

Subacute Thyroiditis

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Abstract:

Subacute thyroiditis is a rare inflammatory disease of the thyroid gland. It is believed to be caused by a viral infection, including COVID-19. It accounts for about 5% of all clinical thyroid diseases. Materials and methods. A clinical case of subacute de Quervain's thyroiditis in a patient with diffuse hypermetabolic fixation of 18-fluorodeoxyglucose by the thyroid gland is presented. Results. A 61-year-old patient with no history of thyroid pathology was under observation. 3 weeks after suffering from COVID-19, body temperature began to rise in the evenings from 37.8 to 39.8°C. Moderate pain appeared in the thyroid gland radiating to the lower jaw, severe weakness, tremor of the upper extremities, trembling in the body, weight loss of 12 kg, and sweating were noted. Duration of symptoms is 3 weeks. On palpation, the thyroid gland is enlarged, dense, sharply painful, especially the left lobe. According to ultrasound examination, the iron is enlarged in size, its structure is heterogeneous with extensive hypoechoic areas in both lobes measuring up to 4x7 mm without clear contours. Color Doppler mapping - blood flow is reduced. Combined positron emission and X-ray computed tomography with 18-fluorodeoxyglucose revealed increased diffuse fixation of the radiopharmaceutical in the thyroid gland against the background of an increase in its lobes, SUVmax 10.55. In the blood, the level of thyroid-stimulating hormone is reduced, and free triiodothyronine and thyroxine are increased, the concentration of ferritin is sharply increased - the phenomenon of thyrotoxicosis. A fine needle aspiration biopsy was performed. Cytological

examination revealed subacute de Quervain's thyroiditis. Glucocorticoids and non-steroidal anti-inflammatory drugs were prescribed. 4 weeks after treatment, clinical manifestations regressed. Examined after 6 months. According to ultrasound examination, the thyroid gland is not enlarged, the contours are smooth, and with color Doppler mapping, the blood flow is normal. Indicators of thyroid-stimulating hormone, triiodothyronine, thyroxine are within normal limits. Conclusion. The SARS-CoV-2 virus can be regarded as the cause of the development of subacute thyroiditis. According to combined positron emission and X-ray computed tomography with 18-fluorodeoxyglucose, diffuse intense accumulation of the radiopharmaceutical in the thyroid gland was observed. Cytological examination is the basis for differential diagnosis. Glucocorticoids and non-steroidal anti-inflammatory drugs constitute the basic therapy.

Keywords: subacute de Quervain's thyroiditis, combined positron emission and x-ray computed tomography with 18-fluorodeoxyglucose, diffuse fixation of radiopharmaceuticals, glucocorticoids.

Introduction. Subacute thyroiditis is an inflammatory disease of the thyroid gland. In the literature, this disease has other names, in particular de Quervain's thyroiditis, giant cell thyroiditis, granulocytic thyroiditis, subacute granulomatous thyroiditis. It is probably of viral origin and usually occurs in 4 phases. The clinical debut of the disease is preceded by an upper respiratory tract infection 2–8 weeks earlier [1]. In terms of frequency of occurrence, it accounts for from 1.6 to 5% of all thyroid diseases [2]. During the coronavirus disease (COVID-19) pandemic, 10–20% of hospitalized patients had clinical manifestations of subacute thyroiditis [3]. However, the impact of COVID-19 on its prevalence is being studied. Women suffer from this disease 4.7 times more often than men, accounting for 70 to 80% of all patients [4]. In the literature, there are isolated reports of cases of the disease in children [5]. In 2018–2020 A retrospective single-center study was conducted in Turkey, which revealed increased seasonal fluctuations and an increase in the number of men suffering from subacute thyroiditis, without affecting the clinical course [6]. At the same time, the results of a cross-sectional study conducted in South Korea from 2017 to 2019 showed the maximum incidence of subacute thyroiditis in 2020. Corticosteroids were more often used to treat this disease [7]. Up to 96% of patients with classic painful thyroiditis report moderate to severe thyroid pain radiating to the jaw (13%) and ears (19%). Fever was observed in 7% of patients [8]. Paresis of the vocal cords may develop. In almost 1/2 of patients, symptoms of thyrotoxicosis appear in the first weeks of the disease - suppression of the function of thyroid-stimulating hormone (TSH), increased concentrations of triiodothyronine (T3) and thyroxine (T4), the duration of thyrotoxicosis is 2-8 weeks. It occurs as a result of the destruction of the glandular parenchyma of the thyroid gland and the release of thyroid hormones [1]. Subsequently, manifestations of hypothyroidism often develop [9]. To visualize subacute thyroiditis, ultrasound examination (ultrasound) of the thyroid gland, laboratory tests - hormones TSH, T3, T4, antibodies to thyroglobulin and thyroid peroxidase, erythrocyte sedimentation rate, C-reactive protein, scintigraphy of the thyroid gland with ^{99m}Tc -pertechnetate and cytological examination of punctate are used, which is rarely required [1]. Thyroid diseases detected using hybrid technology - combined positron emission and X-ray computed tomography (PET/CT) with 18-fluorodeoxyglucose (18-FDG) - make it possible to clarify the nature of the pathological process with focal or diffuse accumulation of radiopharmaceuticals (RP). In the literature, isolated reports are devoted to this [10, 11]. We observed a patient with subacute thyroiditis, in whom 18-FDG PET/CT revealed diffuse hypermetabolism of radiopharmaceuticals. Clinical case Patient N., 61 years old, consulted a doctor with complaints of an increase in body temperature in the evenings from 37.8 to 39.8 ° C, weight loss of 12 kg, pain in the thyroid gland spreading to the lower jaw, loss of appetite, sweating, severe weakness, hand tremor, trembling in body. Considers himself sick for 3 weeks. Symptomatic therapy was carried out with varying success. From the anamnesis it is known that 3 weeks before the onset of the disease he suffered from COVID-19. On palpation, the

