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ORIGINAL ARTICLE

# Clinical characteristics of subacute thyroiditis is different than it used to be – current state based on 15 years own material

**Magdalena Stasiak [1], Renata Michalak [1], Bartłomiej Stasiak [2], Andrzej Lewiński [1,3]**

1 Department of Endocrinology and Metabolic Diseases, Polish Mother`s Memorial Hospital – Research Institute, Lodz, Poland
2 Institute of Information Technology, Lodz University of Technology, Lodz, Poland
3 Department of Endocrinology and Metabolic Diseases, Medical University of Lodz, Lodz, Poland

*Correspondence to:* Andrzej Lewiński, MD, PhD, Professor of Endocrinology, Department of Endocrinology and Metabolic Diseases, Polish Mother`s Memorial Hospital - Research Institute, 281/289 Rzgowska St., 93-338 Lodz, Poland
TEL.: +48 42 271 11 41; E-MAIL: alewin@csk.umed.lodz.pl

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## Abstract

**INTRODUCTION:** The clinical characteristics of subacute thyroiditis (SAT) has been changing in recent years. There are more and more patients with painless SAT, and more cases of SAT with elevated levels of anti-thyroid antibodies were reported. The aim of the study was to evaluate the clinical characteristics of SAT patients with special regard to the differences between the previously described and currently observed features of the disease.

**MATERIAL AND METHODS:** Clinical and laboratory data were retrospectively reviewed for 64 patients with confirmed SAT.

**RESULTS:** Mean age of the patients was 42.67 years. The male to female ratio was 1:7. Neck or ear pain was reported by 93.75% of patients, while fever occurred in 65.63% of patients. The aTPO and aTg levels were increased in 15.5% and 33.3% of patients, respectively. TRAb level was increased in 6% of patients. Transient microhaematuria was present in 63% of analyzed cases. No statistically significant differences in clinical characteristics or laboratory results were found between the groups with- and without neck/ear pain, with- and without elevated TRAb, and with- and without elevated aTPO and/or aTg.

**CONCLUSION:** In our study, several new features of current SAT course, different from what we used to know about the disease, were reported. Higher frequency of painless SAT than it was ever described, was observed. Moreover, in as much as one third of the patients aTPO and/or aTg were present, and in 6% of SAT cases the coexistence of TRAb was demonstrated. Transient microhaematuria was typical for the acute SAT phase.

**Abbreaviations:**

| | |
|---|---|
| AITD | - autoimmune thyroid disease; |
| aTg | - thyroglobulin antibodies; |
| aTPO | - thyroid peroxidase antibodies; |
| CRP | - C reactive protein; |
| ECLIA | - electrochemiluminescence immunoassay; |
| ESR | - high erythrocyte sedimentation rate; |
| FNAB | - fine needle aspiration biopsy; |
| FT3 | - free triiodothyronine; |
| FT4 | - free thyroxine; |
| SAT | - subacute thyroiditis; |
| TBSRTC | - The Bethesda System for Reporting Thyroid Cytopathology; |
| TRAb | - thyrotropin receptor antibodies; |
| TSH | - thyrotropin; |
| US | - ultrasound; |
| WBC | - white blood count. |

## INTRODUCTION

Subacute thyroiditis (SAT) (also called granulomatous thyroiditis, giant cell thyroiditis or de Quervain thyroiditis) is an inflammatory disease of the thyroid, triggered probably by a previous viral infection (occurring approximately 2-6 weeks earlier). The prevalence of SAT is over four times higher in women than in men (Samuels, 2012). Susceptibility to the disease is associated with human leukocyte antigens (HLA), mainly with HLA-B35 antigen (Nyulassy *et al.* 1977).

