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Case report

The Case of Leptospirosis in a Female Patient with Hodgkin's Lymphoma

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SUMMARY

Introduction. Although we could not find the registered cases of leptospirosis co-occurring with lymphogranulomatosis, it is important to note that both diseases can affect the immune system. Therefore, the reported case is unique and will be interesting and useful for the physicians of various specialties.
Case report. We report a case of icterohemorrhagic form of leptospirosis with a fatal outcome in a woman with postmortem diagnosis of Hodgkin's lymphoma. Based on the findings of the autopsy, histological and immunohistochemical studies, it was established that the deceased suffered from Hodgkin's lymphoma during her life, classical form, reticular subtype with depletion of lymphoid tissue and extranodal spread in the liver, ovaries, and epicardium.
Conclusion. The combination of leptospirosis and lymphogranulomatosis was characterized by the complication of the diagnostic process, which should be taken into account by physicians of all specialties.

Keywords: **comorbid pathology, diagnosis, complication of the diagnostic process, clinical manifestations, autopsy**

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INTRODUCTION

Leptospirosis is a group of non-transmissible natural foci infections caused by spirochetes of the genus Leptospira and are rated first among zoonoses in terms of prevalence in natural and anthropogenic foci (1).

Hodgkin's lymphoma (HL) or lymphogranulomatosis is a disease with a primary lesion of the lymphatic system originating from the B-cells, in which a unique cellular microenvironment and activation of numerous signaling pathways support the proliferation of tumor cells and create the immunosuppressive environment for their survival (2, 3).

Although we could not find the registered cases of leptospirosis co-occurring with lymphogranulomatosis, it is important to note that both diseases can affect the immune system. Leptospirosis sometimes progresses to a more severe form known as Weil's disease (4), which can cause liver and kidney failure. Hodgkin's lymphoma can also weaken the immune system, making it more susceptible to infections such as leptospirosis. Therefore, the reported case is unique and will be interesting and useful for the physicians of various specialties.

We report a case of icterohemorrhagic form of leptospirosis with a fatal outcome in a woman with postmortem diagnosis of Hodgkin's lymphoma.

CASE REPORT

A 31-year-old female patient V. received treatment at the Infectious Disease Hospital. It was known from her past medical history that the disease had manifested a week after her husband independently carried out chemical rodent control at home.

Throughout the treatment period, the hemograms revealed anemia (Hb:73–107 g/L; RBC: 2.9–3.4 × 1012/L; color indicator—0.79-0.9), leukocytosis (40–47 × 109 /L), lymphopenia (3–10%), ESR: 25–50 mm/h. The findings of blood biochemistry test showed total bilirubin: 99–102.7 μmol/L; direct bilirubin: 85.8–86.5 μmol/L; indirect bilirubin: 12.5–16.9 μmol/L; total protein: 47–49 g/L; urea: 20.1–21.5 mmol/L; creatinine: 118–121 μmol/L; ALT: 33U/L; AST: 74 U/L.

The patient underwent a multislice chest and abdominal CT that revealed CT-signs of bilateral polysegmental pneumonia (CO-RADS 5), affecting ≥ 25% of the parenchyma, mediastinal lymphadenopathy, bilateral hydrothorax, a small amount of fluid in the pericardial cavity, fatty liver disease, hepatomegaly, abdominal lymphadenopathy, ascites.

The patient was diagnosed with leptospirosis, icterohemorrhagic form, laboratory confirmed Leptospira Gripothyphosae 1:50, 1:800, 1:400, severe course, toxic hepatitis with severe hepatocellular insufficiency, secondary nephropathy, anasarca.

Antibacterial (doxacycline) and detoxification treatment was started, intensive therapy and artificial lung ventilation were carried out, but her condition progressively worsened and the patient died. An autopsy of the dead body was authorized (informed consent and permission to publish this case were signed by the legal representatives).

