Gynecologic manifestations of Sjögren's syndrome

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OBJECTIVE: Sjögren's syndrome is a chronic, inflammatory autoimmune disease in which the salivary and lacrimal glands are progressively destroyed by lymphocytes and plasma cells. Because women are affected 10 times more often than men, we studied gynecologic manifestations of Sjögren's syndrome.

STUDY DESIGN: One thousand questionnaires were sent to women with Sjögren's syndrome in New York, New Jersey, Connecticut, and Pennsylvania. Five hundred thirty-nine women responded.

RESULTS: Women with Sjögren's syndrome reported significant vaginal dryness. There was no relationship of Sjögren's syndrome to either the incidence of infertility or miscarriage, although the 4% incidence of congenital anomalies in offspring was relatively high. Of the congenital anomalies, nine of 19 (47%) were cardiac. A long menstrual cycle (>35 days) was associated with infertility and neuropathy.

CONCLUSIONS: The vaginal dryness in women with Sjögren's syndrome is not surprising, because the nasal and esophageal mucosae are also dry in this disorder. The relationship of infertility to a long menstrual cycle may simply indicate the presence of ovulatory dysfunction or inadequate luteal phase unrelated to Sjögren's syndrome. The relationship of neuropathy to a long menstrual cycle may be related to repeated, prolonged estrogen or progesterone exposure during the long cycles or to involvement of hypothalamic-pituitary-ovarian function. (Am J Obstet Gynecol 1994;170:835-7.)

Key words: Sjögren's syndrome, autoimmune disease, neuropathy

Sjögren's syndrome is a chronic, inflammatory autoimmune disease in which the salivary and lacrimal glands are progressively destroyed by lymphocytes and plasma cells. As a result, afflicted patients have dry eyes and a dry mouth. Sjögren's syndrome may be a primary illness, or it may occur in patients with rheumatoid arthritis or other connective tissue disorders. Because women are affected 10 times more often than men, we studied gynecologic manifestations of Sjögren's syndrome.

Methods

Through the Sjögren's Syndrome Foundation, Inc. (Port Washington, N.Y.), we sent 1000 questionnaires to women with Sjögren's syndrome in New York, New Jersey, Connecticut, and Pennsylvania. Five hundred thirty-nine women responded, although not all the respondents answered every question. Included in the questionnaire were questions on menstrual function, fertility, pregnancy outcome, and ovarian function. Data analysis was performed with the SPSS system.

Results

The mean age of the women studied was 56 ± 17 years (mean ± SD). The mean age at diagnosis of Sjögren's syndrome was 50 ± 14 years. In some cases there were other rheumatic diseases. For example, 196 of 539 women (36%) reported that they also had rheumatoid arthritis.

Women with Sjögren's syndrome had significant vaginal dryness. Seventy-six percent (67/88) of the women ≥54 years old had vaginal dryness, as opposed to the reported 5% in perimenopausal women in this age group without Sjögren's syndrome.

There was no relationship of Sjögren's syndrome to either the incidence of infertility or miscarriage. Of 440 women responding to a question regarding infertility, 42 (10%) said they were infertile, compared with the 10% to 15% of couples in the United States reporting infertility. Of the 329 women who said they had been pregnant at least once, the ratio of miscarriage to pregnancy was 0.17, or 17%, which is similar to the 12% to 16% rate that has been reported for normal women. Six women reported premature ovarian failure (that is, menopause before the age of 40). Oral contraceptive use was reported by 155 women and hormone replacement therapy by 218.

There were 19 congenital anomalies in 433 pregnancies; this 4% incidence in the offspring of
women with Sjögren's syndrome may be compared with the 2% incidence that has been reported for all women. Although we did not have a control group, the 4% observed incidence is significantly greater than the 2% expected incidence ($\chi^2$ 11.7 with Yates' correction, $p < 0.001$).

Nine of the congenital anomalies involved the heart. Three were heart block, and a fourth was described as arrhythmia.

A long menstrual cycle (>35 days) was associated with infertility ($p = 0.00005$, Fig. 1). Moreover, the incidence of neuropathy was closely linked to the length of the menstrual cycle. A short cycle (<25 days) was associated with the lowest incidence of neuropathy, whereas a long cycle (>35 days) was associated with the highest incidence ($p = 0.00005$, Fig. 2). Neuropathy was defined as "nerve disease" on the questionnaire, but no other information was included.

There was no relationship between age of the respondent and menstrual cycle length (age 59 ± 14 years [mean ± SD] for cycle <25 days, 56 ± 13 years for cycle of 25 to 35 days, and 55 ± 17 years for cycle >35 days, $p = 0.23$, one-way analysis of variance.

Comment

The vaginal dryness in women with Sjögren's syndrome is not surprising, because the nasal and esophageal mucosae are also dry in this disorder. Likewise, the relationship of infertility to a long menstrual cycle may simply indicate the presence of ovulatory dysfunction or inadequate luteal phase unrelated to Sjögren's syndrome.

There is a propensity for complete heart block and neonatal lupus in babies of women with Sjögren's syndrome. The heart block, present in at least three of the offspring of women we studied, may be related to maternal anti-Ro (SS-A) antibody.

Neuropathy and other neurologic changes are common complications of Sjögren's syndrome. The neuropathy is found in approximately 10% to 32% of cases and involves multiple peripheral nerves and sometimes the cranial nerves. It may be the result of vascular inflammation of the vasa nervorum or direct infiltration of nerve sheaths with mononuclear leukocytes.

The association of neuropathy with a long menstrual cycle is difficult to explain. It is not an age effect, because there was no significant relationship of age to menstrual cycle length. Perhaps the neuropathy may be related to repeated, prolonged exposure to estrogen and progesterone during the long cycles or to involvement of hypothalamic-pituitary-ovarian function.

In most cases onset of Sjögren's syndrome occurred in the perimenopausal period and was thus associated with a long menstrual cycle.
with estrogen decline. In addition, many women reported use of hormone replacement therapy with no adverse effects. Therefore, unlike other autoimmune diseases, Sjögren's syndrome may be triggered by estrogen deprivation. Further studies might clarify this matter.

REFERENCES