Patients most commonly complain of the anterior neck pain, usually radiating ipsilaterally up to the jaw and ear and to the upper mediastinum. Fever is present in the majority of cases, reaching frequently over 39°C and rising especially at night. Fatigue and malaise often occur. All the initial symptoms may be accompanied by muscle pain. In some cases, symptoms of thyrotoxicosis are present, usually of low to moderate severity (Fatourechi *et al.* 2003; Alfadda *et al.* 2014). In rare cases they can dominate the clinical presentation, with medical history of weight loss and palpitations. The disease typically has a 4-phase course and the characteristic symptoms – described above – are present in the first phase. Thyrotoxicosis phase usually lasts for 2 to 8 weeks, and is a result of the destruction of thyroid follicles and the release of thyroid hormones. In the second phase, pain and fever resolve spontaneously, and hormonal parameters normalize (approximately after 8-16 weeks). In many patients the disease does not resolve spontaneously and subsequent phases appear only after the administration of glucocorticoids. Phase 3 with subsequent hypothyroidism does not occur frequently and persistent hypothyroidism is extremely rare (Fatourechi *et al.* 2003; Alfadda *et al.* 2014).

In laboratory findings, high erythrocyte sedimentation rate (ESR), sometimes reaching even three-digit value, is a characteristic feature of SAT. C reactive protein (CRP) and – to less extend – white blood count (WBC) may also be elevated. Laboratory markers of hyperthyroidism are often found but the levels of antithyroid antibodies are believed to be usually normal (Fatourechi *et al.* 2003; Nishihara *et al.* 2008; Alfadda *et al.* 2014).

The ultrasound (US) features of SAT include hypoechoic and heterogeneous areas with blurred margins, poorly vascularised on colour Doppler (Capelli *et al.* 2014; Vural *et al.* 2015). Sometimes a rapid growth of firm thyroid lesion initially suggests malignancy, but in cytology it reveals to be SAT.

Although the natural course of the disease is often self-limiting, patients frequently suffer from severe symptoms which prevent normal functioning even for months.

The clinical characteristics of the disease has been changing in recent years. There are more and more cases of painless SAT (Daniels, 2001; Karachalios *et al.* 2010; Dalugama, 2018), and elevated levels of antithyroid antibodies, including thyroid peroxidase antibodies (aTPO) and thyroglobulin antibodies (aTg), are more often present (Fatourechi *et al.* 2003; Benbassat *et al.* 2007). Until recently, it was thought that thyrotropin receptor antibodies (TRAb) never occur in SAT, but in the last three decades a few cases of simultaneous coexistence of SAT and elevated TRAb level were reported (Nakamura *et al.* 1996; Fujii *et al.* 2003; Hoang *et al.* 2011).

The aim of the study was to evaluate the clinical characteristics of SAT patients with special regard to the differences between the previously described and currently observed features of the disease

## MATERIAL AND METHODS

Clinical records were retrospectively reviewed for 64 Caucasian patients who were diagnosed with SAT between 2003 and 2018 in the Department of Endocrinology and Metabolic Diseases, Polish Mothers' Memorial Hospital - Research Institute, Lodz, Poland. The study project was approved by Local Medical Ethics Committee. For every patient, the clinical SAT signs and symptoms, possible preceding infection and laboratory results were established based on the clinical examination and medical history.

After admission, patients had laboratory tests performed including blood concentration of: thyrotropin (TSH), free triiodothyronine (FT3), free thyroxine (FT4), aTg, aTPO, TRAb, ESR, CRP, WBC and urinalysis. Serum levels of TSH, FT3, FT4, aTg, aTPO, TRAb were measured by electrochemiluminescence immunoassay (ECLIA), Cobas e601 analyzer (Roche Diagnostics, USA), ESR was determined by Ves-Matic Cube 30 (Diesse, Italy), CRP was determined by VITROS® 4600 Chemistry System (Ortho Clinical Diagnostics, USA), WBC – by flow cytometry, XE-2100 analyser (Sysmex, Kobe, Japan) and urine samples were analysed by the Iris iQ analyser (İris Diagnostics, USA). The results are available for the following number of patients: TSH, FT3 and FT4 – for 63, aTg – for 57, aTPO – for 58, TRAb – for 50, ESR – for 51, CRP – for 59 WBC – for

63, urinalysis – for 27. Thyroid ultrasound examination (US) was performed in every patient using a 7-14 MHz linear transducer (Toshiba Aplio XG; Toshiba, Japan). Scanning was performed in supine position with a pad under the patients' shoulders to provide optimum neck extension. Fine needle aspiration biopsy (FNAB) was performed in 62 patients using a 23-gauge needle. Smears were cytologically evaluated, and the presence of multinucleated giant cells together with mononucleated macrophages, epithelioid cells and follicular epithelial cells against acute and chronic inflammatory dirty background, was considered as a result typical for SAT. Other results, revealing cytological group 2 according to The Bethesda System for Reporting Thyroid Cytopathology (TBSRTC), were considered as exclusion of malignancy.

