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What might cause pain in the thyroid gland? Report of a patient with subacute thyroiditis of atypical presentation

Co boli w tarczycy? Opis pacjenta z podostrym zapaleniem tarczycy o nietypowym przebiegu

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Abstract
Subacute granulomatous thyroiditis (SAT), also known as de Quervain's thyroiditis or painful subacute thyroiditis, is the commonest thyroid condition responsible for neck tenderness. Other causes of pain in the thyroid gland should be taken into consideration during differential diagnosis, especially when a patient presents with misleading or equivocal signs and symptoms.
We report the case of a 39 year-old woman diagnosed as having SAT whose clinical, biochemical and radiological presentation varied significantly from the common SAT manifestation. A tentative diagnosis of SAT was made based on the presented symptoms, ultrasonography and fine-needle biopsy results. However, biochemical analysis suggested neither inflammatory process nor the presence of thyrotoxicosis. Moreover, technetium scan of the thyroid revealed normal uptake of the isotope and there was neither clinical nor ultasonographic response for corticosteroids. The patient's symptoms, despite being prescribed typical treatment, gradually deteriorated and the pain became increasingly debilitating. Eventually, the patient underwent total thyroidectomy. As a result, she has become free of symptoms, but the macroscopic picture of thyroid gland, noted during the operation, gave a suspicion of neoplastic process. Nevertheless, histological study of flow samples confirmed the tentative diagnosis of de Quervain's thyroiditis, despite all previous findings that were not suggestive of it. This report confirms the likelihood that SAT can present atypically. Additionally, it indicates that surgical treatment may be considered in patients with severe, debilitating, persistent thyroid gland pain connected with SAT clinical course. **(Pol J Endocrinol 2012; 63 (2): 138–142)**

Key words: *subacute thyroiditis, de Quervain's thyroiditis, thyroid neoplasms, sonoelastography*

Streszczenie
Podostre ziarniniakowe zapalenie tarczycy, zwane inaczej chorobą de Quervaina lub bolesnym podostrym zapaleniem tarczycy, jest najczęstszą patologią gruczołu tarczowego odpowiedzialną za występowanie bolesności okolicy szyi. Inne przyczyny bólu w tej lokalizacji muszą zostać uwzględnione w diagnostyce różnicowej, zwłaszcza jeśli objawy występujące u pacjenta są niejednoznaczne bądź mylące. Autorzy przedstawili przypadek 39-letniej kobiety, u której rozpoznano podostre ziarniakowe zapalenie tarczycy, którego obraz kliniczny, biochemiczny oraz radiologiczny różnił się znacząco od typowego przebiegu tego schorzenia. Wstępnego rozpoznania podostrego ziarniniakowego zapalenia tarczycy dokonano na podstawie występujących objawów, wyniku badania ultrasonograficznego oraz biopsji aspiracyjnej cienkoigłowej. Jednak przeprowadzone analizy biochemiczne sugerowały nieobecność procesu zapalnego oraz tyreotoksykozy. Co więcej, technetowa scyntygrafia tarczycy wykazała prawidłowy wychwyt izotopu. Nie zaobserwowano klinicznej ani ultrasonograficznej odpowiedzi na glikokortykosteroidy. Mimo zastosowanego leczenia objawy u pacjentki stopniowo narastały, a ból zaczął znacząco upośledzać jej funkcjonowanie. Ostatecznie pacjentka przebyła zabieg całkowitego wycięcia tarczycy. W rezultacie objawy ustąpiły, jednak obraz makroskopowy preparatu operacyjnego gruczołu tarczowego nasuwał podejrzenie procesu nowotworowego. Niemniej jednak badanie histopatologiczne pobranego materiału potwierdziło wstępne rozpoznanie choroby de Quervaina, zatem poprzednie wyniki badań nie pozostawały w zgodzie z tą diagnozą.
Przypadek ten potwierdza możliwość atypowego przebiegu podostrego ziarniniakowego zapalenia tarczycy. Dodatkowo wskazuje na możliwość rozważenia leczenia operacyjnego u pacjentów z ciężkim, przetrwałym, upośledzającym funkcjonowanie bólem gruczołu tarczowego w przebiegu podostrego ziarniniakowego zapalenia tarczycy. **(Pol J Endocrinol 2012; 63 (2): 138–142)**

