ПОДОСТРЫЙ ТИРЕОИДИТ И ЕГО КЛИНИЧЕСКИЕ ХАРАКТЕРИСТИКИ — РЕТРОСПЕКТИВНОЕ ОДНОЦЕНТРОВОЕ КЛИНИЧЕСКОЕ ИССЛЕДОВАНИЕ

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ВВЕДЕНИЕ: Типичными признаками подострого тиреоидита являются такие признаки, как боль в шее, высокая температура тела, нарушения функции щитовидной железы (ЩЖ), повышение воспалительных маркеров и гипоэхогенные характеристики по данным УЗИ ЩЖ. Для лечения применяются нестероидные противовоспалительные средства и глюкокортикостероидные препараты.
ЦЕЛЬ: Изучить клиническую характеристику пациентов с подострым тиреоидитом путем определения уровня тиреоидных гормонов, размеров и структуры ЩЖ по данным УЗИ и сцинтиграфии.
МАТЕРИАЛЫ И МЕТОДЫ: Проведен ретроспективный анализ 122 случаев подострого тиреоидита (пациенты обоих полов, средний возраст 45,05±12,18 года) за период 2015–2020 гг. Оценивались ежемесячная частота возникновения подострого тиреоидита, клиническое состояние пациентов, включая симптомы тиреотоксикоза, температуру тела, лабораторные показатели: Т4 св. и ТТГ, уровень С-РБ и СОЭ, данные УЗИ и сцинтиграфии.
РЕЗУЛЬТАТЫ: Большинство пациентов предъявляли жалобы на боли в шее, повышенная температура тела отмечалась у 66/100 (66%) пациентов. Диагноз подострого тиреоидита обычно устанавливали в тиреотоксической фазе. По данным УЗИ ЩЖ чаще всего выявлялось увеличение размеров ЩЖ, в то время как у 52 пациентов ЩЖ была нормального размера с преимущественно гипоэхогенной негомогенной структурой. На сцинтиграммах определялось отсутствие визуализации ЩЖ у 72/98 (73,47%) пациентов и снижение захвата РФЛП в обеих долях у 26/98 (26,53%).
ЗАКЛЮЧЕНИЕ: Необходимо повысить осведомленность врачей о пациентах с болью в шее для верной постановки диагноза подострого тиреоидита, который часто диагностируют много позже, что приводит к ошибочному чрезмерному использованию антибиотиков. Как правило, нестероидные противовоспалительные препараты эффективны для уменьшения болей в ЩЖ у пациентов с легкими формами заболевания.

КЛЮЧЕВЫЕ СЛОВА: подострый тиреоидит; боль в шее; функция щитовидной железы; ультразвуковое исследование; сцинтиграфия

SUBACUTE THYROIDITIS AND ITS CLINICAL CHARACTERISTICS — A RETROSPECTIVE SINGLE CENTER CLINICAL STUDY

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INTRODUCTION. Typical clinical features of subacute thyroiditis (SAT) are commonly assessed such as – neck pain and high body temperature, as well as thyroid function abnormalities, elevated inflammatory markers, and strongly suggestive hypoechoic ultrasonography characteristics. Non-steroid anti-inflammatory agents and corticosteroids are used.
AIM. To examine the clinical characteristics in patients with SAT, by determining the level of thyroid hormones, the size and structure of the thyroid gland as well as ultrasound and scintigraphy findings.
MATERIALS AND METHODS. We performed retrospective analysis in 122 cases of SAT (both genders, mean age 45.05±12,18 years), in the period 2015-2020. We evaluated monthly frequency of the SAT occurrence, the clinical status of the patients including symptoms, body temperature, laboratory results of FT4 and TSH, CRP and ESR level, ultrasonography and scintigraphy findings.
RESULTS. Most of the patients complained of neck pain, high body temperature was detected in 66/100 (66%) pts. CRP and ESR Patients were usually diagnosed in hyperthyroid phase of the disease. Enlarged thyroid gland was mostly seen on US, while 52 had normal thyroid gland, with predominantly hypoechoic non-chomogenous structure. Scintigraphy noted "empty" scan (without presentation of functional thyroid tissue) in 72/98 (73,47%) and hypofixation mainly in both lobes in 26/98 (26,53%) pts.
CONCLUSION. The awareness of physicians needs to be increased in patients with neck pain for proper diagnosis of SAT, that is often is often misdiagnosed or delayed, leading to erroneous antibiotic overuse. Generally, nonsteroidal anti-inflammatory drugs are effective in reducing thyroid pain in patients with mild cases.