The results of the autopsy, histological and bacteriological examination of the sectional material, the diagnosis of the icterohemorrhagic form of leptospirosis was confirmed. However, during the autopsy, enlarged lymph nodes of the thoracic and abdominal cavities were found, ranging in size from 1 to 4 cm in the largest diameter. They were conjoined into aggregations of a soft-elastic consistency; on the section they were colored gray-pink with crimson softened areas. In addition, a whitish soft nodule up to 4 mm in diameter was found under the epicardium on the lateral wall of the heart. The liver was enlarged and of flaccid consistency, speckled on the surface and on the section due to the presence of yellow and purplish-gray spots. The histological examination of the lymph nodes of the bifurcation of the trachea, mediastinum, pancreoduodenal zone, intestinal mesentery and hilum revealed that the histological structure was smoothed, follicles were not identified, massive necrosis and hemorrhages were pronounced. The preserved areas were infiltrated by the lymphoid atypical cells with the presence of isolated mitoses, including pathological ones. Large-sized cells with multilobed nuclei were noted among the cellular infiltrate (Figure 1). Similar cellular infiltrates were also found in the liver, stroma of the ovaries, and in the node under the epicardium.

Given that similar changes are characteristic of a number of lymphoproliferative diseases, for the purpose of differential diagnosis (5–8), the immunohistochemical study was conducted using markers CD 30, CD 138, CD 20, CD 3, Bcl2, Bcl6, Ki 67, OLA (Figure 2).

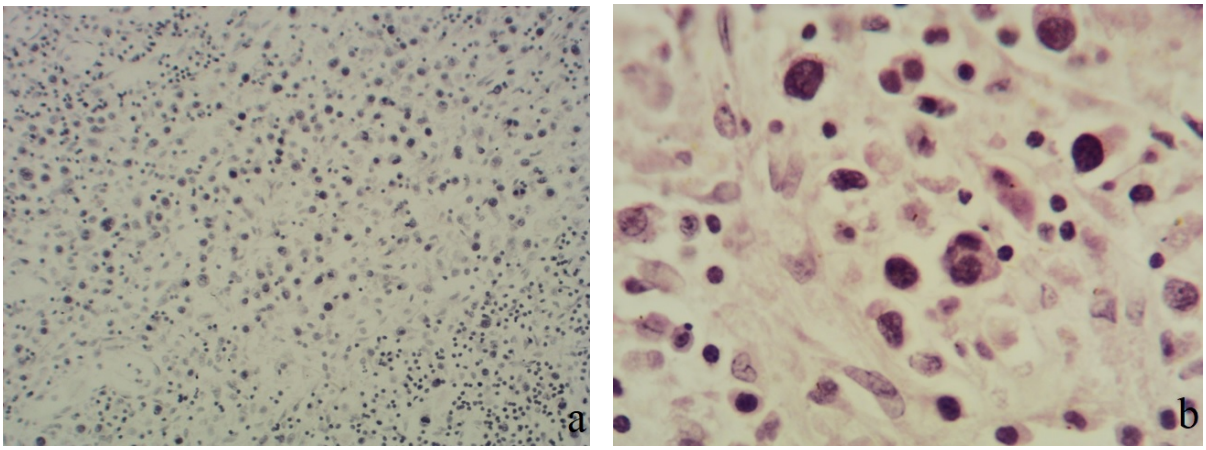
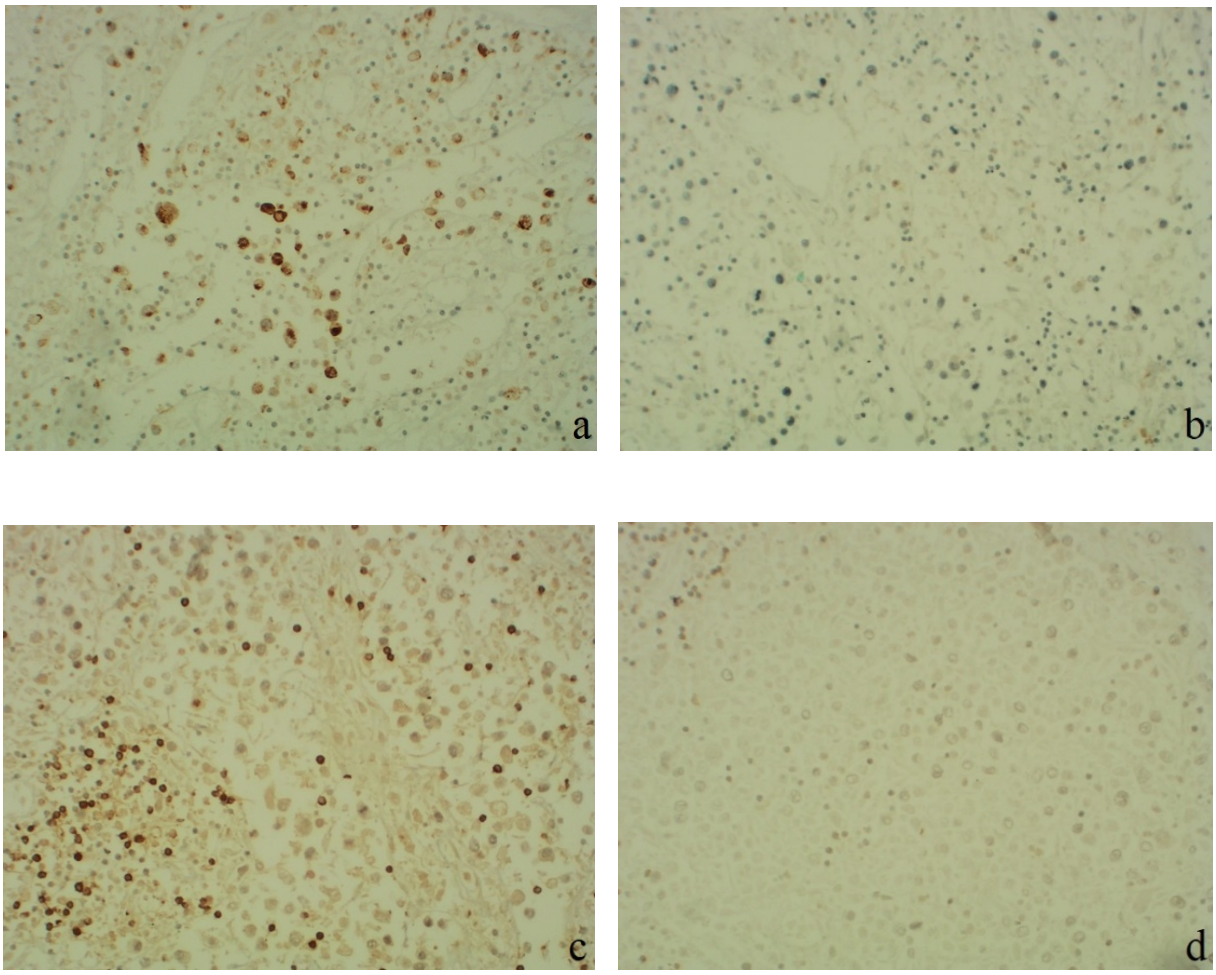