Key words: *podostre zapalenie tarczycy, choroba de Quervaina, nowotwory tarczycy, sonoelastografia*

Introduction

Subacute granulomatous thyroiditis (SAT), also known as de Quervain's thyroiditis or painful subacute thyroiditis, is the commonest thyroid condition responsible for neck tenderness [1]. This transient disorder, often preceded by an upper respiratory tract infection, is presumed to be a post-viral inflammatory process, occurring in genetically predisposed individuals. SAT usually develops during the summer and early autumn,

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mostly in middle-aged females. The neck tenderness of sudden onset radiates up to the ear and mandible, or down to the upper chest, and is often accompanied by systemic manifestations (fever, malaise, myalgias) and thyrotoxicosis (usually mildly expressed and followed by transient hypothyroidism). Markedly elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), typical clinical course, presence of characteristic ultrasound (US) features, and/or low thyroid iodine or Tc-99m uptake are usually sufficient to make a diagnosis [1–4].

Other causes of pain in the thyroid, such as haemorrhage into the thyroid cyst or nodule, malignant lesions, or other forms of thyroiditis (including thyroid tuberculosis) or sarcoidosis are rare, but have to be taken into consideration in differential diagnosis [5–8]. Sometimes, no clear cause of a painful thyroid gland can be found, despite careful clinical, biochemical and radiological analysis [9].

We report the case of a woman diagnosed as having SAT whose clinical, biochemical and radiological presentation varied significantly from the common SAT manifestation.

Case presentation

In October 2010, a 39 year-old woman presenting recurrent low-grade fever (37°C), left anterior neck pain radiating to the ear, profuse night sweats and malaise, was consulted by her family physician. She gave a history of upper respiratory tract infection in mid-September 2010, surgical therapy of an ovarian tumour (teratoma) in 2008, chronic gastritis and nonsteroidal anti-inflammatory drugs (NSAIDs) intolerance. The patient was started on antibiotic treatment with amoxycyline 1,000 mg/day, tapered after ten days, but no improvement in symptoms occurred. In November 2010, the otolaryngologist excluded any pharyngeal or tracheal pathology and recommended thyroid gland examination. Thyroid ultrasonography (US) revealed a hypoechoic, irregular lesion in the left thyroid lobe, which was firm and extremely painful in palpation. Fine needle aspiration biopsy (FNAB) showed a benign condition suspected of being a localised, limited form of subacute granulomatous thyroiditis. Laboratory tests (Table I) showed no rise in inflammatory markers. The patient was biochemically euthyroid and serum titres of antithyroid autoantibodies were within the normal limits. There were also no signs of hypo- or hyperthyroidism on physical examination.

Based on clinical manifestation and demonstrated changes in thyroid parenchyma, she was tentatively diagnosed as having SAT. Standard treatment with NSAID (ibuprofen orally, at a daily dose of 1,000 mg) was administered. In connection with severe stomach pains that occurred after the initiation of treatment, ibuprofen orally was replaced by ketoprofen intravenously (100 mg/day), but unfortunately the symptoms worsened. The whole thyroid became extremely painful, and she developed dysphagia, which resulted in diminished appetite, weight loss and fatigue. Moreover, low-grade fever became constant with a recurrent body temperature rise to 39.8°C, lasting for a few days. In December 2010, she received prednisone orally (40 mg daily), but within four days severe stomach pains recurred, accompanied by high blood pressure values, and the patient decided to discontinue the treatment. Follow-up thyroid function analysis showed consistent euthyroidism. ESR and CRP levels were also within the normal values (Table II). Nevertheless, the patient's symptoms continued to deteriorate. The pain was increasingly debilitating, preventing swallowing and leading to further weight loss, severe dysphonia, permanent high-grade fever and increased general malaise.