KEYWORDS: subacute thyroiditis; neck pain; thyroid function; ultrasonography; scintigraphy

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Table 1. Clinical feature of SAT

Clinical feature			
	Present	**Not present**	**No data**
Neck pain	107/112, (95,54%)	5/112 (4,46%)	10/122 (8,20%)
Body temperature above 37	66/100, (66%)	34/100, (34%)	22/122 (18,03%)

INTRODUCTION

Thyroid inflammatory disorders may present as acute, subacute and chronic. Subacute granulomatous, de Quervain's thyroiditis (also known as giant cell) accounts for 5% of all thyroid diseases. It presents as a self-limiting, non-suppurative, post-viral thyroid inflammation, that is usually followed by infection of an upper respiratory tract (1,2). There is a female predominance (a ratio of 5:1), with peak incidence age in 40–50 years old (3). Several viruses have been linked to the development of subacute thyroiditis (SAT) such as influenza, adenovirus, echovirus, mumps, coxsackie, and H1N1 viruses (4). The major histological features include significant follicular disruption, migration of acute inflammatory cells, and extensive follicular structural damage (5). It has characteristic triphasic clinical course in its natural history: thyrotoxicosis, hypothyroidism, and normal thyroid function afterwards. Typical clinical features of SAT are commonly assessed such as, neck pain and high body temperature, as well as thyroid function abnormalities, elevated inflammatory markers, and strongly suggestive hypoechoic ultrasonography characteristics (1,3). Frequently SAT can be unrecognized for some period of time. Regarding the first stage if misdiagnosed it is treated as hyperthyroidism, so physicians need to differentiate the cause of thyrotoxicosis in a patient, having in mind SAT, to properly manage the patient. Thyreosuppresive therapy is not the first line of treatment SAT, instead non-steroid anti-inflammatory agents and corticosteroids are used. Our aim was to examine the clinical characteristics in patients with SAT, by determining the level of thyroid hormones, the size and structure of the thyroid gland as well as ultrasound and scintigraphy findings.

MATERIALS AND METHODS

We performed retrospective analysis in 122 registered cases of SAT (both genders, mean age 45.05±12,18 years), at our Institution in the period 2015–2020. We evaluated the distribution of the SAT cases during year and monthly frequency of the occurrence, the clinical status of the patients including symptoms the patients complained of, body temperature, laboratory results of thyroid hormone levels of FT4 and TSH, as well as aTPO, CRP and ESR level, ultrasonography and scintigraphy findings. We analyzed the therapy received and the appearance of permanent hypothyroidism after SAT.

Thyroid hormone level was evaluated by Immulite 2000 Immunoassay.

Ultrasound was performed using Phillips H.D. 6, Version 1.1, probe 7,5 Hz.

99mTc-pertechnetate was performed 20 minutes after iv application of 185 MBq of 99mTc-pertechnetate in planar AP position using dedicated gamma camera (static image of 10 minutes, 600 cnts, with and without zoom).

RESULTS

In our study most of the patients complained of neck pain, while only 5/112 (4,46%) pts denied having this symptom, no data existed for 10/122(8,20%) pts. High body temperature was detected in 66/100 (66%) pts varying from 37,5 to 40°Celzius, while 34/100 (34%) pts had no body temperature or they haven't measured it (Table 1). CRP measurement were from 10 to 178 mg/L, while ESR varied from 11 to 140.

Laboratory test showed hyperthyroid phase of the disease in nearly all patients, only 8pts presented in the euthyroid phase, for 6pts we had no data.

Enlarged thyroid gland was seen on US in most of our pts 64, while 52 had normal thyroid gland. Only in 2 pts small thyroid gland was noted on US. Hypoechoic non-chomogenous structure was detected in 100/116 (86,20%) pts, while 16/116 (13,79%) had isoehoic non-chomogenous structure. ST presented only in 1 lobe in 19/120 (15,83%) pts, while all others had bilateral presentation, for 2 pts no data existed (Table 2).

