Lymphocytic Mastitis preceding Sjögren's Syndrome

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Sjögren's syndrome (SS) is a chronic autoimmune disease characterized by lymphocytic infiltration of exocrine glands and B cell hyperreactivity. Lacrimal and salivary glands are the most commonly involved causing keratoconjunctivitis sicca and xerostomia. A wide variety of other glandular and extraglandular manifestations can occur in SS. Lymphocytic mastitis is a rare presentation of several conditions including diabetes mellitus and autoimmune disorders. We report a case of a 43-year-old woman with a four-year history of arthralgias and positive antinuclear antibodies who developed a right painless breast mass. Biopsy revealed lymphocytic mastitis with predominant B cells. One year later she developed severe constitutional symptoms, sicca symptoms, lymphadenopathy, anemia, and interstitial lung disease. Serologies and minor salivary gland were consistent with the diagnosis of SS. This case further supports the association of lymphocytic mastitis with autoimmune diseases and demonstrates that it can even precede the clinical diagnosis of these entities. [*P R Health Sci J 2010;2:127-129*]

Key words: Sjögren's syndrome, Lymphocytic mastitis

Sjögren's syndrome (SS) is a chronic systemic disease characterized by progressive lymphocytic cells infiltration of exocrine glands. This disease exhibits a wide range of organ specific and systemic manifestations. The symptoms are related to the malfunction of the affected glands. The earliest symptoms of SS are related to oral and ocular manifestations, presenting with eyes and mouth dryness. One third of patients with SS, develop a more severe systemic disease, affecting kidneys, liver, lungs and peripheral nerves. (1-2) Lymphocytic mastitis is a fibro-inflammatory breast disease that typically occurs in women with long standing Type 1 diabetes mellitus or other autoimmune diseases. We present a case of a woman who developed a lymphocytic mastitis, several months before the definite diagnosis of Primary SS.To our knowledge, only one prior report of lymphocytic mastitis with primary SS has been published (3).

Case report

A 43 year-old woman with hyperthyroidism and pituitary adenoma was evaluated at our hospital for a four-year history of arthralgias in the hands, wrists and knees. In the past four years, the patient did not complain of other characteristic symptoms (dry mouth or eye dryness) of SS and the only positive finding was elevated antinuclear antibodies (ANA), 1:320, speckled pattern altogether with a negative rheumatoid factor. Her treatment included propylthiouracil 50 mg daily and cabergoline 0.25 mg daily.

Two years later, she began fatigue, low grade fever and abdominal pain; joint pain was persistent. Laboratory work-up revealed positive ANA (1:1280, speckled pattern), antiRo/SSA antibodies (>100U)and anti-smooth muscle antibodies (1:320), and an elevated erythrocyte sedimentation rate (52 mm/hr). Tuberculin, HIV and Hepatitis A, B, C tests were negative. An abdominal ultrasonography was normal and an upper gastrointestinal endoscopy showed non-erosive gastritis.

One year later, she presented a right breast mass measuring 2 X 5 cm. A core needle biopsy was performed and the histologic examination of the breast showed extensive stromal fibrosis with a dense perilobular lymphocytic infiltrate (Figure 1). Immunohistochemical stains revealed that the infiltrate was polyclonal in nature. These findings were consistent with lymphocytic mastitis. Immunohistochemical panel suggested a reactive infiltrate; positive markers included: AE1/AE3, ER, PR, Her-2-neu, CD30, CD4, CD8 and CD20. Prednisone 15mg was started and the breast mass gradually reduced its size and resolved.

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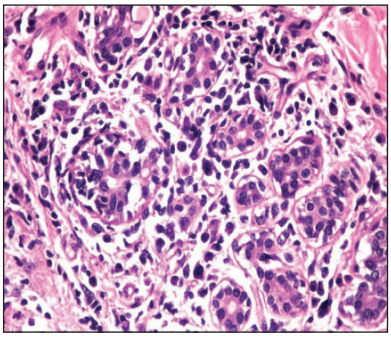

Figure 1. Lymphocytic mastitis characterized by fibrosis and abundant lymphocytes and plasma cells overlying the ducts and lobules(40x).

Two months later, the patient was admitted at another local institution after persistent productive cough and respiratory distress. Chest X-ray showed interstitial infiltrates in the upper segments of both lungs, without evidence of pleural effusions. Chest computed tomography scan demonstrated bilateral pulmonary nodules. Transbronchial biopsy showed extensive bronchial and alveolar macrophages suggestive of chronic bronchitis. No evidence of malignancy or infections (including bacteria, fungi, mycobacteria) was found. The patient was discharged home without a definite diagnosis.