The diagnosis of SAT was based on the diagnostic criteria recently proposed by our team (Stasiak *et al.* 2018, submitted). These criteria are as follows: elevation of ESR (or at least CRP) plus hypoechoic area/areas with blurred margins and decreased vascularisation in US plus FNAB confirmation of SAT, or at least FNAB exclusion of malignancy, plus at least one of the following: hard thyroid swelling and/or pain and tenderness of the thyroid gland/lobe and/ or elevation of serum FT4 and suppression of TSH and/ or decreased radioiodine uptake.

*Statistical analysis*

Data from medical history and laboratory test results were analyzed for all patient. Due to rarity of painless SAT course, and infrequent coexistence of SAT and elevated anti-thyroid antibodies or TRAb, all patients were divided into the following groups: 1. with and without neck/ear pain, 2. with and without elevated aTPO and/or aTg, 3 with and without elevated TRAb. Statistical analysis of clinical and laboratory SAT features was performed for each of these groups individually. Descriptive statistics of the collected data included median, mean, standard deviation, minimum and maximum values, and interquartile range. For comparisons between groups, we used Student's t-test for normally distributed variables, Mann-Whitney U test for the other real-valued data and chi-square test for categorical variables. The normality of data distributions was assessed by Shapiro-Wilk test, and in all the tests $p$ value $< 0.05$ was considered significant.

**Tab. 1.** Clinical features of the studied patients with SAT

| Parameter (No. of patients) | Frequency % (No. of patients) |
|---|---|
| Neck/ear pain (64) | 93.75 (60) |
| Fever (64) | 65.63 (42) |
| Preceding infection (64) | 31.25 (20) |
| Microhaematuria (27) | 62.96 (17) |
| Typical US (64) | 100 (64) |
| Typical FNAB (61) | 81.97 (50) |
| Recurrence | 14.06 (9) |

Abbreviations: FNAB - fine needle aspiration biopsy; US - ultrasound.

## RESULTS

Mean age of the patients was 42.67 years (range 27-69 years). The male to female ratio was 8:56 (i.e. 1:7). Preceding viral infection was reported by 20 patients (31.25%). Neck or ear pain was reported by 60 patients (93.75%), while fever occurred in 42 patients (65.63%). The mean TSH level was 0.258 ± 0.58 mIU/l (decreased in 49 patients and normal in 14 patients). Mean FT3 level was 7.03 ± 4.035. FT3 was increased in 41 patients and in 22 – normal. Mean FT4 was 2.97 ±1.79, FT4 was

**Tab. 2.** Laboratory results of the studied patients with SAT

| Parameter (No. of patients) | mean ± SD | median | abnormal (%)* | min-max (reference range and unit) |
|---|---|---|---|---|
| TSH (63) | 0.259±0.58 | 0.01 | 77.78 | 0.005-2.58 (0.27-4.2 mIU/l) |
| FT4 (63) | 2.98±1.79 | 2.28 | 74.6 | 1.12-7.77 (0.93-1.7 ng/dl) |
| FT3 (63) | 7.03±4.04 | 5.46 | 65.08 | 2.85-17.49 (2.6-4.4 pg/ml) |
| aTPO (58) | 38.34±91.15 | 12.535 | 15.52 | 6.3-600 (<34 IU/ml) |
| aTg (57) | 235.69±575.89 | 51.43 | 33.33 | 3.23-4000 (<115 IU/ml) |
| TRAb (50) | 1.44±5.63 | 0.48 | 6 | 0-40 (<1.75 IU/ml) |
| ESR (61) | 70.39±24.1 | 69 | 100 | 20-132 (0-12 mm/h) |
| CRP (59) | 7.32±6.72 | 5.5 | 98.31 | 0.43-32.98 (<1 mg/dl) |
| WBC (63) | 9.09±3.22 | 8.91 | 28.57 | 3.91-20.81 (4-10 · $10^3$/μl) |

*decreased in the case of TSH, increased in the case of all other parameters

A $p$-value of <0.05 is considered statistically significant. Data are presented as mean ± standard deviation (SD) and as median, and minimum and maximum values.

