Clinical case of concomitant tuberculosis and COVID-19 on the background of Churg-Strauss syndrome

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Conflict of interest: none

BACKGROUND. Tuberculosis (especially chemoresistant), coronavirus disease (COVID-19) and Churg-Strauss syndrome (CSS), both separately are serious illnesses, and in combination with each other (tuberculosis + COVID-19, COVID-19 + CSS). The analysis of the literature also indicates the difficulty of differential diagnosis between these diseases, as they have common clinical and radiological features. The outcome of treatment depends on timely and early diagnosis of each of these diseases with the prescription of corresponding therapy. We haven't found in the available literature described cases of concomitant tuberculosis, COVID-19 and CSS, which may be interesting in terms of diagnostic vigilance of physicians of different specialties.

OBJECTIVE. To demonstrate the features of the simultaneous course of tuberculosis and COVID-19 in a patient with CSS on the example of a clinical case of self-observation.

RESULTS AND DISCUSSION. During the last 19 years of her life, the patient suffered from CSS. From the treatment she received only polcortolon, which was insufficient for such a serious disease. Whereas, according to the literature, for the treatment of eosinophilic granulomatous vasculitis not only glucocorticoids should be prescribed, but also immunosuppressants (cyclophosphamide for induction and azathioprine for maintenance therapy), mepolizumab and others. During these years, the patient developed lesions of the cardiovascular system (metabolic cardiomyopathy of ethanol and eosinophilic-granulomatous-vascular origin, myocardial fibrosis with arrhythmia, heart failure of 1st degree), gastrointestinal tract (chronic gastroduodenitis, peptic ulcer of the duodenum, gallstone disease, chronic calculous cholecystitis, chronic pancreatitis), urogenital system (chronic pyelonephritis), skin (autoimmune dermatitis, hemosiderosis), respiratory system (respiratory insufficiency of the 2nd degree, chronic allergic rhinosinusitis). COVID-19 and multidrug-resistant tuberculosis joined on the background of the depleted organism. COVID-19 treatment was effective. However, the treatment of multidrug-resistant tuberculosis, which the patient received for 3 months, did not have a positive effect (negative radiological dynamics on the background of continued bacterial excretion). Renal dysfunction (creatinine >140 μmol/l) and peripheral eosinophilia also persisted during this period. According to the FFS lethal risk scale, the patient had two factors, which indicated a very severe flow of the disease and a high risk of death. Acute heart failure was the reason of death.

CONCLUSIONS. CSS (eosinophilic granulomatous vasculitis) is a rare disease that requires timely, quality and proper treatment that will prevent the development of damage of various organs and body systems (especially cardiovascular and respiratory). The presented case demonstrates a very severe course of COVID-19 and multidrug-resistant tuberculosis joined. However, death has occurred as a result of acute heart failure after 3 months, that was inevitable.

KEY WORDS: tuberculosis, COVID-19, Churg-Strauss syndrome.
Заголовок: Клінічний випадок

Мета. На прикладі клінічного випадку власного спостереження продемонструвати особливості одночасного перебігу туберкульозу та COVID-19 у хворі на СЧС.

Результати та їх обговорення. Протягом останніх 19 років життя пацієнка страждала на СЧС. Із лікування вона отримувала лише полькортолон, що було недостатнім для такого тяжкого захворювання. За ці роки в пацієнтки розвинулося ураження серцево-судинної системи (метаболічна кардіоміопатія етанолової й еозинофільно-гранулематозно-васкулярної природи, міокардіофиброз із порушенням ритму, серцева недостатність 1 ступеня), шлунково-кишкового тракту (хронічний гастродуоденіт, виразкова хвороба 12-палої кишки, жовчнокам'яна хвороба, хронічний калькулезний холецистит, хронічний панкреатит), сечостатевої системи (хронічний пиелонефрит), шкіри (аутоімунний дерматит, гемосидероз), дихальної системи (дихальна недостатність 2 ступеня, хронічний алергічний риносинусит). На тлі виснаженого організму приєдналися COVID-19 і мультирезистентний туберкульоз. Лікування COVID-19 виявилося ефективним. Водночас лікування мультирезистентного туберкульозу, яке пацієнка отримувала 3 місяці, не мало позитивного ефекту (негативна рентгенологічна динаміка на тлі продовження бактеріовиділення). Протягом цього періоду в пацієнтки зберігалися також порушення ниркової функції (креатинін >140 мкмоль/л) і периферична еозинофілія. За шкалою оцінки ризику летального результату FFS, пацієнка мала два чинники, що вказувало на дуже тяжкий перебіг захворювання та високий ризик летального наслідку. Причиною смерті стала гостра серцева недостатність.

