Etiología de sicca syndrome en una serie consecutiva de 199 pacientes con síndrome de fatiga crónica

Dear Sir,

Chronic fatigue syndrome (CFS) is a heterogeneous and multisystemic disorder of unknown pathogenesis and etiology. It is characterized by prolonged generalized and abnormal fatigue post-exercise (98%), recurrent headache (90%) and problems of concentration and memory (85%) that have lasted for at least 6 months. It is accompanied by such other symptoms as tender lymph nodes (80%), musculoskeletal pain (75%) and psychiatric problems (65%). The prevalence of CFS is estimated to be between 0.5 and 2.5%, predominantly in women (4:1). Many patients with CFS also complain of sicca symptoms in up to 30–87%, and are more likely to have thyroid disorder and sleep disruption;

Bibliografía


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http://dx.doi.org/10.1016/j.reuma.2013.11.003

Etiology of sicca syndrome in a consecutive series of 199 patients with chronic fatigue syndrome

Etiología del síndrome seco en una serie consecutiva de 199 pacientes con síndrome de fatiga crónica

Dear Sir,

Chronic fatigue syndrome (CFS) is a heterogeneous and multisystemic disorder of unknown pathogenesis and etiology. It is characterized by prolonged generalized and abnormal fatigue post-exercise (98%), recurrent headache (90%) and problems of concentration and memory (85%) that have lasted for at least 6 months. It is accompanied by such other symptoms as tender lymph nodes (80%), musculoskeletal pain (75%) and psychiatric problems (65%). The prevalence of CFS is estimated to be between 0.5 and 2.5%, predominantly in women (4:1). Many patients with CFS also complain of sicca symptoms in up to 30–87%, and are more likely to have thyroid disorder and sleep disruption; that may suggest an underlying role of the immune system in these patients. Primary Sjögren’s syndrome (PSS) is a systemic autoimmune disease, that presents chronic exocrine glands hypofunction leading to xerostomia and/or xerophthalmia, and extrapolandular involvement, of which autoimmune hypothyroidism (AIHT) is the most common autoimmune disease developed. Patients with PSS, also experience CFS-like musculoskeletal and neurocognitive symptoms more than 50%, and the two disorders share some similar immunologic defects. The purpose of this study was to determine the causality of sicca symptoms in 199 consecutive patients diagnosed as having CFS, and the possible association with PSS, although few studies that have examined this association (between 2010 and 2012 in our chronic fatigue unit of Joan XXIII University Hospital) according to the Fukuda criteria of 1994. One hundred sixty-seven patients (84%) were women. The age of onset of symptoms was 41 ± 10 years. Mucosal sicca symptoms were complained by 160 patients (80.4%); 11/160 (6.8%) patients were diagnosed with PSS (9 patients were incomplete PSS and 2 patients were complete PSS by positive lower lip biopsy that had MSG focus score >1, using the American-European criteria 2002). 110/160

variables sociodemográficas, datos analíticos, FRCV clásicos, tiempo de evolución de la AR y tratamiento inmunomodulador. Se definió como ITB patológico un valor inferior a 0.96.

De los 60 pacientes incluidos, 3 fueron varones (5%) y 57 mujeres (95%), con una edad media ± desviación estándar de 53,75 años (53,75 ± 15,38; rango 29-87). 38 fueron AR leves (63,3%), mientras que 22 (36,7%) presentaron grandes deformidades. El tiempo de evolución fue de 9,14 años (9,14 ± 6,505; rango 0,6-40); 58 pacientes (96,7%) seguían tratamiento inmunomodulador, la mayoría con metotrexato (75%). El resultado del ITB fue similar en ambas extremidades inferiores: 1,074 (1,074 ± 0,082, rango 0,88-1,28) en la derecha y 1,077 (1,077 ± 0,088, rango 0,92-1,27) en la izquierda, sin diferencias significativas entre ellas. Solo una paciente (1,7%) presentó un ITB patológico: una mujer de 87 años, hipertensa, con AR de 12 años de evolución y uso de corticoides durante prácticamente toda la enfermedad; el ITB en la otra extremidad fue de 0,92. En la figura 1 se muestran los resultados de los ITB.

En nuestra muestra, existe una excesiva representación de mujeres (19:1) respecto a la población con AR (3:1). Sin embargo, el perfil de RCV no difiere respecto a la población general española.

Sólo se ha detectado un caso patológico, frecuencia mucho menor que la de otros estudios, con tasas del 20-25%, si bien el punto de corte que consideraron como patológico fue de 1, en vez del valor de 0,9 actualmente aceptado. Sin embargo, en otra publicación con nuestro mismo punto de corte, la prevalencia fue del 10%, si bien en su muestra la edad media, la duración de la AR y, sobre todo, la prevalencia de FRCV (principalmente diabetes y dislipidemia) eran superiores. Otro de los posibles factores implicados en la ausencia de EAP podría ser el adecuado control de la enfermedad, ya que solo el 3,3% de los pacientes no tenía tratamiento específico y el valor de los reactantes fue normal.

Una de las mayores limitaciones fue la accesibilidad al estudio, ya que el ITB se realizó de forma diferida a la consulta, de manera que muchos de los excluidos fueron aquellos que se negaron a participar, alegando dificultad física para acudir a realizarse la prueba, lo cual puede haber supuesto un sesgo de selección, al haber perdido a los pacientes más graves.

