CASE STUDY

CONTENTS

A case of leptospirosis in transcarpathia complicated with Jarish -Herxheimer reaction

Vlasta V. Vysochanska[1,2], Myroslava S. Babych[2], Anton I. Kohutych[1,2], Andriana A. Halamba[1]
[1]UZHHOROD NATIONAL UNIVERSITY, UZHHOROD, UKRAINE
[2]REGIONAL CLINICAL INFECTIOUS DISEASES HOSPITAL, UZHHOROD, UKRAINE

ABSTRACT

A case report of Jarisch-Herxheimer (JHR) reaction on a 10th day of Leptospirosis caused by *Leptospira Pomona*. JHR occurs as a complication of an antibiotic treatment of various spirochetes and may lead to respiratory distress syndrome, renal failure, hepatic insufficiency, and multiple organ failure. This case represents a skin and cardio-vascular form of JHR with no lung involvement. The patient was treated with benzylpenicillin and low dexamethasone doses for 5th day of the disease with a shift to ceftriaxone and high doses of methylprednisolone. The fastest diagnosis of a sporadic zoonotic disease, early start of antibiotic therapy, and adequate doses of corticosteroids are key to the successful treatment of leptospirosis.

KEY WORDS: Leptospirosis, Jarisch-Herxheimer reaction

Wiad Lek. 2024;77(3):608-612. doi: 10.36740/WLek202403134 DOI

INTRODUCTION

Leptospirosis is not a widespread disease in Ukraine, but some areas may become endemic. Disease is more common in rural and semi-urban areas that are exposed to populations of rodents due to close farming activity [1]. Any mammal may become a source of leptospirosis by excreting *Leptospira* from the proximal tubules of the kidneys [2]. The majority of incidents come from contact of a damaged human skin, or mucosa in oral and respiratory tract with contaminated dust, water, or food [3]. The disease severity may vary from a non-icteric fever with a muscular ache to hemorrhagic fever with multiple organ failure resulting in death in 15-50% of cases [4]. Typical treatment requires penicillin, ceftriaxone, or doxycycline. However, the use of high corticosteroid doses is not supported by high-quality evidence and routine use is not recommended [5].

Jarisch-Herxheimer reaction (JHR) is an acute, self-limiting condition that occurs after antibiotic treatment of spirochetal infections. It is accompanied by the following symptoms: chills, febrile fever, drop of a blood pressure, skin rashes [6], but may result in acute respiratory distress syndrome [7] and disseminated intravascular coagulation syndrome [8], and severe pulmonary hemorrhagic syndrome [9].

JHR is a result of exposure to antigens released from lysis during a high-quantity spirochetemic phase of infection and a massive increase of interleukin-6 (IL-6), IL-8, IL-1β, and tumor necrosis factor (TNF-α) [10]. Corticosteroid infusions before the antibiotic administration as a routine prevention of JHR have shown limited efficacy [11]. The rate of JHR incidents is reported from 19% to 82% of all leptospirosis cases [12,13]. Further studies are required to propose a predictive and clinically efficient protocol for leptospirosis treatment.

CASE REPORT

The patient was informed about the research plan, developed within the framework of the Helsinki Declaration of the World Medical Association "Ethical Principles of Medical Research with the Participation of a Person as an Object of Research,", the Convention of the Council of Europe on Human Rights and Biomedicine, and the legislation of Ukraine, and signed the informed consent to use his medical records and photos. Complete blood count, coagulogram, liver and kidney biochemistry tests, c-reactive protein, procalcitonin were analyzed on 1, 5, 7, 10, 15 days of treatment in Transcarpathia regional infectious disease hospital.