Abbreviations: aTg - anti-thyroglobulin antibodies; aTPO - anti-thyroid peroxidase antibodies; CRP - C reactive protein; ESR - erythrocyte sedimentation rate; FT3 - free triiodothyronine; FT4 - free thyroxine; TRAb - TSH receptor antibodies; TSH - thyrotropin; WBC - white blood cells.

**Tab. 3.** Patients' clinical characteristics in the groups under comparison

| Parameter | Pain-free group | Pain group | *p*-value | aTPO/aTg normal | aTPO/aTg increased | *p*-value | TRAb normal | TRAb increased | *p*-value |
|---|---|---|---|---|---|---|---|---|---|
| Male:Female | 1:3 | 7:53 | 1.00 | 4:30 | 3:17 | 0.983 | 6:42 | 0:3 | 0.786 |
| Preceding infection | 75% | 28% | 0.164 | 32% | 20% | 0.507 | 21.1% | 33.3% | 0.666 |
| Neck/Ear pain | - | - | - | 88% | 100% | 0.291 | 93.8% | 100% | 0.413 |
| Fever | 50% | 66.7 | 0.892 | 65% | 70% | 0.921 | 64.6% | 66.7% | 0.583 |

A *p*-value of <0.05 is considered statistically significant
Abbreviations: aTg - anti-thyroglobulin antibodies; aTPO - anti-thyroid peroxidase antibodies; TRAb - TSH receptor antibodies.

increased in 47 patients and in 16 – normal. Mean aTPO was 38,34 ±91.15 FT4, aTPO was increased in 9 patients and in 49 – normal. Mean aTg was 235.7±575.9, in 19 patients aTg was increased and in 38 – normal. Mean TRAb was 1,44±5.63, in 3 patients TRAb was increased and in 47 – normal. Mean ESR was 70.4 ±24.1 and it was increased in all patients, Mean CRP was 7.32±6.72, CRP was increased in 58 patients and normal in one (1). Mean WBC was 9.09±3.22, WBC was increased in 19 patients, decreased – in 1 patient and normal – in 44 patients. Among 27 patients in whom urinalysis was performed, in 17 microhaematuria was present. Thyroid US was typical for SAT in all the cases, and the cytology was typical for SAT in 50 patients. In the remaining 11 patients cytology excluded malignancy but the smears were not typical for SAT. Nine patients (14%) reported SAT recurrence (at least once). Clinical features of SAT patients are presented in Table 1. Laboratory results of SAT patients are presented in Table 2. No statistically significant difference was found between the groups with- and without neck/ear pain, with- and without elevated TRAb, with- and without elevated aTPO and/or aTg, with regard to clinical characteristics (Table 3) or laboratory results (Table 4).

## DISCUSSION

Subacute thyroiditis is a rare disease but its prevalence is increasing and the clinical course is changing over time. The disease is believed to affect mainly middle aged women (Fatourechi *et al.* 2003) and in our SAT cohort the mean age was 42.67 years and the male:female ratio was 1:7. Predominance of women in our group was even greater than previously suggested by Fatourechi *et al.* (2003), who reported 1:4 ratio. Previous viral infection (occurring approximately 2-6 weeks earlier) is considered as a SAT triggering factor, but in our group only 31.25% of patients reported any preceding symptoms of infection. Thus, probably some other factors can also induce SAT. This theory is supported by reports of SAT affecting a few relatives who lived separately and were not exposed to the same pathogens and did not report any infection (Rubin & Guay, 1991; Kramer *et al.* 2004; Hamaguchi *et al.* 2005). It seems that of key importance is the genetic background, possibly associated with the exposure to some common pathogens leading to symptomatic or asymptomatic infection.

