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Anti-GAD Antibodies and Breast Cancer in a Patient with Stiff-Person Syndrome: A Puzzling Association

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Stiff-person syndrome (SPS) is characterized by painful involuntarty muscle contractions leading to stiffness and spasms [1] affecting the trunk and proximal limb muscles. The condition may occasional-
ly extend to face, hands and feet, or remain focally restricted [2]. An autoimmune, nonparaneoplastic or paraneoplastic origin has been postulated [3, 4]. We present a woman with SPS and breast cancer in whom the two conditions seem unrelated. In January 1998 a 85-year-old woman complained of sustained involuntary muscle contractions leading to permanent stiffness of both thighs and the right arm. Symptoms were amplified by emotional upset or when startled, and disappeared during sleep. Gait was greatly impaired. Since 1977 she was suffering from recurrent bilateral uveitis. In spring 1998 Hashimoto’s thyroiditis was diagnosed. In July 1998 a ductal carcinoma of the breast was treated surgically followed by anthorapyal therapy (tamoxifen). Examination revealed pupillary irregularities due to the uveitis. There were neither oculomotor abnormalities nor nystagmus. There was increased muscle tone in the right arm and in the lower extremities. Palpation of the hamstrings and quadriceps muscles revealed permanent cocontraction with inability to relax. Electromyographic examination revealed continuous motor activity in the hamstring and quadriceps muscles with normal motor unit potentials. Electrical stimulation of the median nerve provoked marked and sustained contractions of both quadriceps. Serum was positive for antithyroglobulin and antimicrosomal antibodies compatible with Hashimoto’s thyroiditis. M2-type antimitochondrial and anti-21-ß-hydroxylase antibodies were present with no signs of biliary cirrhosis or adrenal insufficiency, even after ACTH stimulation. Anti-islet antibodies were markedly elevated (1/640) as determined by immunohistochemistry, as were anti-glutamic acid decarboxylase (GAD) antibodies (250,060 mGAD U/ml, normal <70) determined by radioimmunoassay. CSF contained elevated IgG levels with oligoclonal bands and was positive for anti-GAD antibodies, as determined qualitatively by immunocytochemistry. It is noteworthy that despite elevated anti-GAD antibody titers no diabetes mellitus was present. Fasting glucose and HbA1c values were normal and oral glucose tolerance test was negative. Antiampylinus autoantibodies were negative, as were anti-Hu, anti-Yo and anti-Ri antibodies. MRI imaging of the whole neuraxis was unremarkable. Baclofen treatment (25 mg t.i.d.) slightly improved the patient’s stiffness. Diazepam was not tolerated. Plasmapheresis and IVIG treatment were only of short-lived benefit. High-dose steroid therapy (methylprednisone 500 mg i.v. per day for 5 days) brought substantial improvement allowing the patient to walk freely without support. Treatment was continued successfully with low-dose prednisone orally (0.4 mg/kg every other day) and the patient remained symptom free since. Improvement of SPS patients treated with diazepam [5], baclofen or vigabatrin suggested altered GABA-mediated inhibition as a pathophysiological mechanism for this condition. The association of SPS with pernicious anemia, thyroiditis, adrenal insufficiency, ovarian failure, myasthenia gravis, hypoparathyroidism, adrenalitis, vitiligo and diabetes mellitus hinted at an autoimmune basis for the disease in some patients. These two hypotheses were merged with the report of antibodies to GAD in both serum and CSF of a patient with SPS and diabetes mellitus [3]. Subsequently these antibodies were demonstrated in 70% of patients with SPS [6], and improvement of symptoms was observed with regimens including corticosteroids, plasmapheresis and IVIG [7]. Paraneoplastic SPS was first described in 1993, identifying antiampylinus antibodies in 3 patients with SPS and breast cancer [4]. Recently 2 patients were reported with SPS, breast cancer and anti-GAD antibodies [8, 9], where the SPS was attributed to a paraneoplastic origin. In our patient the SPS appears to be unrelated to the cancer. First, the patient’s symptoms continued to worsen after removal of the neo-

**References**


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**Short Reports**

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