Висновок. СЧС (еозинофільно-гранулематозний васкуліт) є рідкісним захворюванням, яке потребує своєчасного, якісного та правильного лікування, що протидіятиме розвитку ураження різних органів і систем організму (найперше серцево-судинної та дихальної). Представлений випадок демонструє дуже тяжкий перебіг СЧС з ураженням багатьох органів і систем за відсутністю правильного лікування, що могло би забезпечити своєчасний регрес симптомів васкуліту та покращення прогнозу життя пацієнтки. На тлі цього синдрому приєдналися COVID-19 і мультирезистентний туберкульоз. Через 3 місяці в результаті гострої серцевої недостатності настав летальний наслідок, що було неминучим.
Introduction

Today, not only in Ukraine, but all over the world, the epidemic of chemoresistant tuberculosis and the coronavirus disease (COVID-19) pandemic remain relevant issues, which also have a negative impact on each other [1, 10]. And the combined course of these diseases leads to difficulties in treatment, prolonging its duration and increasing the incidence of fatalities.

Churg-Strauss syndrome (CSS, eosinophilic-granulomatous vasculitis) is a rare disease characterized by necrotizing granulomatous inflammation with eosinophilic infiltration in various tissues and organs, often with airway lesions, and autoimmune systemic necrosis vasculitis of vessels of small and medium caliber, which is characterized by blood eosinophilia [1-3, 8, 11]. Manifestations of lesions of the respiratory system in this syndrome are: bronchial asthma, allergic rhinitis, rhinosinusitis, pleural effusion. Among the lesions of the cardiovascular system are eosinophilic endocarditis/myocarditis, coronary vasculitis, pericarditis, symptoms of heart failure. Lesions of the gastrointestinal tract are manifested by eosinophilic gastritis and enterocolitis, necrosis and perforation of the intestine, often by severe abdominal pain and others. Other manifestations of eosinophilic granulomatous vasculitis are polyneuropathy, skin lesions, arthritis, muscle pain and weakness.

The five-factor score (FFS) scale of the lethal result in CSS [4], which includes 5 indicators, is widely used in the world: • renal impairment; • proteinuria (>1 g in 24 hours); • hemorrhage in the digestive tract, heart attack or pancreatitis; • damage of the central nervous system; • cardiomyopathy.

Thus, according to the literature data [3, 4], in the presence of 1 or 5 factors, the disease is considered severe and is accompanied by mortality in up to 30 % of cases; in the presence of 2 or more factors, the disease is considered very severe, and mortality is about 50 % of cases.

P.M. Leru [6] emphasizes that the prognosis of eosinophilic granulomatous vasculitis depends mainly on the cause and mechanism of eosinophilia, the severity of organ dysfunction, as well as the exact diagnosis and response to treatment.

Y. Nguyen and L. Guillemin [8] note that eosinophilic granulomatous vasculitis usually occurs in patients with pre-existing bronchial asthma and affects the skin, lungs and peripheral nerves. And the overall survival of patients depends on the correct treatment. Glucocorticoids should be prescribed to all patients, and immunosuppressants (cyclophosphamide for induction and azathioprine for maintenance therapy) should be used for patients with severe/refractory disease and an unfavorable prognosis on the FFS scale [3, 7, 8, 11].

C. Janson et al. [5] indicate the need for a number of eosinophilic diseases such medicines as mepolizumab, reslizumab, benralizumab, dupilumab, omalizumab and tezepelumab.

