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## ABSTRACT

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## THYROIDITIS AS A COMPLICATION OF COVID-19

**Introduction.** The epidemiological situation around the world does not improve from year to year. Moreover, there is a tendency towards its deterioration. For example, one can take a better look at viral infections to see that 100 years ago, the Spanish influenza pandemic claimed 40 million lives on a global scale; in 2002–2004 – SARS-COV led to 10.9% mortality in patients; 10 years later MERS-COV presented with 34.3% mortality; while the Wuhan pandemic (COVID-19) was accompanied by a mortality rate of 6.5%, in people aged 70 years the rate reached 8%, in people > 80 years – more than 15%. Mortality, of course, is inherent in many complications, since viruses, particularly coronaviruses, have a tropism to the endothelium of vessels and the epithelium of various organs, so complications can affect different organs and systems. Peculiarities of their course and diagnosis substantiate the urgency of the problem.

**Objective.** To share the features of the clinical course and diagnosis of rare complications of COVID-19, primarily in the thyroid gland.

**Materials and Methods.** We observed 2 patients who, in addition to general clinical examinations, had ultrasound and thyroid panel tests performed.

**Results and Discussion.** In two patients (a female and a male), in addition to general clinical and respiratory syndromes, gastrointestinal disorders prevailed, namely, a complete loss of appetite and decreased body weight of more than 10 kg. After a complete examination, autoimmune thyroiditis was diagnosed.

**Conclusions.** The signs of intoxication, along with loss of body weight, should prompt a doctor to consider endocrine organs (primarily the thyroid gland) examination with ultrasound.

**Keywords:** COVID-19, complications, thyroiditis, diagnosis, pleural effusion syndrome.

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## ТИРЕОЇДИТ – УСКЛАДНЕННЯ COVID-19

**Вступ.** Епідеміологічна ситуація в усьому світі з року в рік не кращає. Більше того, спостерігається тенденція до її погіршення. Достатньо прослідкувати ситуацію з вірусною інфекцією: 100 років тому «іспанка» забрала 40 млн життів у світовому масштабі, у 2002–2004 рр – SARS-COV призвів до летальності 10,9 % захворівших, через 10 років MERS-COV – 34,3 %, Уханська пандемія (COVID-19) супроводжувалася летальністю 6,5 %, а у осіб 70 рр – 8 %, після 80 рр – понад 15 %. Летальність, зрозуміло, притаманна багатьом ускладненням оскільки віруси, зокрема й коронавіруси, мають тропність до ендотелію судин і епітелію різних органів, отже ускладнення можуть вражати різні органи й системи. Особливості їх перебігу і діагностики обґрунтовують **актуальність проблеми**.

**Мета роботи.** Поділитися особливостями клінічного перебігу і діагностики рідкісних ускладнень COVID-19, передусім з боку щитоподібної залози.

**Матеріали і методи.** Ми спостерігали 2 хворих, у яких окрім загальноклінічних обстежень було застосовано УЗД і визначення гормональної функції щитоподібної залози.

**Результати та обговорення.** У двох хворих (жіночої і чоловічої статі) окрім загальноклінічних і респіраторних синдромів превалювали порушення з боку шлунково-кишкового тракту, а саме, повна втрата апетиту та втрата маси тіла понад 10 кг. Після повного обстеження констатовано аутоімунний тиреоїдит.

**Висновки.** Наявність ознак інтоксикації із втратою маси тіла повинно налаштувати думку лікаря на обстеження ендокринних органів (передусім щитоподібної залози) та вивчення їх за допомогою УЗД.

**Ключові слова:** COVID-19, ускладнення, тиреоїдит, діагностика, синдром плеврального випоту.

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## INTRODUCTION / ВСТУП

Infectious diseases are usually accompanied by a significant number of complications, which often lead to fatal cases. This is determined by the nature of the causative agent and its sensitivity to antibacterial drugs. At the same time, it is well-known that such drugs do not affect viral pathogens. An example is the Spanish influenza pandemic, which took the lives of 40 million people all over the world one hundred years ago.