Figure. 1. *Microscopic changes in the lymph nodes of the deceased V.: a – general view, × 100; b – atypical polymorphic cells, × 400. Staining with hematoxylin and eosin*



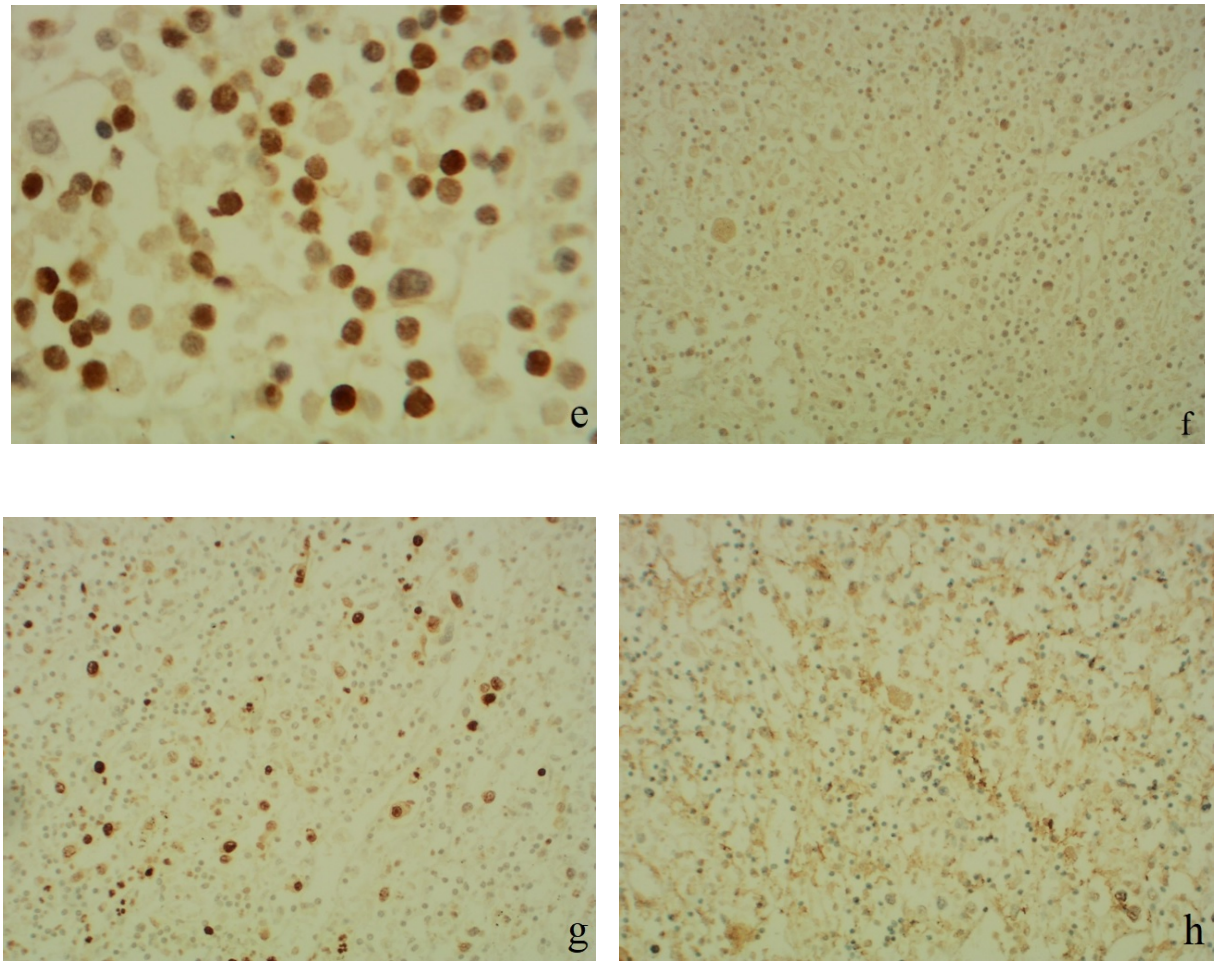


Figure. 2. *Immunohistochemical examination of the tissue of the lymph nodes of the deceased V.: a – CD 30 (× 100); b – CD 138 (× 100); c – CD 3 (× 100); d – CD 20 (× 100), e – Bcl2 (× 400), f – Bcl6 (× 100); g – Ki 67 (× 100); h – OLA (× 100)*

Based on the findings of the autopsy, histological and immunohistochemical studies, it was established that the deceased suffered from Hodgkin's lymphoma during her life, classical form, reticular subtype with depletion of lymphoid tissue and extranodal spread in the liver, ovaries, epicardium.

Thus, the patient had two diseases, which can be considered as concurred, because each of them could lead to the death of the patient.

DISCUSSION

A ubiquitous spread of leptospirosis is associated with a wide range of reservoir hosts of pathogenic Leptospira and animal species susceptible to them. Rats, mice, and dogs are carriers of Leptospira. The largest epidemic foci of leptospirosis are noted in countries with tropical and subtropical climates, where outbreaks involving hundreds and thousands of people are registered annually (1, 10). This infectious pathology has an important medical and social significance, since the annual morbidity constitute 1 million people, of which more than 50 thousand people die and many remain disabled (11).

Infection occurs through a direct contact with the reservoir host or indirectly through soil, urine of infected animals, and contaminated water. Icteric and anicteric forms of the disease are distinguished. Moreover, the mortality rate in the anicteric form is significantly lower compared to the icteric form. Ninety percent of cases of the disease are asymptomatic or have a mild form, and the symptoms are non-specific, which complicates the clinical diagnosis of leptospirosis (12, 13). Noteworthy, the course of leptospirosis can be affected by concomitant pathology. Therefore, it is important to study not only the clinical and morphological features and the improvement of the diagnostics of infectious di-

seases, but also the course, morphological and pathophysiological aspects of infectious diseases in coinfection and in the combination of an infectious disease with a non-infectious one, including tumor pathology (2, 3, 14, 15).