thyroid gland is diffusely enlarged, dense, sharply painful, especially on the left. Cervical and supraclavicular lymph nodes are not palpable. According to the ultrasound results, the right lobe measures 5.9×2.6×2.3 cm, the left – 5.4×2.5×2.0 cm. The volume of the lobes does not correspond to gender and age. The contours are smooth. The echostructure is heterogeneous, with extensive hypoechoic areas in both lobes, up to 4x7 mm in size, without clear contours. Color Doppler mapping - blood flow is reduced. Conclusion: signs of diffuse focal changes in the thyroid gland. The patient was referred to an endosurgeon to resolve the issue of surgical treatment. According to spiral CT of the chest and ultrasound of the abdominal organs, no focal pathology was detected. 18-FDG PET/CT was performed. An increase in the size of both lobes was revealed: the left – up to 28×19 mm, the right – up to 26×16 mm with diffuse hyperfixation of the radiopharmaceutical SUVmax 10.55. The lymph nodes of the neck are not enlarged and metabolically inactive (Fig. 1). A fine-needle aspiration biopsy of the left lobe of the thyroid gland was performed under ultrasound guidance. Cytological examination revealed subacute granulomatous de Quervain's thyroiditis (Fig. 2). In the blood serum, the concentration of TSH is reduced - 0.053 mIU/l, and free T3 and free T4 are increased - 8.88 and 29.7 nmol/l, respectively. The ferritin level was significantly increased - 1876.5 ng/ml. These indicators are characteristic of thyrotoxicosis. Antibodies to thyroid peroxidase – 0.305 IU/ml, which indicates normality. An analysis for infectious diseases - hepatitis, mycoplasmosis, chlamydia - showed a negative result. Antibodies to Epstein–Barr virus and cytomegalovirus class G were not detected. Erythrocyte sedimentation rate – 65 mm/h. Echocardiography revealed no evidence of endocarditis. A diagnosis was made: “subacute de Quervain’s thyroiditis, thyrotoxicosis.” Corticosteroids were prescribed - prednisolone in a daily dose of 20 mg for 2 weeks, followed by a dose reduction, duration of therapy - 6 weeks, as well as non-steroidal anti-inflammatory drugs. By the end of treatment, the clinical symptoms completely regressed, and the level of thyroid hormones returned to normal. Examined after 6 months. On ultrasound, the thyroid gland is not enlarged, the contours are smooth, the structure is homogeneous, the nature of the blood flow is normal. The hormonal function of the thyroid gland is not impaired. The presented case is interesting due to the presence of a connection between the disease of subacute thyroiditis and the SARS-CoV-2 virus, as well as a favorable outcome after glucocorticoid therapy.

Discussion The first description of subacute thyroiditis was made by the Swiss surgeon de Quervain in 1902.[12]. Its etiology is still unclear. The onset of the disease is caused by several viruses: Coxsackie, Epstein-Barr, influenza, parvovirus, rubella, HIV, hepatitis, measles [13]. Upper respiratory tract infections were the initial diagnosis in 1/3 of patients [14]. The main morphological changes in the thyroid gland are caused by the migration of acute inflammatory cells with pronounced damage to the follicles [15]. C. Xu et al. in 2023 published the results of a bibliometric analysis of the literature on various aspects of subacute thyroiditis from 2001 to 2022 according to the Web of Science database. A total of 568 studies published in 282 academic journals from 900 institutions and 61 countries were analyzed. The authors believe that over the past 20 years, major research has focused on the prevalence of this disease, especially in patients with COVID-19, including genetic changes, and its treatment. During the COVID-19 pandemic, there has been a sharp increase in the number of publications regarding subacute thyroiditis [16]. Numerous cases of association of subacute thyroiditis with SARS-CoV-2 infection have been published [17]. The first such case associated with SARS-CoV-2 was registered in May 2020 [18]. Also, a systematic review of the literature showed that subacute thyroiditis can occur within 2 months after vaccination against COVID-19 [19]. The clinical picture of the disease is accompanied by local pain and tenderness on palpation in the thyroid gland in combination with fever, chills, and weight loss [20]. At the onset of the disease, thyrotoxicosis is observed, followed by the development of hypothyroidism and a return to the euthyroid state several months after treatment. However, recently the clinical picture has undergone certain changes. Thus, fever began to be observed less frequently, and the frequency of the painless variant increased to 6.3% [4]. A typical symptom was persistent hypothyroidism, the likelihood of which is associated with changes in the

