take account of laboratory abnormalities as well as clinical features
Acknowledgements

- Immunology and haematology laboratories UHW
- Alison Keenor, P.A. to virology consultants UHW
- Rachael Steven, Senior BMS UHW

Thank you for your attention