To re-evaluate the presumed diagnosis, US re-examination with subsequent FNAB and thyroid Tc-99m scintigraphy were performed. The thyroidal trapping of Tc-99m was normal (Figure 1), whereas US examination once more visualised a hypoechoic lesion in the left thyroid lobe (Figure 2). Additionally, a thyroid sonoelastography showed that the elasticity of the focal lesion was not decreased compared to the surrounding thyroid

Table I. *Laboratory tests in November 2010*

Tabela I. *Badania laboratoryjne wykonane w listopadzie 2010 roku*

Parameter	Value	Unit	Reference range
ESR	9	[mm/h]	0–12
CRP	0.28	[mg/L]	0–5
WBC	5.79×10^3	[1/μL]	$3.9–11.0 \times 10^3$
RBC	4.27×10^6	[1/μL]	$3.5–5.2 \times 10^6$
TSH	0.82	[μIU/mL]	0.27–4.2
TPOAb	6	[IU/mL]	0–34
TgAb	91	[IU/mL]	10–115
TRAb	0.26	[IU/L]	0–2

Table II. *Repeated laboratory tests in December 2010*

Tabela II. *Powtórzone badania laboratoryjne wykonane w grudniu 2010 roku*

Parameter	Value	Unit	Reference range
ESR	8	[mm/h]	0–12
CRP	0.83	[mg/L]	0–5
TSH	0.67	[μIU/mL]	0.27–4.2

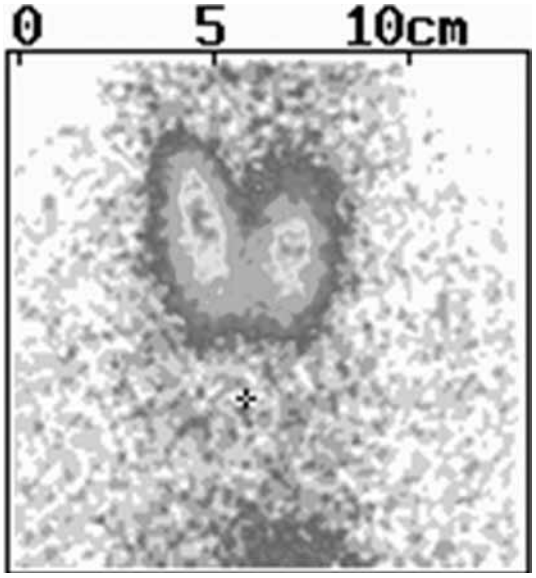

Figure 1. *Thyroid Tc-99m scintiscan, revealing normal isotope uptake*

Rycina 1. *Scyntygrafia tarczycy Tc-99m, przedstawiająca prawidłowy wychwyt izotopu*