B. Özdemin et al. [9] analyzed literature data (6 clinical cases) and self-observation data (5 clinical cases) on patients with eosinophilic-granulomatous vasculitis with COVID-19 and patients diagnosed with eosinophilic-granulomatous vasculitis or who underwent an outbreak that imitates COVID-19. First, the authors point to similarities in clinical and radiological data in eosinophilic granulomatous vasculitis and COVID-19, as both diseases may present with respiratory distress syndrome, especially in patients with negative polymerase chain reaction (PCR). Among 11 analyzed clinical cases, in 7 cases (63.6 %) eosinophilic granulomatous vasculitis imitated COVID-19. In 4 cases (36.4 %) the combined course of these two pathologies was determined, with all 100 % having a history of bronchial asthma, and computer tomography (CT) of thoracic cavity organs (TCO) revealed changes of "frosted glass" type. The authors indicate that there was a positive dynamics in all 4 cases.

R.M. Mroz et al. [7] described changes in CT of the TCO by the type of "frosted glass" and "consolidation" in patient with CSS in their clinical case, which is also characteristic of the radiological manifestations of COVID-19.

G. Zonzin et al. [11] described a clinical case of self-observation of CSS in a pregnant woman. In the 4th week of pregnancy, the woman showed the first symptoms of CSS (dry cough, nasal congestion, rhinorrhea and shortness of breath), no X-ray examination was performed, there was no dynamics of symptoms for the prescribed antibiotic. After that, the woman was consulted by an allergist, who prescribed a course of hormone therapy, including inhaled corticosteroids. However, the woman did not receive this treatment. Two weeks after delivery, the symptoms in the woman in labor worsened sharply with fever, pleural pain and hemoptysis. After that, an X-ray examination of the thoracic cavity organs (X-r TCO) was performed, where bilateral interstitial infiltrates were detected. Although mycobacterium tuberculosis (MBT) was not found twice in the sputum of the patient and the tuberculin tests were negative, it was decided to start empirical treatment of tuberculosis. On the background of antimycobacterial therapy (AMBT), the patient’s condition only worsened, and she was transferred to the intensive care unit. Therefore, the AMBT course was stopped. On the control CT of TCO bilateral interstitial infiltrates remained without dynamics, and on CT of the head chronic sinusitis was revealed. Such symptoms as epigastric pain, weight loss of 6 kg and
arthritis were observed. In the general blood analysis high leukocytosis and eosinophilia were revealed. After thoracoscopy and biopsy were made, necrotic eosinophilic granulomas in the vessels and alveoli were revealed. Based on the obtained data, a course of pulse therapy with methylprednisolone and cyclophosphamide was prescribed. And only after that the positive dynamics with saving of patient's life was received. Therefore, the authors point out the difficulty of differential diagnosis between CSS and tuberculosis, and the importance of timely diagnosis of relevant diseases.

Thus, tuberculosis (especially chemoresistant), COVID-19 and CSS, both separately are serious diseases, and in combination with each other (tuberculosis + COVID-19; COVID-19 + CSS). The analysis of the literature also indicates the difficulty of differential diagnosis between these diseases, as they have common clinical and radiological features. The outcome of treatment depends on timely and early diagnosis of each of these diseases with the prescription of corresponding therapy. We haven't found in the available literature described cases of concomitant tuberculosis, COVID-19 and CSS, which may be interesting in terms of diagnostic vigilance of physicians of different specialties.

Purpose: to demonstrate the features of the simultaneous course of tuberculosis and COVID-19 in a patient with CSS on the example of a clinical case of self-observation.

**Materials and methods**

Clinical case of self-observation of simultaneous tuberculosis and COVID-19 on the background of CSS in a patient who was treated in the pulmonary tuberculosis department № 2 of clinical base of the phthisiatry and pulmonology department of Zaporizhzhia State Medical University on Public Non-profit Enterprise of the "Zaporizhzhia Regional Clinical and Diagnostic Center of Phthisiatry and Pulmonology" of Zaporizhzhia Regional Council (PNE "ZRDCCPP" ZRC).

**Results and discussion**

Patient P., 53 years old. From the anamnesis of life: at the age of 34, the patient was diagnosed CSS (eosinophilic-granulomatous vasculitis), allergic rhinitis.

On September 29, 2020, due to contact with a father with coronavirus infection (who lived in the same apartment), testing for COVID-19 was conducted. The PCR result on COVID-19 was positive. As the patient had no symptoms of the disease, the family physician recommended her the self-isolation. From October 4, 2020, hyperthermia appeared, after that azithromycin 500 mg a day was prescribed on an outpatient basis. The general condition continued to worsen.

