

Demographic and clinical features of patients with subacute thyroiditis: Results of 169 patients from a single University Center in Turkey

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ABSTRACT. Background: Turkey is an endemic area for thyroid diseases. The Aegean region is well documented for increased prevalence of thyroid disorders. In this study we investigated the demographic and clinical features of subacute thyroiditis (SAT) patients who had been diagnosed and treated in Ege University. **Methods:** The hospital files of patients admitted to the endocrinology clinic of Ege University between January 1987 and December 2001 were retrospectively evaluated. Patients who had been diagnosed as having any thyroid disorder were determined. **Results:** 176 fulfilled diagnostic criteria for SAT. The majority of patients with SAT were diagnosed as having subacute granulomatous thyroiditis (169/176) (134 females, 35 males, mean age 34.0 ± 17.8 yr); 69% of the patients were between 30-50 yr of age. Thyroid pain was present in 97.1% of female patients, and in 100% of male patients. High fever was evident in 78 patients

(46.2%). Mean erythrocyte sedimentation rate (ESR) was 43.42 ± 39.68 mm/h. Anti-thyroglobulin antibody was positive in 20%, and anti-thyroid peroxidase antibody was positive in 4% of patients. Among patients who were treated with non-steroidal anti-inflammatory drugs (NSAD) 10 female patients (10.6%), and 3 male patients (12%) developed recurrence of the disease. Among patients who were treated with prednisolone 7 female patients (17.5%), and one male patient (10%) developed recurrence. There was no significant difference regarding the recurrence rates between patients who were treated with NSAD and patients who were treated with prednisolone. **Conclusion:** With the exception of ESR, demographic, clinical, laboratory, and imaging findings and prognoses of our patients were comparable to the previous reports.

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INTRODUCTION

Subacute thyroiditis (SAT) (de Quervain thyroiditis, or granulomatous thyroiditis) is an inflammatory disorder of the thyroid (1-3). Patients with SAT suffer thyroid pain associated with symptoms of hyperthyroidism. SAT is the most common cause of the painful thyroid and may account for up to 5% of clinical thyroid abnormalities. Women are more frequently affected than men. The peak incidence of the disease appears in the 4th and 5th decades (4). TSH

levels are suppressed, thyroid uptake of radioactive iodine (I^{131}) is low, and erythrocyte sedimentation rate (ESR) is elevated in those patients (5, 6). Clinical and laboratory findings are usually sufficient for the diagnosis of SAT, and tissue diagnosis is rarely needed (5, 7, 8). SAT is possibly of viral etiology, and is a self-limited disease. The clinical features of SAT and outcome of the disease have been previously documented in many non-population-based studies (9-12). The pathogenesis of SAT, frequencies of autoantibodies, seasonal variations, scintigraphic and ultrasonographic findings, late complications and recurrence rates of the disease were investigated in those trials. However, community and incidence cohort studies are rare (13, 14).

Turkey is an endemic area for thyroid diseases. Several regions of Turkey, including the Aegean region, are well documented for increased prevalence of thyroid disorders. Ege University is in Izmir and is the

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main referral center accepting patients from all over the Aegean region. Therefore, the patient population of Ege University can reflect the general population in that area. In this study we aimed to outline the demographic and clinical features of our SAT patients, and to compare our results with previous studies in the literature.

MATERIALS AND METHODS

The hospital files of patients admitted to the endocrinology clinic of Ege University were retrospectively evaluated and patients who had been diagnosed as having any thyroid disorder were determined. Patients with SAT were selected among those patients. The inclusion criteria for the diagnosis of SAT were any one of the following: a) pathological diagnosis (surgical specimen or biopsy); b) painful thyroid and either suppressed uptake of I¹³¹ or elevated ESR, or both; or 3) unilateral thyroid pain with abnormally low uptake I¹³¹ and elevated ESR.

