

Thyroid disease in primary Sjögren's syndrome

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The thyroid and the salivary glands have a number of functional similarities, including the uptake of iodine by both glands (1). It is also interesting to compare the histopathological features of salivary glands and thyroid tissue, and in primary Sjögren's syndrome (SS) with concomitant thyroiditis the inflammatory picture is similar in the glandular structures of the two organs. The term "autoimmune epithelitis" has been proposed (2) reflecting possible pathogenic mechanisms in common of the epithelial cells in different organs of patients with SS.

Thyroid disease in primary Sjögren's syndrome

Several studies on thyroid disease in SS have not included a control population, and furthermore the results can be difficult to compare owing to different diagnostic criteria of SS. In three uncontrolled studies of patients with SS, hypothyroidism or thyroiditis was found in 13, 24 and 54%, respectively, and hyperthyroidism in 10%, 6% and 0%, respectively (3,4,5). See Table 1.

Two studies include control populations. Foster et al reported overt thyroid disease in 9.5% of 42 SS-patients compared to 1.9% in a local control population (6). Hansen found autoimmune thyroiditis in 18% of SS patients compared to 2% in a general female population (7). In conclusion, thyroiditis and hypothyroidism are common in SS, whereas hyperthyroidism is less frequent.

Table 1. Thyroid disease in primary Sjögren's syndrome

Reference	No of pat.	Hypothyroid/Thyroiditis	Hyperthyroid	Controls
Karsh 1980	24	54 % hypothyroidism	0 %	-
Hansen 1991	28	18 % thyroiditis	0 %	yes
Foster 1993	42	9 % overt thyroid disease	0 %	yes
Perez 1995	33	24 % thyroiditis	6 %	-
Punzi 1996	121	13 % hypothyroidism	10 %	-

Thyroid autoantibodies in primary Sjögren's syndrome

Patients with autoimmune thyroiditis usually have autoantibodies to thyroid tissue, e.g. thyroglobulin (anti-TGB) and/or thyroid peroxidase (anti-TPO). However, these autoantibodies are also common in otherwise healthy populations.

As shown in Table 2, thyroid autoantibodies seem to be more common in SS than in healthy controls although only two studies have compared the frequencies in SS with those in a normal population (3,6). Besides anti-TPO and anti-TGB, Perez et al found autoantibodies to thyroxine in 42%, and to triiodothyronine in 36% (4).

Table 2. Occurrence of anti-thyroid antibodies in primary Sjögren's syndrome

Reference	anti-TPO SS-patients	anti-TGB SS-patients	anti-TPO controls	anti-TGB controls
Karsh 1980	42 %	21 %	-	-
Loviselli 1988 (8)	25 %	12 %	-	-
Bouanani 1991	-	100 %	-	-
Foster 1993	33 %	14 %	5 %	2 %
Perez 1995	45 %	18 %	-	-
Punzi 1996	17 %	13 %	9 %	1 %

The thyroglobulin epitopes bound by Sjögren's syndrome sera are different from those bound by sera from patients with Hashimoto's thyroiditis according to Bouanani. SS-sera bind multiple regions while Hashimoto-sera bind only a single region of the thyroglobulin molecule. A higher

percentage of patients with SS and concomitant thyroid disease bind this region compared to patients with SS without thyroid disease (9).

Foster et al have proposed a common genetic predisposition between SS and thyroid disease based on their investigation of 42 patients with SS and 207 of their relatives. Thyroid disease, SS and their associated autoantibodies were the commonest autoimmune abnormalities observed in the relatives compared to a local control population. Furthermore, the HLA-DR3 phenotype was associated with SS as well as with hypothyroidism (6).

Primary Sjögren's syndrome in patients with autoimmune thyroiditis

If thyroiditis is common in SS; how frequent is the opposite, i.e. SS in patients with thyroiditis?

Controlled epidemiological studies have not been performed. In three studies of patients with Hashimoto's thyroiditis from the 1960's there was no increase of SS compared to age and sex matched controls (10,11,12). However, Sjögren's syndrome was defined in a different way and the distinction between primary and secondary Sjögren's syndrome was not done in those days.

In a study of 246 patients diagnosed as Hashimoto's thyroiditis during the period 1935-1967 only one patient with Sjögren's syndrome was found (13), and in 1998 Gaches et al reported 6 patients with SS retrospectively found among 140 patients with thyroiditis (4%) (14). For comparison, the frequency of SS was 2.7% in a Swedish healthy population aged 52-72 years (15).

In 1997 Coll et al reported 176 patients with autoimmune thyroid disease (88 Grave's disease, 40 Hashimoto's thyroiditis, 48 primary myxoedema). SS was diagnosed in as many as 24% and the frequency was about the same in the three subgroups. However, the occurrence of antibodies to SS-A and SS-B was not reported, only 38 of 176 patients were lip biopsied, and SS was defined by the presence of keratoconjunctivitis sicca and/or xerostomia. (xerostomia defined by labial biopsy score IV according to Chisholm and Mason or score III and positive glandular scintiscan) (16).

In an excellent review from 1996 Scofield concluded that there appears to be no increase in the prevalence of SS in patients with autoimmune thyroid disease (17).

Autoantibodies to SS-A and SS-B in patients with autoimmune thyroiditis

From a total of 63 patients with autoimmune thyroiditis Hansen et al found one single patient with precipitating antibodies to SS-A and not one with precipitating antibodies to SS-B. In contrast, 27% had antibodies to SS-B as tested with ELISA. Nineteen cases were further evaluated, and 6 patients (10% of all 63 patients) fulfilled the Copenhagen criteria for primary Sjögren's syndrome (7).

In 1994 Gudbjörnsson et al reported the serological and clinical data of 40 women with postpartum thyroiditis. No patient had precipitating antibodies to SS-A or SS-B during the period of postpartum thyroiditis or five years later. However, with an ELISA method antibodies to SS-A were detected in 46% and to SS-B in 34%. Five of 24 examined patients had objective signs of keratoconjunctivitis sicca, and 3 of these also had xerostomia (7.5% of all patients). Seven patients underwent biopsy and two had sialoadenitis compatible with SS. The patient group was not compared to any control population (18).

We have investigated the occurrence of anti-SS-A antibodies in 130 patient sera previously shown to contain antibodies to TPO and/or TGB as tested by solid phase assays (ELISA). A positive anti-thyroid antibody test was defined as an antibody level above the 97th percentile in 100 blood donor sera. The presence of anti-SS-A antibodies was screened using a commercial ELISA kit, and with a cut-off level recommended by the manufacturer. Positive anti-SS-A antibody tests were followed up by Ouchterlony immunodiffusion technique for the demonstration of precipitating antibodies against SS-A and SS-B. By ELISA-screening 3% (4/130) proved to contain anti-SS-A antibodies. Precipitating anti-SS-A antibodies were confirmed in two of these patient sera. None of the four sera had precipitating antibodies against SS-B. Thus, antibodies to SS-A seem to be

uncommon in an unselected material of anti-TPO/anti-TG-containing patient sera (Eriksson & Dahle, unpublished observations).

Conclusions

In patients with concomitant SS, symptoms and treatment of thyroid disease does not differ from non-SS patients with thyroid disease. However, one should be aware of the possibility of primary Sjögren's syndrome when hypothyroid symptoms (for instance tiredness) do not improve upon thyroid hormone replacement. Extreme tiredness is a common complaint in SS. Since thyroiditis is important to diagnose and treat, and since it occurs in 10-54% of SS patients, it is advisable to examine thyroid function regularly in patients with SS.

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