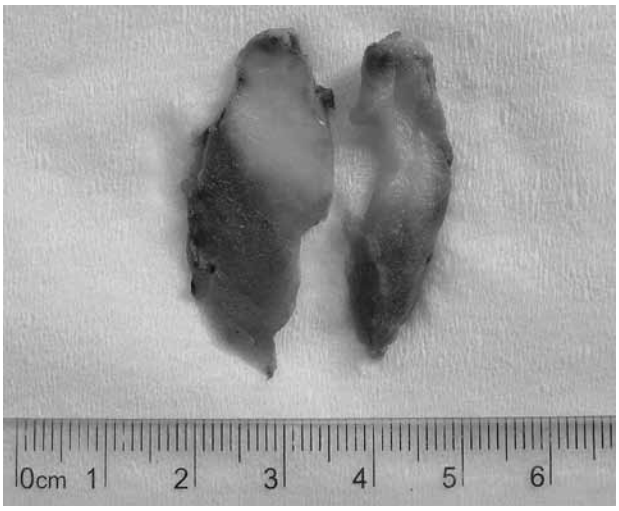

Figure 3. *Macroscopic picture of the surgical specimen after thyreoidectomy*

Rycina 3. *Obraz makroskopowy preparatu operacyjnego po tyreoidektomii*

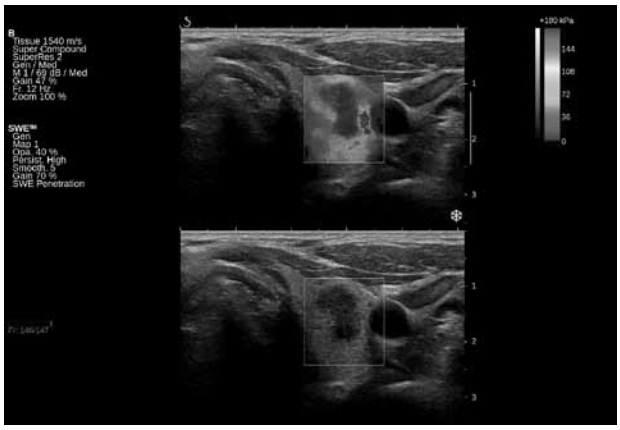

Figure 2. *Sonoelastographic (upper part) and ultrasonographic (lower part) picture of lesion in left thyroid lobe*

Rycina 2. *Obraz sonoelastograficzny (powyżej) i ultrasonograficzny (poniżej); zmiany w obrębie lewego płata tarczycy*

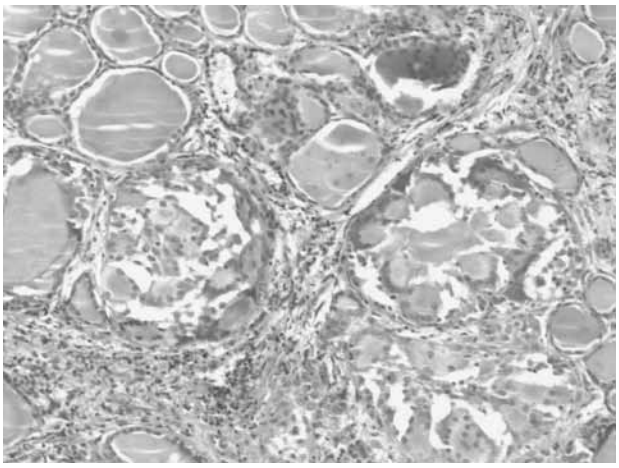

Figure 4. *Histopathological examination of the surgical specimen, revealing granulomas and marked fibrosis*

Rycina 4. *Badanie histopatologiczne preparatu operacyjnego, uwidaczniające ziarniniaki i znacznego stopnia włóknienie*

parenchyma elasticity (Figure 2). Cytological examination revealed inflammatory cells (lymphocytes, histiocytes, and a single multinucleated giant cell) and a few groups of follicular cells. This indicated in all probability the presence of thyroiditis, and a SAT could not be ruled out. Methylprednisolone intramuscularly was prescribed at a single dose of 120 mg, but the symptoms did not resolve. Eventually, the patient underwent total thyroidectomy in January 2011. The surgery was uneventful, but during the operation, a mass noted in the thyroid tissue gave a suspicion of a thyroid malignant process (Figure 3). Histological study of the left lobe revealed inflammatory zone with numerous granulomas, accompanied by giant multinucleated cells and fibrosis (Figure 4). This confirmed the diagnosis of limited SAT. Pain relief was achieved almost instantly following the surgery. L-thyroxin substitution with a daily dose of 88 μg was administered. She became euthyroid and free of symptoms.

Discussion

The differential diagnosis of a painful thyroid has to include: subacute granulomatous thyroiditis, acute suppurative thyroiditis, Riedel's disease, acute exacerbation of chronic thyroiditis, Graves' disease, haemorrhage into the thyroid cyst or nodule, primary or metastatic

neoplastic process (carcinoma, lymphoma), sarcoidosis and tuberculosis [6–11].

Establishing a final diagnosis of SAT in the described case was a true challenge. The patient presented with systemic inflammatory signs and symptoms accompanied by extreme thyroid pain that were preceded by pharyngitis, which all together favoured the diagnosis of SAT [12]. However, subsequent findings caused us to re-evaluate the primary diagnosis.