For years, neck pain was considered the main and most characteristic symptom of SAT. In recent years, several cases of painless SAT have been described in the literature (Daniels, 2001; Karachalios *et al.* 2001; Dalugama, 2018) but painless course of SAT is still considered as extremely rare. However, in our group, such a course of the disease concerned as many as 6.25% of patients (with cytological SAT confirmation in all cases), which clearly indicates the increasing frequency of pain-free SAT cases. This may result from a changing course of the disease, or – perhaps – previously painless SAT was simply not diagnosed, because of poorer diagnostic possibilities, mainly with the respect to US and FNAB. Our results did not reveal any potential characteristic feature of painless SAT, because in the studied cohort no significant difference was found between patients with- and without neck/ear pain in the aspects of all analysed laboratory parameters and clinical features. The long-known SAT diagnostic criteria required confirmation of pain or tenderness of the thyroid, which is currently not always present. Thus, we have recently suggested new diagnostic criteria for SAT, with pain being only a complementary criterion (Stasiak *et al.* 2018, submitted). Painless SAT often presents as fever of unknown origin (Daniels, 2001; Karachalios *et al.* 2001). Two of our pain-free patients (50%) complained mainly of fever and mild symptoms of thyrotoxicosis, while the other two had firm thyroid nodule which appeared suddenly and required exclusion of malignancy. In the whole group, fever was less frequent that it had been believed to occur, since it was present only in 65.63% of our patients. Laboratory findings revealed thyrotoxicosis in the majority of patients, with mean TSH 0.258 ± 0.58 mIU/l. Decreased TSH was observed in 77.78% and increased FT3 and FT4 were observed in 65.08% and 73.33%, respectively. These results are consistent with previously published observations (Nishihara *et al.* 2008; Benbassat, 2007).

The absence of anti-thyroid antibodies was believed to be a typical SAT feature. However, sporadic occurrence of increased levels of thyroid antibodies in SAT has been reported with the frequency ranging from 4% for aTPO to 20% for aTg (Fatourechi *et al.* 2003;

**Tab. 4.** Comparison of the laboratory results and age in groups with and without neck/ear pain, with and without increased aTPO and/or aTg, and with and without increased TRAb.

| Parameter | Pain-free group | Pain group | *p*-value | aTPO/aTg normal | aTPO/aTg increased | *p*-value | TRAb normal | TRAb increased | *p*-value |
|---|---|---|---|---|---|---|---|---|---|
| age | μ=41.50 SD=6.46 | μ=42.75 SD=9.57 | 0.989 | μ=41.77 SD=9.22 | μ=42.75 SD=9.50 | 0.628 | μ=42.62 SD=9.88 | μ=45.33 SD=13.58 | 0.733 |
| TSH | μ=0.23 SD=0.29 | μ=0.26 SD=0.59 | 0.563 | μ=0.28 SD=0.62 | μ=0.17 SD=0.55 | 0.910 | μ=0.21 SD=0.52 | μ=0.49 SD=0.54 | 0.179 |
| FT3 | μ=4.15 SD=0.83 | μ=7.22 SD=4.09 | 0.111 | μ=6.79 SD=3.37 | μ=7.33 SD=4.28 | 0.956 | μ=6.83 SD=3.65 | μ=7.97 SD=8.24 | 0.595 |
| FT4 | μ=2.04 SD=0.47 | μ=3.04 SD=1.83 | 0.345 | μ=2.79 SD=1.32 | μ=3.29 SD=2.19 | 0.790 | μ=2.91 SD=1.62 | μ=3.27 SD=3.38 | 0.462 |
| aTPO | μ=10.17 SD=3.62 | μ=37.87 SD=93.18 | 0.184 | - | - | - | μ=32.84 SD=87.97 | μ=70.00 SD=91.63 | 0.123 |
| aTg | μ=22.27 SD=16.43 | μ=245.38 SD=598.4 | 0.198 | - | - | - | μ=239.56 SD=627.30 | μ=369.17 SD=237.64 | 0.066 |
| TRAb | μ=0.51 SD=0.61 | μ=0.66 SD=0.89 | 0.622 | μ=0.46 SD=0.26 | μ=0.52 SD=0.39 | 0.619 | - | - | - |
| ESR | μ=45.00 SD=28.53 | μ=72.17 SD=23.01 | 0.151 | μ=68.88 SD=25.50 | μ=78.10 SD=23.26 | 0.187 | μ=72.00 SD=24.95 | μ=60.67 SD=14.43 | 0.425 |
| CRP | μ=5.39 SD=2.88 | μ=8.49 SD=10.35 | 0.959 | μ=8.75 SD=12.15 | μ=8.45 SD=8.00 | 0.736 | μ=8.79 SD=11.01 | μ=3.15 SD=1.78 | 0.148 |
| WBC | μ=10.49 SD=7.00 | μ=9.00 SD=2.90 | 0.699 | μ=8.79 SD=3.33 | μ=9.29 SD=3.10 | 0.453 | μ=9.05 SD=3.23 | μ=11.42 SD=3.84 | 0.253 |