Five-year follow-up data was recorded for each patient. Accordingly, patients who had been diagnosed between January 1987 and December 2001 were included in this study. Age and sex distributions, frequencies of symptoms such as fever and pain, laboratory findings including ESR and autoantibodies, scintigraphic and ultrasonographic findings, treatment modalities, treatment responses, and recurrence rates of the patients with SAT were evaluated in detail. Anti-thyroglobulin antibody and anti-thyroid peroxidase antibody levels were measured with chemiluminescent sequential immunometric assay in Immulite 2000.

Statistical analysis

The Statistical Package for Social Sciences (SPSS) version 10.0 was used to analyze the data. Descriptive statistics, chi-square test, Fisher's exact chi-square test, and Student's t-test were used for statistical analyses.

RESULTS

Among 19,750 patients admitted to the endocrinology clinic of Ege University between January 1987 and December 2001, 6,496 patients (32.9%) were diagnosed as having thyroid disorder, such as thyroiditis, Graves' disease, toxic multinodular goiter, toxic adenoma, and solitary nodules. A total of 176 patients fulfilled the above-mentioned diagnostic criteria for SAT. The prevalence of SAT was 0.9% among the whole population of patients (no.=19,750), and the prevalence of SAT was 2.7% among patients with thyroid disorders (no.=6,496) (Table 1). The majority of patients with SAT were diagnosed as having subacute granulomatous thyroiditis (169/176, 96.0%), and 7 patients were diagnosed as having subacute lymphocytic thyroiditis (Table 1). We then evaluated various features of the 169 patients with subacute granulomatous thyroiditis in more detail. One hundred and thirty-four patients were female (79.3%), and 35 patients

were male (20.7%) (Table 1). Mean age of the whole group of patients with subacute granulomatous thyroiditis was 34.0±17.8 yr. Mean age of females was 34.5±18, and mean age of males was 31.8±16.7 yr (Table 1). Age distribution was as follows: 13.8% of the patients were below 30 yr of age, 69% of the patients were between 30-50 yr of age, and 17.2% of the patients were above 50 yr of age (Table 1). Thyroid pain was present in 97.1% of female patients, and in 100% of male patients. There was no significant difference regarding the presence of thyroid pain between females and males ($p=0.124$) (Table 2). High fever (i.e. >38.3 C) was evident in 78 patients (46.2%) (Table 1). There was no significant difference regarding the presence of high fever between females and males. Mean ESR was 43.42±39.68 mm/h in the whole group of subacute granulomatous thyroiditis patients. Mean ESR was 41.18±36.72 mm/h in females, and 53.05±50.48 mm/h in males ($p=0.230$) (Table 2). ESR was markedly elevated (i.e. >60 mm/h) in 56.7% of the patients. ESR was <20 mm/h in 14.1% of the patients (Table 1). The mean time of admission of patients with low ESR after the onset of their symptoms was 45 days, and 4 of them were using prednisolone.

Table 1 - Clinical and demographical features of patients with subacute thyroiditis (SAT).

	%
SAT among the whole population of patients	0.9
SAT among patients with thyroid disorders	2.7
Subacute granulomatous thyroiditis	96.0
female	79.3
male	20.7
below 30 yr of age	13.8
between 30-50 yr of age	69.0
above 50 yr of age	17.2
Presence of thyroid pain in female	97.1
Presence of thyroid pain in male	100
High fever (>38.3 C)	46.2
ESR was >60 mm/h	56.7
ESR was <20 mm/h	14.1
Anti-thyroglobulin antibody was positive	
female	20.0
male	21.2
Anti-thyroid peroxidase antibody was positive	
female	4.0
male	4.0
Treated with NSAD	70.4
Treated with prednisolone	29.6
Recurrence of the disease with NSAD drugs	
female	10.6
male	12.0
Recurrence of the disease with prednisolone	
female	17.5
male	10.0

ESR: erythrocyte sedimentation rate; NSAD: non-steroidal anti-inflammatory drugs.