A 72-year-old male was admitted to a Transcarpathian regional Infectious hospital with complaints of headache, loss of appetite, frequent urination, thirstiness, pain in the joints, and yellowing of the skin and eyes. The patient considered himself sick for 5 days. The sickness started with a rise in body temperature to 38°C,

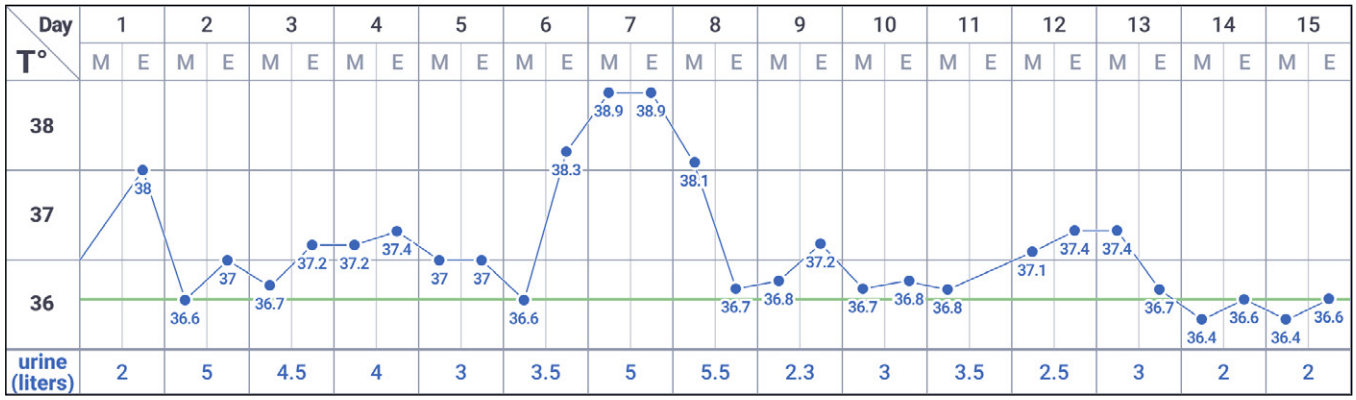

Fig.1. Dynamics of body temperature and volume of urination.