Table 2. Ultrasound and scintigraphy feature of SAT

Ultrasound and scintigraphy feature					
Echogenicity					
Hypoechoic non-chomogenous	100/116 (86,20%)	Isoechoic non — chomogenous	16/116 (13,79%)	No data	6/122 (4,92%)
Thyroid lobe (one or both)					
One lobe	19/120 (15,83%) Left lobe — 9 Right lobe — 10	Both lobes	101/120 (84, 17%)	No data	2/122 (1, 64%)
Scintigraphy					
Empty scan	72/98 (73, 47%)	Hypofixation	26/98 (26,53%)	No data	24/122 (19, 67%)

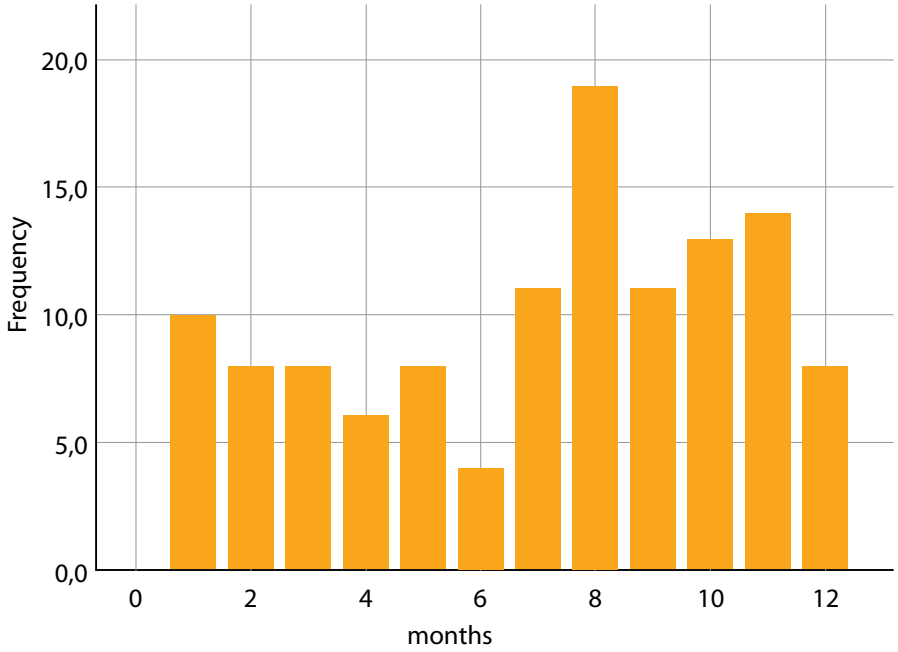

Figure 1. Histogram of months when SAT was diagnosed

Scintigraphic evaluation of ST was performed in 98/122 pts, detecting "empty" scan (without presentation of functional thyroid tissue — lat. functio laesa) in 72/98 (73,47%) pts and hypofixation mainly in both lobes in 26/98 (26,53%) pts.

The frequency of SAT showed August and November as the most frequent months (Figure 1).

We found 11 pts with hypothyroidism, 6 months to 1 year after the onset of SAT, and they were treated with Levothyroxine.

DISCUSSION

Subacute thyroiditis presents as a viral infection that was first described by Swiss surgeon De Quervain in 1902 (6). Patients typically present with a history of an upper respiratory infection (usually two to eight weeks before the onset of SAT (7). The diagnosis of SAT is usually based upon clinical grounds, with thyroid function tests and ultrasound for confirmation. Clinically patients usually complain of a neck pain, that can irradiate to the ears, cause an ear pain, and sometimes to the jaw (jaw pain) and that is why patients first visit ENT specialist or specialist of internal medicine. Because of the pain and high body temperature patients are prescribed drugs, antibiotics that are not used in the treatment guideline of SAT. Symptoms can last for one or two months, and even get worse leading the patient to seek further help. When they visit endocrinologist or nuclear medicine specialist usually the diagnosis is final, especially when we perform palpation of the thyroid gland, revealing enlarged gland and tender on palpation.

This thesis was also confirmed in the study of Anaforoglu, with 70% of pts having flu-like symptoms before the neck pain; 57% had initially visited other specialty for treatment and 28% even received antibiotics for misdiagnosis of an upper respiratory tract infection (8).

In our study most of the patients complained of neck pain, while only 5 pts denied having this symptom, possibly due to early and only focal inflammatory involvement of the thyroid gland in this few cases. High body temperature was detected in 66 pts varying from 37,5 to 40 Celzius degrees, while 34 patients had no body temperature or they haven't measured it. CRP measurement were from 10 to 178 mg/L, while ESR varied from 11 to 140.

Distribution of SAT more in spring and fall was seen in the study of Fatourechi, with no statistical significance (P = 0.26). They registered (of the 160 patients in 38 yr), 46 in spring, 45 in fall, 36 in summer, and 33 in winter (9).