On October 8, 2020, the X-ray examination of TCO was held, where the following changes were revealed: on the right in the lower lobe, on the left in the upper lobe, an inhomogeneous haze: hepatomegaly symptoms, diffuse changes in the liver parenchyma, microlithiasis of both kidneys (chronic pyelonephritis). In the X-ray examination of TCO with contrast, changes were observed in the wall of the pulmonary vessels and alveoli. Based on the obtained data, a molecular genetic study of sputum for COVID-19 was conducted. The PCR result on COVID-19 was positive, there was a some positive clinical dynamics. During this time, sputum culture was obtained, where it was found MBT to be resistant to isoniazid (H), R, ethambutol (E), pyrazinamide (Z) and kanamycin (Km).

Therefore, the patient was transferred to in-patient department of the hospital of an anti-tuberculosis institution with a diagnosis of multidrug-resistant tuberculosis (10.2020), infiltrative left lung, destruction+ MBT+ M+ MG+ Rif+ K+. Resistance I (HREZ), resistance II (Km). Histology 0. Category 4 (newly detected tuberculosis, NDTB). CSS (eosinophilic-granulomatous vasculitis), metabolic cardiomyopathy (ethanol and eosinophilic-granulomatous-vascular origin), myocardial fibrosis with arrhythmia. Bilateral non-hospital pneumonia of the group III, coronavirus disease (PCR positive from 29.09.2020).


Taking into consideration the general condition of moderate severity and changes in X-ray examination of TCO, the patient was hospitalized in the pulmonology department with a diagnosis of bilateral nosocomial pneumonia of group III, coronavirus disease (PCR positive from 29.09.2020).

At the time of admission to the pulmonology department, it was established that the patient was registered at a cardiologist and family doctor for: CSS (eosinophilic-granulomatous vasculitis), metabolic cardiomyopathy (of ethanol and eosinophilic-granulomatous vascular origin), heart failure of the 1st degree, chronic allergic rhinosinusitis. That is why she received pircocortolon on a regular basis.

Also accompanying diseases in the patient are: gallstone disease, chronic calculous cholecystitis, chronic pancreatitis, chronic gastroduodenitis, peptic ulcer of the duodenum. Chronic pyelonephritis and hemosiderosis.

Collecting the anamnesis of the disease, it was revealed that from June 2020 the patient had subfebrilitis. The patient stated that she did not have tuberculosis before, and she denied contact with a tuberculosis patient. Given the presence of prolonged subfebrilitis a molecular genetic study of sputum on the MBT was performed. Revealed MBT+ were resistant to rifampicin (R+).

However, having the positive result on COVID-19, the patient began treatment in the pulmonology department before receiving a negative result. Medicines that were prescribed: leflocin, Refined, polycortolon, omeprazole, pancreatin, yogurt.

After a week of treatment, the PCR result on COVID-19 was negative, there was a some positive clinical dynamics. During this time, sputum culture was obtained, where it was found MBT to be resistant to isoniazid (H), R, ethambutol (E), pyrazinamide (Z) and kanamycin (Km).

According to the general condition of moderate severity and changes in X-ray examination of TCO, the patient was transferred to in-patient department of the hospital of an anti-tuberculosis institution with a diagnosis of multidrug-resistant tuberculosis (10.2020), infiltrative left lung, destruction+ MBT+ M+ MG+ Rif+ K+. Resistance I (HREZ), resistance II (Km). Histology 0. Category 4 (newly detected tuberculosis, NDTB). CSS (eosinophilic-granulomatous vasculitis), metabolic cardiomyopathy (ethanol and eosinophilic-granulomatous-vascular origin), myocardial fibrosis with arrhythmia. Bilateral non-hospital pneumonia of the group III, coronavirus disease (PCR positive from 29.09.2020).


Upon admission to the PNE "ZRDCCPP" ZRC the patient was examined.

Blood tests for RW and HIV were negative. GBA result: HB – 132 g/l, er – 4.25×10^12/l, thrombocytes (Tr) – 442×10^9/l, L – 10.1×10^9/l, ef – 10 %, r/s – 5 %, s/s – 37 %, hf – 41 %, mn – 7 %, ESR – 3 mm/h. Biochemical blood analysis: bilirubin – 11.0 μmol/l, thymol test – 8.58 μL, ALT – 0.69, AST – 0.41, TP – 60 g/l, glucose – 6.42 mmol/l, creatinine – 145 μmol/l.