The diagnosis of leptospirosis was not difficult for the clinicians to make, based on the past medical history (the woman assisted her husband to remove rat corpses after deratization) and clinical and laboratory tests. However, clinicians sometimes cannot diagnose the second disease because of its atypical picture. Therefore, it is important to analyze the diagnostic steps that clinicians had to take to diagnose Hodgkin's lymphoma.

Due to the specific cellular interaction, two main forms of HL are to be distinguished: a classical and nodular one with a predominance of lymphocytes, which differ in prevalence, morphology, immunophenotype of cellular composition, and clinical picture. Classical Hodgkin's lymphoma, in turn, has four different subtypes: with nodular sclerosis, mixed-cell, with a predominance of lymphocytes, and with depletion of lymphoid tissue (4).

The deceased woman was diagnosed with Hodgkin's lymphoma with depletion of lymphoid tissue, which is the least common subtype with the incidence of less than 1% (17). The diagnosis of classical Hodgkin's lymphoma with lymphocyte depletion is difficult and is often detected at the advanced stages, and patients with this disease have the lowest survival rates, especially in the presence of adverse factors (18), which in this case were leptospirosis (extranodal disease), involvement of more than three groups of lymph nodes, lesions of mediastinal lymph nodes, high ESR.

Clinical manifestations of Hodgkin's lymphoma and leptospirosis commonly concur, which can lead to inaccurate diagnosis in cases of comorbid pathology. Both diseases can be manifested by an increase in body temperature, myalgia, headache, back and abdominal pain, anorexia, hepatomegaly, thrombocytopenia, and increased ESR. However, lymphadenopathy is a characteristic symptom of Hodgkin's lymphoma. Therefore, clinicians having detected enlarged mediastinal and abdominal lymph nodes, reveled by CT, should suspect another disease manifested by this symptom and perform a diagnostic puncture of lymph nodes in order to exclude lymphoproliferative disease (19, 20). After all, considering the pathogenesis of leptospirosis, lymphadenopathy is not characteristic of this disease.

Notwithstanding the absence of the direct link between leptospirosis and Hodgkin lymphoma, some studies have shown that infection with certain bacteria, viruses, or parasites can increase the risk for the development of lymphomas, including Hodgkin's lymphoma (8, 21). However, this correlation is not fully understood and more investigations are needed to determine its exact mechanisms.

CONCLUSION

For the first time ever, we described a case of comorbid pathology of leptospirosis and lymphogranulomatosis. The combination of these diseases was characterized by the complication of the diagnostic process, which should be taken into account by physicians of all specialties.

Conflict of interests

The authors have no existing or potential conflicts of interest to declare.

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Slučaj leptospiroze kod bolesnice sa Hodžkinovim limfomom

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S A Ž E T A K

Uvod. Iako nismo mogli pronaći registrovane slučajeve leptospiroze koja se javlja zajedno sa limfogranulomatozom, važno je napomenuti da obe bolesti mogu uticati na imunosistem; zbog toga je prijavljeni slučaj jedinstven i biće zanimljiv i koristan lekarima različitih specijalnosti.
Prikaz slučaja. Predstavljamo slučaj ikterohemoragijske forme leptospiroze sa fatalnim ishodom kod bolesnice sa dijagnozom Hodžkinovog limfoma postavljenom *post mortem*. Na osnovu nalaza obdukcije, histoloških i imunohistohemijskih studija utvrđeno je da je preminula bolesnica tokom života patila od klasičnog oblika Hodžkinovog limfoma retikularnog podtipa, praćenog smanjenjem limfoidnog tkiva i ekstranodalnim širenjem u jetru, jajnike i epikard.
Zaključak. Lekari svih specijalnosti treba da imaju na umu da kombinaciju leptospiroze i limfogranulomatoze karakteriše komplikacija dijagnostičkog procesa.

Klučne reči: **komorbidna patologija, dijagnoza, komplikacija dijagnostičkog procesa, kliničke manifestacije, autopsija**