At the time of our initial evaluation, the patient reported weight loss (50 lbs), persistent cough, xerostomia, eye itching, heartburn, dysphagia, abdominal pain and arthralgias. On physical exam, she appeared cachectic and pale. She had mouth dryness, dry skin and mild cervical adenopathy. Lungs auscultation revealed bibasilar crackles. The remainder of the physical examination, including musculoskeletal system, was unremarkable. The results of laboratory tests were notable for the presence of anemia (hemoglobin of 9.8 g/dl), elevation of the Westergren erythrocyte sedimentation rate (80mm/hr), and positive ANA (1:640), anti-Ro/SSA antibodies (815 U/ml) and thyroid peroxidase (TPO) antibodies (2255U/ml).

A fine needle biopsy of the cervical node showed an infiltrate of abundant small and medium sized lymphocytes. Lower lip biopsy (minor salivary gland) showed chronic inflammation with a lymphocytic infiltrate.

Patient was started on prednisone 1mg/kg/day and hydroxychloroquine 200mg twice per day. Patient's symptoms, including generalized malaise, cough, abdominal pain and arthralgias, gradually improved with therapy.

Discussion

In our patient, a diagnosis of primary SS was made after four years of extensive evaluation. The patient meets four of the six European criteria for the diagnosis of Sjögren's syndrome: subjective ocular and oral symptoms, the presence of autoantibodies, and histopathological features (1). Patient's history and physical exam excluded other rheumatologic conditions such as rheumatoid arthritis, systemic lupus erythematosus or systemic sclerosis. Our patient presented autoimmune thyroid disease, a common condition associated to primary SS (2).

SS is a slow progressive disease affecting the function of exocrine glands. The most common clinical features of SS are xerostomia, keratoconjuntivitis sicca, parotid gland enlargement, dry skin and vaginal dryness (2, 4). Systemic manifestations are diverse, including fatigue, arthritis, lung disease, nephritis, small vessel vasculitis, Raynauds phenomenon, gastrointestinal involvement and peripheral neuropathy (2, 4).

Our patient presented with lymphocytic mastitis, an extremely uncommon manifestation of SS. Lymphocytic mastitis is a fibro-inflammatory breast disease that typically occurs in women with long standing type 1 diabetes mellitus or other autoimmune diseases. It usually presents with a unilateral painless breast mass (3-7). The major histological findings are mature lymphocytic infiltrates with stromal fibrosis (5-7). The presence of this morphologic changes are suggestive of an autoimmune etiology.

The most common conditions associated with lymphocytic mastitis are diabetes mellitus and thyroid disease (3-7). Only few authors have reported cases of lymphocytic mastitis in patients with rheumatologic diseases (3, 6). Asthon et al., reported a 31 year old woman with SLE and a palpable hard breast mass with lymphocytic infiltrates (6). Valdez R et al., reported a 81 year old non-diabetic woman with past medical history of SS. This patient presented a breast mass with histological changes suggestive of lymphocytic mastitis and no evidence of lymphoma (3). In summary, we report a case of a 43-year-old woman with developed a right painless lymphocytic mastitis who one year later developed full blownSS. The other reported cases of lymphocytic mastitis suggest a relationship of this entity with autoimmune diseases such as diabetes mellitus, thyroid disease, SLE and SS. Clinicians should be aware that lymphocytic mastitis can be an unusual presentation of autoimmune disorders that may precede the clinical diagnosis of these entities.

Resumen

El síndrome de Sjögren es una enfermedad inflamatoria crónica, la cual se caracteriza por infiltrados de linfocitos en las glándulas exocrinas e hiperactividad de células B. Las glándulas lacrimales y salivares son más comúnmente afectadas causando keratoconjunctivitis sicca y xerostomia. En este síndrome ocurren un sin numero de manifestaciones asociadas a otras glándulas y fuera de las glándulas exocrinas. Mastitis linfocítica es una presentación rara de varias condiciones incluyendo diabetes mellitus y otros desórdenes auto-inmunes. Nosotros presentamos un reporte de una paciente mujer de 43 años con un historial por cuatro años de artralgias y anticuerpos positivos contra el núcleo (ANA) antes de que desarrollara una masa

indolora del seno derecho. La biopsia de esta masa presentó una mastitis linfocítica con predominancia de células B. Un año más tarde, desarrolla síntomas constitucionales, resequedad en ojos y boca (síndrome de sicca), linfadenopatía, anemia y enfermedad intersticial del pulmón. Las pruebas serológicas positivas y la biopsia de glándula salivar fueron consistentes con el síndrome de Sjögrens. Este caso comprueba la asociación de mastitis linfócitica con enfermedades autoinmunes y demuestra que ésta puede preceder el diagnóstico clínico de estas entidades.

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