Anti-thyroglobulin antibody was positive (normal value: 0-40 IU/ml) in 20% of female patients with subacute granulomatous thyroiditis, and in 21.2% of males (Table 1). Anti-thyroid peroxidase antibody was positive (normal value: 0-35 IU/ml) in 4% of females and in 4% of males (Table 1). Seventeen percent of patients with subacute granulomatous thyroiditis had been given antibiotics before admission; 119 patients (70.4%) were treated with non-steroidal anti-inflammatory drugs (NSAD) (94 females and 25 males), and 50 (29.6%) of them were treated with prednisolone (40 females and 10 males) (Table 1). Prednisolone was started at a dose of 35-60 mg/day. The dose of prednisolone was decreased by 5 mg approximately 7-10 days after the initiation of the treatment, and then tapered and discontinued within 6-8 weeks. Among patients who were treated with NSAD 10 female patients (10.6%), and 3 male patients (12%) developed recurrence of the disease (Table 1). Among patients who were treated with prednisolone 7 female patients (17.5%), and one male patient (10%) developed recurrence. There was no significant difference regarding the recurrence rates between patients who were treated with NSAD and patients who were treated with prednisolone ($p=0.317$) (Table 2). The mean ages of patients who had recurrence and who did not have recurrence were 30.52 ± 18.37 yr and 34.54 ± 17.73 yr, respectively ($p=0.337$) (Table 2). Likewise, sex distributions of patients with or without recurrent disease were comparable. Recurrence developed in 12 patients who had had high fever (no.=78), and in 9 patients who had remained afebrile (no.=91) ($p=0.247$) (Table 2). There was no significant difference regarding recurrence rates between patients with or without anti-thyroglobulin antibodies, and between patients with or without anti-thyroid peroxidase antibodies. A total of 17 female patients and 4 male patients had recurrent disease. Among those patients with recur-

rent disease 12 females and 3 males were treated with prednisolone, and 5 females and 1 male were treated with NSAD.

Thirty-five patients (20.7%) (27 females, 8 males) developed transient hypothyroidism. There was no association between the development of transient hypothyroidism and clinical findings (pain, fever), laboratory findings (ESR, anti-thyroglobulin antibodies, anti-thyroid peroxidase antibodies) or the treatment modalities. Permanent hypothyroidism was seen in 4 patients (2.3%) after surgical interventions, and in 3 patients (1.8%) due to autoimmune thyroiditis.

Technetium 99 thyroid scanning demonstrated low uptake in all patients. Thyroid ultrasonography demonstrated normal findings in 17.3%, diffuse enlargement in 15.2%, single nodule in 60.8%, and multiple nodules in 6.7% of female patients; and diffuse enlargement in 26%, single nodule in 42%, and multiple nodules in 32% of male patients. Thyroid ultrasonography was performed in 50 patients who did not have recurrence. Among those patients, 9 had normal findings, 25 had single nodule, and 8 had multiple nodules in the thyroid gland. Thyroid ultrasonography was available in 15 patients who had disease recurrence. Among those patients, 3 had diffuse enlargement, 11 had single nodule, and 1 had multiple nodules in the thyroid gland. The thyroid ultrasonographic findings were comparable between patients with or without recurrent disease ($p=0.232$) (Table 2).

DISCUSSION

In this study we presented the clinical and demographic data of 169 patients with subacute granulomatous thyroiditis who were diagnosed and treated in the endocrinology clinic of Ege University between January 1987 and December 2001.

Table 2 - Clinical and demographical features of patients (values are expressed as mean±SD).

	mean±SD	p
Presence of thyroid pain between females and males		0.124
Mean ESR		
female	41.18±36.72 mm/h	0.230
male	53.05±50.48 mm/h	
Recurrence rates; NSAD and prednisolone		0.317
The mean ages of patients		
who had recurrence	30.52±18.37 yr	0.337
who did not have recurrence	34.54±17.73 yr	
Recurrence developed		
patients who had high fever (12/78),		0.247
patients who had remained afebrile (9/91)		
The thyroid ultrasonographic findings were comparable between patients with or without recurrent disease		0.232

ESR: erythrocyte sedimentation rate; NSAD: non-steroidal anti-inflammatory drugs.