A *p*-value of <0.05 is considered statistically significant. Data are presented as: mean (μ) and standard deviation (SD).
Abbreviations: aTg - anti-thyroglobulin antibodies; aTPO - anti-thyroid peroxidase antibodies; CRP - C reactive protein; ESR - erythrocyte sedimentation rate; FT3 - free triiodothyronine; FT4 - free thyroxine; TRAb - TSH receptor antibodies; TSH - thyrotropin; WBC - white blood cells.

Benbassat, 2007; Erdem *et al.* 2007). Unfortunately, the majority of the studies did not assess anti-thyroid antibodies or assessed them only in very small subgroups of patients (Alfadda *et al.* 2014; Nishihara *et al.* 2008; Latrofa *et al.* 2012). In our cohort, aTPO and aTg were evaluated in 58 and 57 patients, respectively, and an increased level was observed in 15.52% and 33.33%, respectively. This phenomenon may be considered as a reflection of the increasing incidence of autoimmune thyroid disease (AITD) and the overlapping of SAT and AITD. However, increased thyroid antibodies level, especially aTg, can also be a simple consequence of the release of thyroid antigens due to the gland damage during SAT. Presumably, genetic susceptibility is the most important factor determining the consequent development of AITD after SAT. In people without such susceptibility, it seems that the increased concentration of antibodies, mainly aTg, may be transitory (Latrofa *et al.* 2012). The presence of increased level of aTPO is more likely to be persistent and associated with AITD. Thus, the presence of thyroid antibodies cannot be considered a feature that is inconsistent with SAT. In comparison of patients with- and without elevated aTPO and/or aTg levels, no significant difference was found in the aspects of all analysed laboratory parameters and clinical features. This means that the presence of these antibodies does not change the course of SAT, nor does it affect clinical symptoms or the severity of the disease. In patients with chronic thyroiditis and SAT, features of thyrotoxicosis were similar to those present in other patients with SAT.

Until recently, it was thought that TRAb are never elevated in SAT, but in the last decades a few authors presented case reports of coexistence of SAT and Graves' disease (Nakamura *et al.* 1996; Fujii *et al.* 2003; Hoang *et al.* 2011). Interestingly, in our group, elevated TRAb were present in as many as 3 patients (6%). In comparison of patients with- and without elevated TRAb levels, no significant difference was found in the aspects of all analysed laboratory parameters and clinical features. All TRAb-positive patients were women, but the group was too small to conclude that this is a differentiating feature, because our results have demonstrated that SAT is 7 times more common in women than in men. Lack of the difference is surprising in the aspects of severity of thyrotoxicosis and, indeed, the levels of TSH, FT3 and FT4 were similar in both groups (Table 4). Therefore, it seems that the presence of TRAb does not influence the course of SAT, namely its clinical symptoms or severity. This is probably due to the fact, that it is SAT that initiates the process of TRAb production. It is believed that SAT may trigger autoreactive B cells to produce TRAb, resulting – in some patients – in subsequent TRAb-associated thyroid dysfunction (Iitaka *et*

*al.* 1998; Fatourechi *et al.* 2003). This hypothesis can be confirmed by the fact that there have been much more case reports on TRAb occurrence after SAT resolution than of the simultaneous presence of SAT and TRAb (Wartofsky & Schaaf, 1987; Fukata *et al.* 1992; Bartalena *et al.* 1996; Hallengren *et al.* 2015). Perhaps this is mainly due to the lack of assessment and monitoring of TRAb levels during the course of SAT. Thus, the earlier theory about the absence of TRAb in SAT is outdated, and now we observe that SAT may coexist with both chronic thyroiditis and - although less frequently - Graves' disease.

