Crohn’s Disease Is Associated With Restless Legs Syndrome: a New Extraintestinal Manifestation

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INTRODUCTION

• Crohn’s disease (CD) is chronic gastrointestinal (GI) disease primarily affecting small intestine and colon1 – Intestinal blood loss and other mechanisms may cause iron deficiency4 1
• CD is associated with bacterial overgrowth and increased, chronic inflammation2 1
• Iron deficiency may cause fatigue and sleep disorders7
• Patients at risk for iron deficiency are also at risk for development of restless legs syndrome (RLS)5
• RLS is central nervous system disorder that elicits compelling urge to move legs at rest and contributes to sleep disturbances and poor quality of life8 1
• Idiopathic or secondary to many disorders7 1 – In prospective clinical trial of 13 patients with irritable bowel syndrome (IBS) and RLS, 77% of patients (10 of 13) reported ≥80% improvement from baseline of RLS symptoms after rifaximin treatment for IBS5

OBJECTIVE

• To determine if CD is associated with RLS because both conditions may display iron deficiency

METHODS

Study design

• Prospective evaluation of RLS in patients with CD seen in 3 academic outpatient GI clinics from either August 2007 or February 2008 to March 2008 and in 1 community GI clinic from August 2007 to March 2008

Assessments

• Diagnosis of RLS according to criteria set by International Restless Legs Syndrome (RLS) Study Group4
• Incidence (presence of RLS during any period of life) and prevalence (display of RLS symptoms at time of survey) of RLS in patients with CD
• Prevalence of RLS in spouses of patients with CD, as determined by patient query
• Past and current reported history of iron deficiency or anemia
• Onset and duration of RLS symptoms
• Statistical analysis via chi-square test with P<0.05 considered significant

RESULTS

• 272 patients were included in analysis
• RLS symptoms at any point during lifetime were reported in 93 of 218 patients with CD (43%) queried for RLS incidence (Table)

Table. Demographics and Baseline Characteristics of Patients With CD

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Patients with RLS* (n=93)</th>
<th>Patients without RLS (n=179)</th>
</tr>
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<tbody>
<tr>
<td>Mean age ± SD, y</td>
<td>42 ± 16</td>
<td>47 ± 13</td>
</tr>
<tr>
<td>Male:Female, n</td>
<td>40:53</td>
<td>81:98</td>
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<tr>
<td>CD location, n (%)</td>
<td></td>
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<tr>
<td>Small intestine</td>
<td>53/68 (78)</td>
<td>78/117 (67)</td>
</tr>
<tr>
<td>Colon</td>
<td>27/68 (40)</td>
<td>74/117 (63)</td>
</tr>
<tr>
<td>Currently taking iron supplementation, n (%)</td>
<td>10/67 (15)</td>
<td>14/118 (12)</td>
</tr>
<tr>
<td>Currently reporting iron deficiency, n (%)</td>
<td>3/65 (5)</td>
<td>5/106 (5)</td>
</tr>
</tbody>
</table>

CD, Crohn’s disease; RLS, restless legs syndrome; SD, standard deviation. *Patients with RLS at any point in lifetime. 1Reduction in total due to nonqueried data in questionnaires from 1 study site.

Figure 1. Restless legs syndrome (RLS) prevalence in patients with Crohn’s disease (CD) and their spouses. Patients with CD were more likely to have current RLS (62 of 272 patients; 30%) than their spouses (17 of 202 spouses, 8%; P<0.0001; Figure 1)

DISCUSSION AND CONCLUSIONS

• RLS symptoms in patients with CD did not correlate with iron deficiency

Figure 2. Percentage of patients with CD describing onset of RLS symptoms before or during/after onset of GI symptoms. Substantially more patients with CD reported onset of RLS symptoms during or after GI symptoms than before GI symptoms. CD, Crohn’s disease; GI, gastrointestinal; RLS, restless legs syndrome.

• In this prospective multicenter study, RLS was found to be comorbid condition in patients with CD, with incidence of 43% and prevalence of 30%
• RLS symptoms occurred during or after onset of CD symptoms in majority of patients, suggesting link between CD and RLS
• Systemic iron deficiency was not associated with RLS in patients with CD, suggesting that other factors may be involved in RLS pathophysiology within this patient population; however, total body iron concentrations do not always correlate with central nervous system iron levels, which may be more relevant to RLS4
• Pathophysiology may include small intestinal bacterial overgrowth and systemic inflammation. In vitro studies report that some proinflammatory cytokines, such as interleukin-6, increase production of hepcidin, which affects iron transportation9
• Further research on potential association and clinical impact of RLS in CD is warranted