A relative of that virus is the coronavirus infection, which, having undergone a specific mutation during this period, declared itself in the regions of South-East Asia in 2002–2004 as a type of severe respiratory infection (SARS-COV-2), which was accompanied by a mortality rate of 10.9% [1]. But 10 years later, in Saudi Arabia, a similar disease with a more severe course struck the country's population – MERS-COV. The mortality rate for this disease reached 34.4% [2]. Hardly had the residents of this region recover from the new mutant disease when, in December 2019, a new type

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of coronavirus infection (COVID-19) started in Wuhan, China, and spread throughout the country; within a few months, it was diagnosed in European and Asian countries, capturing Australia, South America, and North America [3, 4].

The first publications about the coronavirus infection in journals indicated a significant frequency of complications in many organs. The complications occurred in different periods of the disease course, but more often, they occurred at the end of the first week and the beginning of the second week after the disease onset.

Having processed a considerable amount of materials, V. Trykhlil reported on the frequency of some of these complications. Thus, pneumonia was registered in 15.7% to 100% of all patients. Acute respiratory distress syndrome (ARDS) was observed in 3% to 90% of hospitalized patients. Cardiac involvement occurred in 4% to 53% of cases. Deep vein thrombosis and thromboembolism were reported in almost 31% of patients, coagulopathy – in up to 38%, anemia – in up to 15%, kidney damage – in 3% to 8%, sepsis – in 4% to 8%, cerebro-neurological disorders – in 6% to 10% [5].

The group of authors presented data on the surgical treatment of 63 patients with complications after COVID-19: there were 18 (29.1%) people with pleural empyema, 8 (12.6%) people with non-specific pleuritis, 7 (11.1%) people with spontaneous pneumothorax, 4 (6.3%) people with subpleural (subcortical) hematoma, 7 (4.7%) people with hemopneumothorax. Patients with these complications were admitted to the clinic of the institute with delay because the complications were diagnosed late. Other pathological processes (17) were not related to the complications of COVID-19, but surgical intervention was indicated for them [6]. Most authors pay attention to thromboembolic complications [7, 8].

Previously, while consulting patients in other institutions, we reported 3 cases of complications in the pleural cavity organs [9]. These complications were discovered late. One patient had hemopneumothorax on the 18th day of the disease; the other two patients had pneumothorax on the 11th and 9th day. The first patient, after drainage, still had to be operated on using videothoracoscopy to remove the hematoma of the pleural cavity. Two other patients were drained, but despite this and mechanical ventilation, no favorable result was achieved.

**Rationale.** The mentioned complications and mortality data in these patients and our observations

on the course severity of some complications substantiate the relevance of the problem regarding the features of COVID-19 complications and the timeliness of their diagnosis, which should prevent fatal consequences and reduce the tension in society associated with new outbreaks of COVID-19 infection.

**Study Objective.** To share with the medical community the observations of rare complications of COVID-19 infection, not described by other authors, and the peculiarities of the course of combined complications.

#### **Materials and Methods**

We observed 2 patients diagnosed with thyroiditis at the stage of discharge from the hospital (recovery from the coronavirus disease). One of them had thyroiditis combined with left-sided pleural effusion syndrome (LPES).

#### **Clinical case description:**

Patient L., 59 years old, a non-manual worker, a city resident. Subacute disease: weakness, joint and muscle pain, sore throat, dry cough, shortness of breath, body temperature up to 38 °C, loss of appetite, pain in the peritoneal cavity with no precise localization, periodic diarrhea. The patient had a clinical examination and computed tomography (CT) performed. The connection of the disease with coronavirus infection was confirmed, as well as the focal infiltrative lesions of up to 45% of the lung fields, mainly in the lower lobes. After a week of antiviral therapy, despite some general improvement in condition (reduced shortness of breath and cough), the patient lost appetite and began to lose body weight; pain appeared in the heart area and behind the sternum, and shortness of breath began to increase. Due to the last two complaints, the patient had to consult a cardiac surgeon. Aorto-coronary examination helped to rule out coronary thrombosis. However, effusion in the right pleural cavity was revealed during the study. The patient was consulted by the thoracic surgeon, who confirmed the syndromic diagnosis; this was the reason for a video-assisted thoracoscopic surgery. After making sure that there were no contraindications to invasive examination, a video-assisted thoracoscopic surgery (VATS) was performed under local anesthesia. VATS revealed the following findings: no changes in the visceral pleura, hyperemia of the parietal pleura, a slight uniform injection of arterial small vessels along its entire length, the intercostal spaces clearly visible: unchanged arterial and venous vessels. In our opinion, the visual picture of the pleura was indicative of toxic manifestations. At the

