Tuberculosis in rheumatic patients treated with biological therapies – is screening enough?

Romão VC1,2; Saavedra MJ3; Vieira-Sousa E1,2; Costa M2; Polido-Pereira J1,2; Rodrigues AM1,2; Ramos F2; Macieira C2; Capela S2; Resende C1; Madruga-Dias J1,2; Ponte C1,2; Campanilho-Marques R1,2; Castro A1,2; Furtado C1,2; Fernandes S1,2; Gonçalves MJ1,2; Pereira da Silva JA2; Canhão H1,2; Fonseca JE1,2

1 Rheumatology Research Unit, Instituto de Medicina Molecular – Faculdade de Medicina da Universidade de Lisboa; 2 Rheumatology Department, Lisbon Academic Medical Centre, Lisbon, Portugal

Introduction

An increased risk of active tuberculosis (TB) has been reported in patients with rheumatic diseases treated with biological therapies, especially TNF inhibitors. Most TB cases result from an activation of a previous latent infection (LTB). In Portugal, stringent screening guidelines for detection of LTB have been issued and regularly updated since 2003. The aim of this study was to analyze TB cases in biological-treated patients from a single center.

Methods

We included patients from Hospital Santa Maria treated with biological therapy and registered in Reuma.pt that had a diagnosis of TB after starting treatment. Data were obtained through Reuma.pt and clinical files.

Results

We identified 736 treatments with biological therapies, 627 of which with TNF inhibitors, corresponding to 510 patients. There were 3 cases of TB after the start of biological treatment (0.59% of patients, 0.41% of treatments) - Table 1.

Table 1 - Characteristics of the 3 patients diagnosed with TB after the start of a biological.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Rheumatic disease</th>
<th>Biological</th>
<th>Year of biological start</th>
<th>Disease duration (years)</th>
<th>Screening§</th>
<th>Previous TB (year)</th>
<th>LTB Treatment</th>
<th>Time on biological to TB (months)</th>
<th>TB site</th>
<th>Contact with active case</th>
<th>TB diagnosis</th>
<th>Treatment</th>
<th>Evolution</th>
<th>Biological reintroduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>27</td>
<td>Male</td>
<td>Psoriatic Arthritis</td>
<td>Infliximab</td>
<td>2009</td>
<td>5</td>
<td>Negative</td>
<td>No</td>
<td>No</td>
<td>5.1</td>
<td>Pulmonary</td>
<td>No</td>
<td>Clinical*, sputum, imaging*</td>
<td>HRZE</td>
<td>Resolution</td>
<td>No</td>
</tr>
<tr>
<td>2</td>
<td>48</td>
<td>Female</td>
<td>Psoriatic Arthritis</td>
<td>Infliximab</td>
<td>2003</td>
<td>18</td>
<td>Positive (TST 20mm)</td>
<td>Yes, treated (1960)</td>
<td>Yes, INH 9m</td>
<td>18</td>
<td>Miliary</td>
<td>Yes</td>
<td>Clinical*, lymph node pathology, imaging*</td>
<td>HRZE</td>
<td>Resolution</td>
<td>No</td>
</tr>
<tr>
<td>3</td>
<td>17</td>
<td>Female</td>
<td>Spondyloarthritis</td>
<td>Adalimumab</td>
<td>2010</td>
<td>4</td>
<td>Negative</td>
<td>No</td>
<td>No</td>
<td>14.5</td>
<td>Miliary</td>
<td>Yes</td>
<td>Clinical*, BAL, imaging*</td>
<td>HRZE</td>
<td>Resolution</td>
<td>No</td>
</tr>
</tbody>
</table>

§Including epidemiological risk factors, two-step tuberculin skin test (TST), IGRA and chest X-ray (CXR); *clinical signs and symptoms; *CXR and/or CT-scan. BAL, bronchoalveolar lavage; HRZE, quadruple therapy with isoniazid, rifampin, pyrazinamide and ethambutol; INH, isoniazid; LTB, latent tuberculosis; TB, tuberculosis.

Conclusions

In biological-treated rheumatic patients TB occurred even after appropriate screening measures. No particular pattern could be seen in positive cases, except that all three patients were treated with anti-TNF monoclonal antibodies and two of them had contact with active TB cases. TB occurred between 5 and 18 months after starting treatment, in patients with positive and negative screening tests, with and without previous LTB treatment. This highlights that even with thorough screening for LTB, there is still a risk of developing active TB at any time after the start of biological therapies, especially with TNF inhibitors. Thus, close vigilance is mandatory and patients should be clearly aware of the continuous increased risk of TB.

References