Similar to the results of previous reports, subacute granulomatous thyroiditis was more prevalent in females in our study, with a female:male ratio of approximately 4:1. Hence, like all other thyroid diseases there is female predominance in patients with subacute granulomatous thyroiditis (female:male ratio 3.8). Likewise, similar to previous trials, the majority of our patients were between 30-50 yr of age (15, 16). The mean age of our patients with subacute granulomatous thyroiditis was 34.0 ± 17.8 yr. The mean age of SAT patients was 40 yr in a series of 1,127 patients (17). Litaka et al. (18) reported 3,344 SAT patients with a mean age of 38.4 yr. Frequencies of presenting symptoms of our patients including pain and fever were also similar to previous reports. Pain (neck pain, thyroid pain or sore throat) was present in 97.1% of females, and in 100% of male patients in our study. Pain was reported in 91% of SAT patients by Aiginer et al. (19), in 89% of patients by Volpe et al. (20), and in 93% of patients by Hwang et al. (21). There was no difference regarding the presence of pain between females and males in those previous studies and in our study. On the other hand, 46.2% of our patients had high fever. High fever was present in 57% of patients reported by Aiginer (19), in 54% of patients reported by Volpe et al. (20).

We demonstrated that only 57% of our patients with subacute granulomatous thyroiditis had ESR higher than 60 mm/h. However, nearly all patients with SAT had ESR higher than 60 mm/h in previous trials (20, 22, 23). Delayed admission to our clinic after onset of the symptoms and previous therapies with NSAD or steroids might be possible explanations for the lower prevalence of markedly elevated ESR in our group.

Mild or moderately active patients regarding clinical symptoms and laboratory values were treated with NSAD. Patients with severe symptoms (high fever, severe thyroid pain, tenderness of the thyroid, severe thyrotoxic symptoms) and laboratory values including elevated thyroid function tests, ESR higher than 60 mm/h, heterogenities in ultrasonographic evaluations were treated with glucocorticoids (24).

The therapy of choice was prednisone, starting with an initial dose of usually 35-40 mg/day, reduced stepwise over 3 months under control of the clinical picture and the sedimentation rate. Some of the patients' clinical symptoms of the disease that had disappeared transiently redeveloped under reduction of prednisone without increase of the ESR. Raising the dose of prednisone to 60 mg/day for a short while led to prompt disappearance of symptoms.

The frequency of thyroid autoantibodies does not generally increase in SAT. Those antibodies show mild elevations and disappear within a few months (25). We demonstrated that anti-thyroglobulin an-

tibody was positive in 20% of females and 21% of males. On the other hand the frequency of anti-thyroid peroxidase antibody was much lower in both sexes (4% in both females and males). The prevalence of those autoantibodies in our patients was comparable to previous studies (23).

Nodular enlargement : diffuse enlargement ratio in thyroid ultrasonographies of SAT patients was 4:1 in a previous study (26, 27). Likewise, we demonstrated that nodular enlargement : diffuse enlargement ratio was 4.4:1 in females and 2.8:1 in males. It was suggested that hypodensities, hypodensities with pseudocysts, and multiple hypodense areas could be erroneously accepted as nodules in ultrasonographic examinations during the acute phase of SAT. Hence nodular enlargement : diffuse enlargement ratio increases in thyroid ultrasonographies of those patients.

In accordance with a study by Aiginer et al. (19), we reported that 17.1% of our patients with subacute granulomatous thyroiditis had been treated with antibiotics, mostly by penicillin.

Previous studies showed a recurrence rate of approximately 10% in SAT patients (23, 28-32). Likewise, 10.6% of females and 12% of males developed recurrence of the disease after treatment with NSAD, and 17.5% of females and 10% of males developed recurrence in our study.

In summary, we herein reported the demographic and clinical features of our patients with subacute granulomatous thyroiditis. We demonstrated that, with the exception of ESR, demographic, clinical, laboratory, and imaging findings and prognoses of our patients were comparable to the previous reports. Our study was retrospective and presents the usual limitations of a retrospective design. Moreover, as it is not a population-based study identifying all patients with SAT, there may be referral bias in our patient population. However, it is difficult to establish SAT epidemiologically since it occurs sporadically and infrequently. On the other hand, since Ege University is the main referral center for endocrinologic diseases in the Aegean region of Turkey, our results can reflect the general population in that region.

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