We detected most of the cases to be in August, followed by November and October.

Clinical pattern of the disease starts with a hyperthyroid state (elevated FT4, suppressed TSH), that resolves by its own for 6–8 weeks, followed by hypothyroid state and then euthyroid state. The first phase of self-limiting thyrotoxicosis that is with variable duration, make the patients to complain of symptoms that occur due to thyrotoxicosis such as palpitations, tremor, sweating, anxiety.

The precise cause of SAT is unclear. It's uncertain whether follicular injury in SAT is caused by a straightforward viral infection of the gland or from the host's immune reaction to the virus. However, it is thought that viral infection results in production of an antigen that binds strongly to the macrophages human leukocyte antigen-B35 molecule, triggering cytotoxic T lymphocytes via helper T1 cells (Th1 cells). Invasion of thyroid follicles causes the basement membrane to burst and the follicles to rupture. The damage is detected by cytolytic T-cells, giving the explanation of the thyrotoxic phase of the condition. Furthermore, thyroidal iodine uptake hypofunction occurs when thyroid follicular cells are damaged, and hypothyroidism follows thyroid hormone shortage. However, this hypothyroidism (due to impaired thyroid biosynthesis) is transient, lasting for approximately 1 month, with the subsequent restoration of normal thyroid function in most patients (1, 10, 11).

Our patients mainly presented as hyperthyroid, with suprresed TSH level, only 8pts were detected in the euthyroid phase.

Typical pattern on the ultrasound imaging is connected to SAT, such as hypoechoic non-chomogenous structure of an enlarged gland, that can mimic a thyroid nodule. It can be distributed in both thyroid lobes, or sometimes starts in one lobe and then spreads to the other lobe called «creeping thyroiditis.» The presence of ill-defined hypoechoic thyroid lesions without a round or oval shape is diagnostic for SAT in the proper clinical setting (12). Doppler sonography can help distinguish SAT from Graves' disease, with low vascularity being presented in SAT. Bilateral SAT on US was shown in 64% of patients, all lesions being diffusely heterogeneous or focally hypoechoic areas, like «lava flow» (13).

Tenderness involved the entire gland in 44 patients, 14 in the left lobe and 16 in the right lobe. Localized tenderness of 1 of the lobes was noted in 10 patients (9).

Regarding our study, enlarged thyroid gland was seen on US in most of our patients 64, while 52 had normal thyroid gland. Hypoechoic non-chomogenous structure was detected in 100/116 (86,20%) pts, while 16/116 (13,79%) had isoehoic non-chomogenous structure. SAT presented only in 1 lobe in 19/120 (15,83%) pts, while all others had bilateral presentation.

Scintigraphy pattern of "empty scan" is a characteristic finding in SAT. Poor image quality is seen because of low uptake of the radioactive $^{99m}TcO4^-$ in the thyroid gland (14). Scintigraphic evaluation of SAT was performed in 98/122pts, noting "empty" scan (no thyroid tissue detected) in 72/98 (73,47%) pts and hypofixation mainly in both lobes in 26/98 (26,53%) pts.

No definitive cure for SAT is proposed so far and no consensus on initial therapy exists. The treatment's primary goal is intended to reduce the inflammation and to effectively relieve the symptoms and allow an asymptomatic way of the disease. For amelioration of the symptoms NSAIDs, beta-blocker agents and steroids are proposed. American Thyroid's Association clinical guideline for SAT recommends NSAIDs for mild symptoms and 40 mg/day of prednisolone for severe disease or those who fail to respond to NSAID treatment (15). After one to 2 weeks of this treatment, the dosage is tapered over a period of 6 weeks (16). From our group of pts, 15 pts were treated with corticosteroid therapy, 3 only were prescribed Thyrozol, while the rest had symptomatic treatment with analgetics and antipyretics.

No correlation was detected between the onset of hypothyroidism and thyroid hormone levels at SAT onset, as well as with the antibody titers (17, 18). We found 11 pts with hypothyroidism, 6 months to 1 year after the onset of SAT, and they were treated with Levothyroxine. In the study of Zhao they found that the early maximum TSH value was closely related to the incidence of hypothyroidism at 1 and 2 years after the onset of SAT (19).

CONCLUSION

The awareness of physicians needs to be increased in patients with neck pain for proper diagnosis of SAT, that is often misdiagnosed or delayed, leading to erroneous antibiotic overuse. Generally, nonsteroidal anti-inflammatory drugs are effective in reducing thyroid pain in patients with mild cases.

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