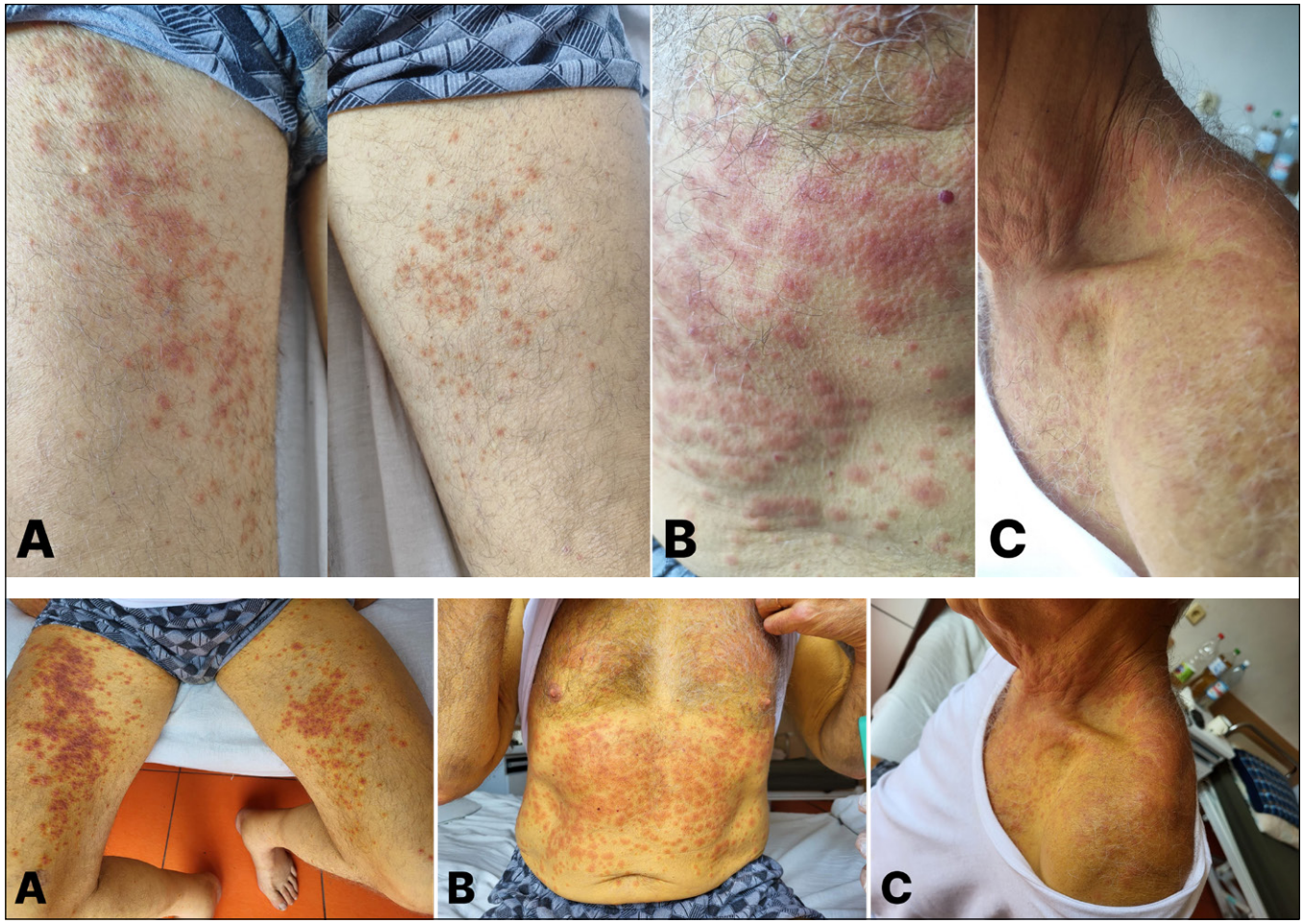

Fig. 2. Jarisch-Herxheimer reaction on a 5th day of antibiotic therapy (8-hour difference). A. thigh area; B. trunk area; C. neck and shoulders.

muscle aches, and sudden weakness. The patient took paracetamol with no improvement in the condition. In a few days, the man noticed urine became darker. On the night before hospitalization, the patient was suffering from intense pain in muscles and first seen eyes turned yellow. The patient lives in a rural area and has a grain storage next to his house.

Primary examination in hospital: low-grade fever (37.9°C), breathing rate 14/min, and blood pressure of 155/90 mmHg. Skin is pale with a yellowish tone and dry. Sclera are subicteric. The tongue is covered with a white coating. Lymph nodes are not enlarged. Auscultation: hard bronchial breathing in the lungs, arrhythmic tones of the heart with a systolic murmur. Moderate swelling of the lower extremities (feet to ankle-foot joint). Urination: 2 liters per day of dark-colored urine (Fig. 1).

Indirect agglutination test was negative for *Leptospira* on 6h day of disease. Based on clinical examination, anamnesis, and laboratory tests a previous diagnosis of leptospirosis was put and the patient was treated with

Table 1. Laboratory examination and etiological treatment during treatment period in hospital

Day in hospital	1th	5th	7th	10th	15th
Treatment	**Benzylpenicillin 16 M/day Dexamethasone 8 mg**		**Ceftriaxone 2 g, Methylprednisolone 500/250 mg**		**-**
WBC (*10^9/l)	18.03	17.24	19.16	11.59	6.39
LYM (*10^9/l)	0.34	0.58	0.79	1.14	1.28
MID (*10^9/l)	0.06	0.05	0.11	0.72	0.41
GRA (*10^9/l)	17.64	16.6	18.26	9.73	4.7
LY %	1.9	3.4	4.1	9.8	20
MI %	0.3	0.3	0.6	6.2	6.5
GR %	97.8	96.3	95.3	83.9	73.5
RBC (*10^{12}/l)	4.03	3.45	3.5	3.31	3.46
HBG (g/l)	105	100	99	91	99
HCT %	33.92	27.97	29.3	28.38	32.97
PLT (*10^9/l)	36	141	348	537	244
TP (g/l)	53.8	52.1	54.4	52.1	48.5
ALB (g/l)	33.3	27.7	28.6	28.4	28
UCB (umol/l)	194.4	251.7	163.4	64.7	41.9
TBil (umol/l)	256.6	366.8	264.3	94.4	74.2
ALT (U/l)	136.8	72.1	72	108.2	98.5
AST (U/l)	185	104.9	96	101.4	74.2
GGT (U/l)	38.9	35.2	57.5	55.3	58.1
ALP (U/l)	101	421.6	420	-	-
Cr (umol/l)	437	186.6	204.8	140.7	132.5
Urea (mmol/l)	29.15	17.08	14.93	11.23	8.31
GLU	7.96	8.65	6.7	5.2	4.18
PT (sec)	14.44	16.84	15.44	14.32	-
PA %	100.9	86.01	94.13	101.8	-
INR	1.09	1.24	1.15	1.08	-
PTI %	94	81	88	95	-
APTT (sec)	34.12	36.96	33.8	27.4	-
Fibrinogen (g/l)	6.09	5.39	5.61	4.12	-