Como conclusión, sobre la base de nuestros resultados no consideramos justificada la realización rutinaria de un ITB en pacientes con AR asintomáticos desde el punto de vista cardiovascular.
Patients (68.75%) were mainly due to xerogenic medications. Severe obstructive sleep apnea syndrome (OSAS) was diagnosed in 6/160 patients (3.75%) (according to the American Academy of Sleep Medicine, Chicago Criteria 1999) by polysomnographic analysis. Thirty-eight (23.75%) patients were sero-positive for thyroperoxidase antibody (TPO-Ab) and/or thyroglobulin antibody (Tg-Ab) (of these patients 33/160 (20.6%) were diagnosed as having AIHT), 15 (10.2%) had a positive antinuclear antibody (ANA) assay (titer count >1:160), and 5 (3.5%) had a positive parietal cell antibody (titer count >1:160). All were sero-negative for anti-Ro/SS-A and anti-La/SS-B. In previous studies mucosal sicca symptoms were described as one of the common clinical manifestations of CFS, as seen in our serie. Nishikai et al. and Siros et al. had found sicca symptoms in 73% and 52% of their series respectively. As possible causes in our study, we determined that the prevalence of sicca symptoms (especially xerostomia) induced by psychotropic medications with anticholinergic side effects (amitriptyline, clonazepam, etc.) was high as described in several studies. Drugs with anticholinergic actions decrease salivary gland secretion by neurochemical blockade. It is usually dose related and reversible when medication is discontinued. We also found a group of CFS patients with sicca symptoms that may be attributed to AIHT and OSAS. This suggests that these two disorders share common pathophysiological features with CFS. Interestingly, in patients with OSAS, CFS symptoms were improved by using continuous nasal positive airway pressure (CPAP). Any potential relationship between CFS and PSS is complicated by the lack of a sensitive test or agreement regarding the diagnostic criteria for PSS. Nishikai et al. examined a group of 75 seronegative patients diagnosed with CFS and found that 22 (29%) met the European criteria 1993 for PSS. Siros et al. also examined 25 patients diagnosed with CFS and found that 32% met diagnostic criteria for PSS according to the European criteria 1993. These results were not similar to ours in the study we present (11 patients if we included patients with incomplete PSS) as we described previously (Table 1). In searching of causes of this poor association, several considerations have to be taken into account in our study. 1st, in our study we used the 2002 criteria that require mandatory: (1) a positive salivary gland biopsy (only done in 5 patients), or (2) the presence of antibodies to SSA/Ro and/or to SS-B/La (negative in all patients). The serological item was also met in the 1993 criteria (used by Nishikai et al. and Siros et al.) but only if a test for rheumatoid factor or ANA was positive. This condition has probably increased the prevalence of PSS in their studies. 2nd, symptoms or signs of PSS do not always begin at the same time and that patients with incomplete SS may be will meet the diagnostic criteria 2002 at some point in the future. In summary, in our study about 70% of CFS patients with sicca syndrome are related to be drug-induced. Therefore, xerogenic medications, as possible cause, must be excluded. However, we recommend that patients who have been diagnosed with CFS and manifest mucosal sicca symptoms should be also screened for SS, AIHT and/or OSAS; and should be regarded as a comorbidity of CFS, not a diagnostic exclusion criterion.

Conflict of interest

The authors declare no conflict of interest.

References


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http://dx.doi.org/10.1016/j.reuma.2013.11.002

Pigmented villonodular synovitis diagnostic delay due to coexistence with ankylosing spondylitis

Retraso en el diagnóstico de sinovitis villonodular pigmentada por coexistencia con espondilitis anquilosante

Dear Editor,

A 57-year-old man with longstanding ankylosing spondylitis (AS) was treated successfully with etanercept since January 2006, except for persistent left elbow swelling. Three local corticosteroid injections and radiosynovectomy with 3 mCi 186–Rhenium proved to be useless. Elbow involvement is sporadically seen in AS, and the persistence despite the intra-articular treatment made us consider the possibility of a coexistent arthropathy, such as an opportunistic infections (mycobacteria, fungi), synovial sarcoma, joint metas- tasis or lipoma arborescens. A first magnetic resonance imaging (MRI) was ordered, showing an unspecific synovial hypertrophy. Joint aspiration revealed an inflammatory non-hemorrhagic fluid with repeatedly negative cultures, and an open biopsy resulted in non-specific synovitis, ruling out infections and malignancies. In June 2010, an X-ray highlighted the development of bone erosions. A new MRI (Fig. 1) demonstrated at this time an enhancing

Table 1

<table>
<thead>
<tr>
<th>Causes of sicca symptoms in chronic fatigue syndrome’ patients</th>
<th>N: patients (%)</th>
</tr>
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<tbody>
<tr>
<td>Xerogenic medications</td>
<td>110 (68.75)</td>
</tr>
<tr>
<td>Autoimmune hypothyroidism</td>
<td>33 (20.6)</td>
</tr>
<tr>
<td>Primary Sjögren syndrome</td>
<td>11 (6.8)</td>
</tr>
<tr>
<td>(incomplete/complete)</td>
<td>(9/2 patients)</td>
</tr>
<tr>
<td>Obstructive sleep apnea syndrome</td>
<td>6 (3.75)</td>
</tr>
</tbody>
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