Elevated ESR is a laboratory hallmark of SAT, and SAT diagnosis should be excluded in a patient with normal ESR. In our cohort mean ESR was 70.4 ±24.1 and it was obviously increased in all patients. Such observation is consistent with previous reports (Nishihara *et al.* 2008; Benbassat *et al.* 2005; Alfadda *et al.* 2014). C-reactive protein is usually increased, but normal value does not exclude SAT. Therefore, CRP is not equivalent to ESR in SAT diagnostics. In our group, mean CRP value was 7.31±6.72, and CRP level was increased in 58 patients and normal - in one (1). Nishihara et al. (2008) reported even lower mean CRP level of 3.16± 3.34 mg/dl in a group of 282 SAT patients, which additionally confirmed the greater usefulness of ERS than CRP in the diagnosis of SAT. Increased WBC level is less often present and WBC has not been assessed in most papers published so far. In our study group, mean WBC was 9.09±3.21, with increased value in 19 patients, decreased value – in one (1) patient and normal – in 44 patients. Thus, WBC cannot be considered as a diagnostic SAT parameter. Interestingly, among 27 patients in whom urinalysis was performed, in 17 (63%) transient microhaematuria was present. In the majority of these patients (14 out of 17) the coexisting fever may be considered as the causative factor, however, in the remaining 4 patients the body temperature was normal. It seems that the severe systemic inflammation in the course of SAT was the causative factor. Simultaneous resolution of haematuria and SAT symptoms is the confirmation of such pathogenesis. To our best knowledge, this is the first observation of frequent prevalence of microhaematuria in SAT. Urinalysis is often performed in patients with inflammatory diseases. Thus, clinicians should be aware of common microhaematuria in patient with SAT, even in those without fever. Before planning further diagnosis of haematuria, the urinalysis should be repeated in these patients after the resolution of the most severe SAT symptoms.

Thyroid US was typical for SAT in all studied cases and revealed poorly defined hypoechoic areas involving a part of the thyroid or whole thyroid lobes, associated with diminished blood flow. Neck US is an excellent tool for SAT evaluation due to the characteristic features of the disease. Other authors also observed great usefulness of US in SAT diagnostics and in subsequent monitoring (Frates *et al.* 2013; Lee & Kim, 2016). Thyroid US image changes over time, the SAT-specific areas may appear in the contralateral lobe, but finally the SAT-typical lesions disappear, which indicates the cure of the disease. Such disappearance of the SAT lesions was observed in all patients in our group. Most authors had the same observations (Frates *et al.* 2013) but a few reported persistent SAT-like lesions after SAT resolution (Lee & Kim, 2016). Such an US image can be associated with either uncured SAT or its relapse, or with the presence of a SAT-similar lesions of other origin, requiring FNAB. Cytological evaluation of SAT lesions allows to finally confirm the diagnosis and to exclude a malignancy. It should be recalled that thyroid cancer can co-exist with SAT (Gul *et al.* 2018). In the studied cohort, cytology was typical for SAT in 50 patients, while in the remaining 11 patients cytology excluded malignancy but the smears were not typical for SAT. None of the patients had malignant thyroid lesion, although the prevalence of thyroid malignancy in SAT was recently reported as exceeding 4% (Gul *et al.* 2018).

Despite the proper treatment, the frequency of SAT recurrence is rather high, although it varied significantly between studied groups, ranging from 1.6% (Nishihara *et al.* 2008) to 20% (Mizukoshi *et al.* 2001). The observed discrepancies between different studies seem to be dependent on the studied population (Caucasian and Asian). In Caucasian patients, the recurrence rate of several percent is usually reported (Erdem *et al.* 2007; Mizukoshi *et al.* 2001). In our cohort, nine patients (14%) reported SAT recurrence (at least once).

To conclude, in our study, several new features of current SAT course, different from what we used to know about the disease, were reported. Mainly, higher frequency of painless SAT than it was ever described, was observed. Moreover, in as much as one third of the patients aTPO and/or aTg were present, and in 6% of SAT cases the coexistence of TRAb was demonstrated. Transient microhaematuria occurred in 63% SAT patients and resolved spontaneously with the resolution of SAT symptoms. No significant differences in clinical and biochemical characteristics between groups with- and without new features of SAT (painless course or elevated aTg, aTPO or elevated TRAb) were observed.

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