*WBC: White blood cell count; LYM: absolute lymphocyte count; MID: cells include less frequently occurring and rare cells correlating to monocytes, eosinophils, basophils, blasts and other precursor white cells that fall in a particular size range; GRA: absolute neutrophils, monocytes, eosinophils, and basophils count; RBC: red blood cells; HGB: Hemoglobin; HCT: hematocrit; PLT: Platelets; TP: total protein; ALB: albumin; UCB: unconjugated bilirubin; TBil: total bilirubin; ALT: alanine transaminase; AST: aspartate transaminase; GGT: gamma-glutamyl transferase; ALP: alkaline phosphatase; Cr: creatinine; GLU: glucose; PT: prothrombin time; PA: prothrombin activity according to Kwik; INR: international normalized ratio; PTI: prothrombin index; APTT: activated partial thromboplastin time.

2 000000 units of benzylpenicillin 8 times per day, 8 mg of dexamethasone, disintoxication therapy, furosemide, metoclopramide and oral lactulose.

On the 5th-day patient's condition worsened: fever of 39,5°C, tachycardia, tachypnoea (20/min.), blood pressure 90/60 mmHg, SpO2 - 98%. Skin and sclera became intensively icteric. The rash appeared on the trunk and spread to the lower and upper limbs, abdomen, neck, and trunk, on the thighs it became bluish, confluent in nature; on the front surface of the lower legs – petechiae (Fig. 2). Patient complained to a horrible itch and pain in the rash's sites. Auscultation: hard bronchial breathing with wet rales in the lungs (Fig. 3 chest X-ray, Table 1). The abdomen was soft on palpation and somewhat sensitive in the right hypochondrium. On percussion, the liver was slightly enlarged by 1 cm. The spleen was not palpable. Urinary output was about 5 liters, urine was dark yellow and foamy. Excretions 1 time/day formed, acholic.

The antibiotic was changed to 2 grams of ceftriaxone per day. Instead of dexamethasone, 500 mg of methylprednisolone was prescribed for the first infusion and 250 mg during the next days. Indirect agglutination