Firstly, biochemical analysis suggested neither an inflammatory process nor the presence of thyrotoxicosis. It has been found by Nishihara et al. that abnormal laboratory findings (increased FT4, FT3, Tg, CRP and aminotransferases levels) reach their peak levels in the first week after onset [13]. If we consider that the average hyperthyroid phase lasts for 6–8 weeks, we may assume that the TSH might have been mildly suppressed at the very beginning of the patient's clinical course. Secondly, US examination showed a hypoechoic, irregular thyroid lesion that did not resolve with treatment. Typical US findings in SAT are: enlarged thyroid volume, ill-defined hypoechoic lesion with a nonhomogeneous pattern, and no vascular flow on colour Doppler US [14–16]. However, cases of SAT presenting as a focal mass mimicking thyroid malignancy have also been reported [17]. FNAB is considered to be inevitable in such cases [18]. In general, in US there are no permanent echo abnormalities, and all changes resolve during the recovery process, while in this case there was neither clinical nor ultrasonographic response to corticosteroids [14]. Indeed, if corticosteroids are used and no response occurs within 72 hours, SAT is unlikely to be the aetiology [19]. Thirdly, technetium scan of the thyroid revealed normal uptake of the isotope, which is usually decreased, due to an association with SAT thyroid parenchyma destruction [20]. Finally, the macroscopic picture of the thyroid gland, noted during the operation, which gave a suspicion of neoplastic process, convinced our team to change the tentative diagnosis.

Acute suppurative thyroiditis (AST) caused by bacterial, fungal or parasitic infection is an extremely rare condition occurring mostly in individuals with immune incompetency. Initially, its clinical course may be hard to distinguish from SAT. During the US examination, abscess creation may be shown. The normal radioactive iodine and technetium uptake is parallel to one observed in the reported case. FNAB seems to be the most useful diagnostic test, and it excluded this diagnosis [1].

The coexistence of Riedel's thyroiditis and recurrent SAT was reported by Cho et al. in 2007 [10]. This disorder is characterised by the spread of fibrosis beyond the limits of thyroid capsule and the total destruction of normal thyroid structure. The invasion of the neck structures and symptoms caused by oesophagus or bronchus compression (dysphagia, dyspnoea) resemble those of thyroid carcinoma [21]. The FNAB was necessary to make a distinction or rule out both of these conditions.

Primary thyroid lymphoma (PTL) is also highly infrequent, and responsible for only 1–5% of all thyroid malignancies. Two recently described cases of PTL not only presented initially clinically as a SAT look-alike condition, but also were interpreted cytologically as a SAT [8]. Characteristic cytological feature of SAT may also be mimicked by other granulomatous pathologies, tuberculosis and/or sarcoidosis [22].

Histological examination provided the ultimate diagnosis of SAT. Typically, it contains an inflammatory cell mix (mainly lymphocytes), destruction of follicular unit, and plethora of multinucleated giant cells and non-caseating granulomas. Fibrotic areas may also be observed [23].

Additionally, after standard US examination, Shear Wave Elastography (SWE) was performed. This novel technique of thyroid tissue elasticity assessment has already been described as being potentially useful in thyroid nodules evaluation [24]. Moreover, the sonoelastographic picture of SAT has also been recently reported. These studies have demonstrated markedly decreased elasticity of the affected area to be typical for this disorder [25, 26]. On the contrary, SWE in our patient showed no stiffness increase of the presented lesion compared to the surrounding thyroid tissue.

No response for the classic anti-inflammatory agents resulted in the need for unconventional therapy. Surgery has already been proven to be successful in unexplained severe pain of the thyroid gland and acute exacerbation of chronic thyroiditis [9, 27, 28]. Our case lends support to the possible advantages of surgical treatment in extremely painful and persistent SAT.

In conclusion, this report confirms the likelihood of SAT presenting atypically. In such cases, clinical, ultrasonographic, scintigraphic, and biochemical findings may not be sufficient to reach the correct diagnosis. Careful analysis is necessary to distinguish SAT from other causes of a painful thyroid. Moreover, in our opinion, surgical treatment may be considered in patients with severe, debilitating, persistent thyroid gland pain connected with SAT clinical course.

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