Conclusion of ultrasound examination of the abdominal cavity: hepatomegaly symptoms, diffuse changes in the liver and pancreas, gallstone disease, chronic calculous cholecystitis, calciocoele of the 1st degree, diffuse changes in the liver parenchyma, microlithiasis of both kidneys (chronic pyelonephritis).

Therapist’s advisory opinion: myocardial fibrosis, ventricular extrasystole. Heart failure of 1st degree. Chronic calculous
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Conclusion X-r TCO + tomogram (TG) of the left lung 8.0 on admission to PNE “ZRDCCPP” ZRC (fig. 1, 2): in the upper part of the left lung there is a focal infiltration with destruction up to 1.5 cm with a wide path to the root.

Taking into consideration the data of additional examination and tuberculosis diagnosis, the patient was prescribed the AMBT of category 4, considering the data of the drug sensitivity test. Necessary pathogenetic and symptomatic therapy of concomitant pathology was also prescribed according to the recommendations of relevant specialists.

After 3 months of inpatient treatment negative radiological dynamics was determined on the background of the continuation of the sputum from 01.2021 (MBT+). Conclusion X-r TCO + TG of the left lung 8.0 from 21.01.2021 (fig. 3, 4): on the left in the upper lobe there is a partial resorption of infiltration and foci, reduction of destruction to 1.2 cm; the root is deformed and altered fibrosly; in the lower left lobe there was an infiltration of lung tissue with destruction up to 2.5×1.2 cm.


Considering severe accompanying diseases, the patient was under constant supervision of a physician. AMBT of category 4, pathogenetic and symptomatic therapy the patient received fully. However, on January 24, 2021, the patient’s condition worsened sharply due to the development of acute heart failure. Despite the therapy and resuscitation measures, at 08:00 on 24.01.2021 biological death was stated.


From the presented clinical case of the simultaneous course of tuberculosis and COVID-19 on the background of CSS, we see the following: during the last 19 years of her life, the patient suffered from CSS. From the treatment she received only polcortolon, which was insufficient in the treatment of such a serious disease. Whereas, according to the literature [3, 5, 7, 8, 11], for the treatment of eosinophilic granulomatous vasculitis not only glucocorticoids should be prescribed, but also immunosuppressants (cyclophosphamide for induction and azathioprine for maintenance therapy), mepolizumab and others. During these years, the patient developed lesions of the cardiovascular system (metabolic cardiomyopathy of ethanol and eosinophilic-granulomatous-vascular origin, myocardial fibrosis.
with arrhythmia, heart failure of 1st degree), gastrointestinal tract (chronic gastroduodenitis, peptic ulcer of the duodenum, gallstone disease, chronic calculous cholecystitis, chronic pancreatitis), urogenital system (chronic pyelonephritis), skin (autoimmune dermatitis, hemosiderosis), respiratory system (respiratory insufficiency of the 2nd degree, chronic allergic rhinosinusitis). COVID-19 and multidrug-resistant tuberculosis joined on the background of the depleted organism.

COVID-19 treatment was effective. However, the treatment of multidrug-resistant tuberculosis, which the patient received for 3 months, did not have a positive effect (negative radiological dynamics on the background of continued bacterial excretion). Renal dysfunction (creatinine >140 μmol/l) and peripheral eosinophilia also persisted during this period. According to the FFS lethal risk scale, the patient had two factors, which indicated a very severe flow of the disease and a high risk of death. Acute heart failure was the reason of death.

Conclusions
1. CSS (eosinophilic granulomatous vasculitis) is a rare disease that requires timely, quality and proper treatment that will prevent the development of damage of various organs and body systems (especially cardiovascular and respiratory).
2. The presented case demonstrates a very severe course of CSS with damage of many organs and body systems in the absence of proper treatment, which could lead to timely regression of vasculitis symptoms and improve the patient’s prognosis. On the background of this syndrome, COVID-19 and multidrug-resistant tuberculosis joined. However, death has occurred as a result of acute heart failure after 3 months, that was inevitable.
КЛІНИЧНИЙ ВИПАДОК

Література


References