same time, atelectasis of the middle lobe was discovered. No enlarged lymph nodes were detected. A pleural biopsy was performed in three pleural sites. Considering the general condition of the patient, it was decided to postpone the bronchoscopy test for 1–2 days. No pathological changes were found during bronchoscopy. Toilet bronchoscopy was performed with antiseptics; lungs were massaged through the chest wall, and aspiration of bronchial secretions was performed.

In parallel with this, biochemical analysis and hormone tests were carried out. The following results were obtained: thyrotropin – 0.10  $\mu$  IU/ml (reference value: 0.3–0.4  $\mu$  IU/ml); triiodothyronine free – 29.52 nmol/l (reference value: 3.1–6.8 nmol/l); free thyroxine – 72.67 nmol/l (reference value: 12.0–22 nmol/l); thyroglobulin antibodies – 286.0 IU/l (reference value: 0–115 IU/l); thyroperoxidase antibodies – 184.7 IU/l (reference value: 0–35 IU/l). Increased C-reactive protein level was recorded (19.41 mg/l). These findings were registered against the background of lymphopenia (8%) and eosinophilia (9%).

Ultrasound examination of the thyroid gland: the gland was enlarged; echogenicity was normal; the echostructure was heterogeneous due to hypoechoic areas and fibrous inclusions; parenchymal blood flow in the PDI mode increased; in the upper pole, there was a hyperechoic solid nodule of rounded shape with clear smooth contours of 8 × 8 mm, TR 3 category by ACR TI-RADS 2017. The capsule was unchanged. Peripheral lymph nodes were not visualized.

#### CONCLUSIONS / ВИСНОВКИ

The signs of intoxication, along with loss of body weight secondary to COVID-19 infection, should prompt a doctor to consider endocrine organs

#### CONFLICT OF INTEREST / КОНФЛІКТ ІНТЕРЕСІВ

The authors declare no conflict of interest.

#### FUNDING / ДЖЕРЕЛА ФІНАНСУВАННЯ

None.

#### AUTHOR CONTRIBUTIONS / ВКЛАД АВТОРІВ

All authors substantively contributed to the drafting of the initial and revised versions of this paper. They take full responsibility for the integrity of all aspects of the work.

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The patient was consulted by an endocrinologist, who, with our help, verified thyrotoxicosis, autoimmune thyroiditis, nodular goiter.

Taking into account the complications, anti-inflammatory non-specific therapy (Nimid), and hormonal drugs (deoxycorticosterone 5 mg 2 times a day, tyrosol 10 mg 4 times a day, Xarelto 15 mg) were prescribed. The pleural cavity was drained according to the Subbotin-Bulau method. After 4 days, the drain was removed. The patient developed an appetite and began to gain weight. In 2 weeks, he was discharged for outpatient rehabilitation. The patient came for a follow-up visit after 2 weeks. He complained of weakness, which did not affect his working capacity significantly. Breathing on the right is weakened; no other pathological phenomena were found. Radiological findings: pleural thickening on the right, minor lung spots of up to 20% in the lower lung fields.

Another observation related to a 48-year-old female, a city resident, who had stage II obesity. The disease progressed with similar clinical signs. The leading signs were loss of appetite and decreased body weight (up to 15 kg in 2 weeks after disease onset). Hormonal test findings: triiodothyronine – 32.5 nmol/l, free thyroxine 66.6 nmol/l; thyroglobulin antibodies – 290.0 IU/l; thyroperoxidase antibodies – 220.6 IU/l. Ultrasound findings: increased blood flow in the thyroid gland and alternation of hypo- and hyperechoic fields.

After verification of autoimmune thyroiditis and thyrotoxicosis, the patient was referred to an endocrinologist for further treatment.

(primarily the thyroid gland). Appropriate ultrasound studies should be started in the first days of observing patients with suspected COVID-19 infection.

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