volume of the thyroid gland, determined by ultrasound before and after treatment [21]. This is accompanied by multidirectional diagnostic and tactical errors in treatment. From the moment of clinical debut to diagnosis, the time varies from 2 weeks to 6 months [22], which leads to a delay in treatment and a deterioration in the quality of life. In the presented case, the clinical picture was classical. Nevertheless, the patient was examined and received symptomatic treatment in a local clinic for 4 weeks, after which he was hospitalized in an infectious diseases hospital, where he remained for 3 weeks. During the examination, a diagnosis of “mass formation of the thyroid gland” was made and surgical treatment was recommended. Thus, the diagnosis of subacute thyroiditis was made 7 weeks after the clinical debut of the disease. Ultrasound of the thyroid gland is one of the main methods of diagnosis and follow-up of patients with subacute thyroiditis [1]. Subacute thyroiditis can affect diffusely or focally, one or both lobes of the thyroid gland [13]. A number of works have been published in the available literature on the ultrasound characteristics of subacute thyroiditis, which describe 27 patients. Of these, 23 had unilateral lesions, and 4 had bilateral lesions. Moreover, all formations were unclear, hypoechoic with an uneven edge, which imitated a malignant tumor [13]. A valuable method for diagnosis, especially differential diagnosis, is 18-FDG PET/CT. Focal accumulation of radiopharmaceuticals in the thyroid gland is most often caused by a malignant tumor. Several reports of cases of subacute thyroiditis with diffuse intense accumulation of radiopharmaceuticals, reminiscent of a malignant neoplasm, have been published in the literature [23]. Most likely, intense hypermetabolism of 18-FDG is due to active inflammation. The described case demonstrated the possibility of diffuse intense uptake of 18-FDG by the thyroid gland in subacute thyroiditis. The standardized maximum accumulation factor SUV_{max} was 10.55. In such cases, for the purpose of differential diagnosis, it is necessary to perform a fine-needle aspiration biopsy followed by a cytological examination, which will establish the true nature of the process. The main goal of treatment of subacute thyroiditis is pain relief and anti-inflammatory therapy, for which glucocorticoids and non-steroidal anti-inflammatory drugs are used, and corticosteroids are considered a factor in reducing the risk of relapse of the disease. Short-term use of prednisolone is comparable to long-term use and has a better safety profile [24]. Early relapse develops in 10–22% of cases during treatment with glucocorticoids or within 2 months after its completion [25]. Late relapses occur in 0.9–2.3% of patients 8–23 years after completion of therapy [26]. In addition, intrathyroidal administration of corticosteroids under ultrasound guidance is possible, which can reduce the duration of oral administration of the drug [27]. In such cases, for the purpose of differential diagnosis, it is necessary to perform a fine-needle aspiration biopsy followed by a cytological examination, which will establish the true nature of the process. The main goal of treatment of subacute thyroiditis is pain relief and anti-inflammatory therapy, for which glucocorticoids and non-steroidal anti-inflammatory drugs are used, and corticosteroids are considered a factor in reducing the risk of relapse of the disease. Short-term use of prednisolone is comparable to long-term use and has a better safety profile [24]. Early relapse develops in 10–22% of cases during treatment with glucocorticoids or within 2 months after its completion [25]. Late relapses occur in 0.9–2.3% of patients 8–23 years after completion of therapy [26]. In addition, intrathyroidal administration of corticosteroids under ultrasound guidance is possible, which can reduce the duration of oral administration of the drug [27]. In such cases, for the purpose of differential diagnosis, it is necessary to perform a fine-needle aspiration biopsy followed by a cytological examination, which will establish the true nature of the process. The main goal of treatment of subacute thyroiditis is pain relief and anti-inflammatory therapy, for which glucocorticoids and non-steroidal anti-inflammatory drugs are used, and corticosteroids are considered a factor in reducing the risk of relapse of the disease. Short-term use of prednisolone is comparable to long-term use and has a better safety profile [24]. Early relapse develops in 10–22% of cases during treatment with glucocorticoids or within 2 months after its completion [25]. Late relapses occur in 0.9–2.3% of patients 8–23 years after completion of therapy [26]. In addition,

intrathyroidal administration of corticosteroids under ultrasound guidance is possible, which can reduce the duration of oral administration of the drug [27].

Conclusion. Subacute thyroiditis is a rare virus-associated inflammatory disease of the thyroid gland. The presented case is associated with the SARSCoV-2 virus. Thyroid pain and tenderness, as well as fever, are characteristic symptoms of subacute granulomatous de Quervain's thyroiditis. According to PET/CT with 18-FDG, in subacute thyroiditis, both focal and diffuse increased fixation of radiopharmaceuticals is observed in the thyroid gland, SUVmax 10.55. The last option is much less common. In this regard, in such cases, performing a fine-needle aspiration biopsy should be considered a mandatory option in order to conduct a differential diagnosis, taking into account the results of a cytological study. The main treatment method is the use of glucocorticoids and non-steroidal anti-inflammatory drugs.

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