Diagnostic value of ADENOSINE DEAMINASE in TB pleural effusions

Brechtje Grotenhuis, Dutch Elective Student
Introduction

- Pleural TB is present in 4% of all TB cases\(^4\)
- Resolves spontaneously vs progressive disease / high recurrence rate\(^4\)
- Diagnosis of TB pleuritis is difficult: \(^1,3,4\)
  - Non-specific clinical presentation
  - Insufficient efficiency diagnostic methods:
    - Pleural biopsy often requires several attempts, results of histology and culture $\rightarrow$ diagnosis in 85%
    - Thoracoscopy is most accurate + expensive
Adenosine Deaminase (1)

- Effusion is result of delayed-type hypersensitivity reaction of T-cells

<table>
<thead>
<tr>
<th>tuberculous focus ruptures</th>
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<tbody>
<tr>
<td>release of tubercle bacilli</td>
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<tr>
<td>activate macrophages + present to T-cells</td>
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<tr>
<td>entrance pleural cavity</td>
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<td>production ADA during proliferation</td>
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Adenosine Deaminase (2)

- Enzyme that catalyses the deamination of adenosine and deoxyadenosine $^{1,3,4}$
- Found in most cells
- 2 isoenzymes: $^3$
  - ADA-1: found in many tissues
  - ADA-2: $>$ major component of total ADA activity
    - $>$ greatest affinity for adenosine
    - $>$ found only in macrophages
    - $>$ release when entrance micro-organism
Adenosine Deaminase (3)

- High levels ADA in effusions due to: 1,3,4
  - TB
  - Bacterial infections
  - Rheumatologic diseases
  - Lymphoproliferative disorders

- Determination of the isoenzymes of help in distinguishing 3
Research (1)

- Existing diagnostic methods insufficient efficient or expensive
- Sensitivity / specificity using ADA in detecting tuberculosis in pleural effusions
- Tygerberg research, ’03
  - 51 pt undiagnosed exudative pleural effusions
  - Prospective, direct comparison between pleural microbiology and biochemistry (ADA), closed needle biopsy and thoracoscopy.
  - Sensitivity combined histology / culture:
    - closed needle biopsy 79 %, thoracoscopy 100%.
  - Sensitivity pleural fluid ADA of >50 U/L 95%, specificity 89%
Sensitivity + specificity ADA in diagnosing TB in pleural effusions

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<thead>
<tr>
<th></th>
<th>Cut-off value (U/L)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
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<tbody>
<tr>
<td>Review articles 4,5</td>
<td>40 – 55</td>
<td>85 – 100</td>
<td>80 – 95</td>
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<tr>
<td>ADA-2 3</td>
<td>40</td>
<td>100</td>
<td>96</td>
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<tr>
<td>Tygerberg 1</td>
<td>50</td>
<td>95</td>
<td>89</td>
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Discussion

- False-positive results are relatively high, due to empyema, and in low-prevalence TB countries.
- Drawback of relying on ADA alone: adding cytology and bacterial culture increase the values.
- South-Africa: Effect of HIV on ADA-activity.
Conclusion

- Combination of:
  - Pleural fluid adenosine deaminase
  - Closed needle biopsy, for histology and culture

→ Has a high diagnostic accuracy in undiagnosed pleural effusions in areas with high TB-incidences. 1,2,3,4,5

- Substitution for thoracoscopy at lower expense in poor countries

- Most of the studies are on total ADA level; ADA isoenzymes may be more accurate. 3

With special thanks to:
• Prof. N. Beyers, TB research, Tygerberg
Remember...

- Maastricht
- Amsterdam