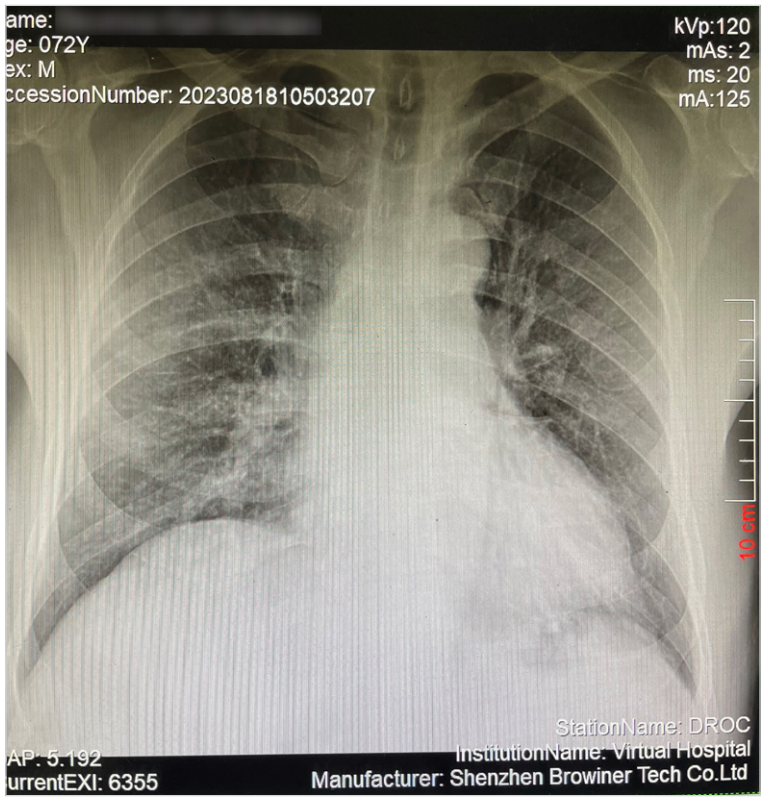

Fig. 3. X-ray of the chest in the frontal direct projection on a 5th day in hospital.
The sinuses are free. The domes are not relaxed. The roots are structural. Lung parenchyma has no focal infiltrative changes. Shadow of the heart of the usual configuration. Conclusion: There are no focal infiltrative changes in the lung parenchyma.

test came positive for *Leptospira Pomona* in 1:400 titer. Procalcitonin 1.16 ng/ml, CRP 72.36 mg/l.

In 2 days, body temperature normalized and the patient's condition began to improve. The intensity of itching and pain on the skin has dramatically decreased. The patient was discharged on the 15th day.

The main contributors of JHR are serogroup *interrogans* of the *Leptospira* genus, delay of antibiotic therapy for more than 3 days after the onset of symptoms, and treatment with amoxicillin [12]. Also, it was reported that JHR occurs within 24 hours of antibiotic therapy [14]. Comparison of symptom severity, and complication rate showed no statistical difference between the patients who developed JHR and those who did not. Renal failure, severe thrombocytopenia, and a lung hemorrhage were reported not to be statistically associated with JHR. Our case represents a typical symptom of JHR with an itchy and painful skin rash and a short-term cardio-vascular insufficiency with a delay in the onset of reaction to a 5th day of antibiotic therapy. The described case was caused by an *L. interrogans* serovar *Pomona* which serves in favor of the theory described above [15].

CONCLUSIONS

Leptospirosis is an underestimated disease despite a high mortality rate. The earliest antimicrobial therapy is crucial for the successful treatment and prevention of bacteria and secondary immune-associated complications. Corticosteroids can reduce the mortality of patients with severe leptospirosis but routine administration requires further investigation.

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The article was written within the framework of the research topic of the Department of Microbiology, Virology, and Epidemiology, as part of the infectious diseases course at the State University "UzhNU" "Health and Recreation. Peculiarities of the clinical and epidemiological course of infections and parasitoses typical for the Trans*carpathian region" State registration number 0117002833. Theme code 02070832. UDC index: 614.4. Subject code 76.33.*

CONFLICT OF INTEREST

The Authors declare no conflict of interest

CORRESPONDING AUTHOR

Vlasta V. Vysochanska
Uzhhorod National University
1 sq. Narodna, 88000 Uzhhorod, Ukraine
e-mail: lachupakabramail@gmail.com

ORCID AND CONTRIBUTIONSHIP

Vlasta V. Vysochanska: 0000-0003-0998-554 A D F
Myroslava S. Babych: 0009-0005-1123-9855 B
Anton I. Kohutych: 0000-0003-3838-9106 E
Andriana A. Halamba: 0000-0003-0175-9943 E

A – Work concept and design, B – Data collection and analysis, C – Responsibility for statistical analysis, D – Writing the article, E – Critical review, F – Final approval of the article

RECEIVED: 11.11.2023
ACCEPTED: 28.02.2024