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A CASE REPORT

THE CHALLENGES OF TREATMENT OF PATIENT WITH VIRAL HEPATITIS C AND BRUCELLOSIS:

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Abstract

Brucellosis is a widespread zoonotic illness with significant morbidity rates in Armenia. It causes a wide range of clinical consequences as it progresses, from mild ones that don't require changing the composition or length of an antibiotic prescription to fortunately uncommon, fatal situations involving the heart or central nervous system. According to the National Institutes of Health's Annual Statistical Records, the number of cases with Brucellosis that were initially diagnosed in Armenia was 309 in 2015, 362 in 2017, and 201 in 2018; simultaneously no data for 2016 has been provided. As Brucellosis is an endemic disease for Armenia, sometimes there can be co-infection of Brucellosis with other diseases. Management of such cases is difficult because of drug-drug interactions and hepatotoxicity of drags.

The aim of the case report is to discuss the challenges of management of patient with Brucellosis and Viral Hepatitis C infection.

A 59-year-old man was admitted to the hospital, Intensive Care Unit with gastrointestinal bleeding with a primary diagnosis of liver encephalopathy. Based on the clinical and laboratory findings, the patient was diagnosed with liver cirrhosis of mixed etiology (alcohol + Viral Hepatitis C), Child-Pugh C class (decompensated disease) Meld-Na22, splenomegaly, grade 3 ascites, stage 3 liver encephalopathy. 2 months after the first hospitalization the patient started to develop an increase in body temperature (up to 39C), pain in the spine, neuropathies and paresthesia. Patient was tested for Brucellosis, Wright-Hedelson (agglutination test) positive results (positive, 1:200 respectively), and positive serology results (high levels of IgG and IgM) confirmed diagnosis. Patient was treated based on international guidelines and drug-drug interaction information.

Keywords: *brucellosis, viral hepatitis C, co-infection, management, treatment.*

Introduction

Brucellosis is a widespread zoonotic illness with significant morbidity rates [*Corbel M, 2006, Hasanjani Roushan M, Ebrahimpour S, 2015; Unuvar G et al., 2019*]. It causes a wide range of clinical consequences as it progresses, from mild ones that don't require changing the composition or length of an antibiotic prescription to fortunately uncommon, fatal situations involving the heart or central

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nervous system. According to recent findings, brucellosis can affect patients with underlying conditions to experience a decline in their overall well-being [*Shi Q et al., 2024*]. For the human species, the causative agents include B.melitensis, B.suis, and B.abortus, with B.melitensis being the most virulent of the opportunistic infections, therefore, causing hematologic or rheumatologic disorders, osteoarticular system, musculoskeletal system dysfunctions. Nonspecific symptoms are fever, chills, night sweats, joint pains, weight loss, lymphadenopathy, and myalgia [*Jiang W et al., 2019; Qasim Set al., 2020*]. In systemic disorders involvement of the spine is observed mostly in the elderly, leading to complaints of back pain and sciatica radiculopathy spinal lesions, hepatosplenomegaly, and osteoarticular complications (10-85%) mostly affecting the lumbar vertebra (60%) [*Yildirim A et al., 2022*]. Travelers returning from endemic regions (such as those in Central and South America, Asia, the Balkans, and Sub-Saharan Africa) are most commonly affected by brucellosis, which is why doctors advise against consuming raw dairy products [*Ljubas D et al., 2020*]. Transmission in humans occurs by direct or indirect contact with a contaminated animal product, aerosols infused with the pathogen, blood, urine, infected tissues, or aborted fetus [*Doganay M, Aygen B, 2003; Sun G et al., 2020*]. Reservoirs are cattle, goats, camels, etc. [*González-Espinoza G et al., 2021*]. Brucella often predisposes to the liver because of the microbe's propensity for survival, which causes moderate hepatomegaly and is accompanied by hepatic granulomas in the patients [*Giambartolomei G, Delpino M, 2019*]. Although chronic brucellosis is a rare but complicated chronic hepatic suppurative disease, scientists like Wesley Spink have cited the etiological role of brucellosis in the development of cirrhosis; however, this was once thought to be merely contentious research [*Spink W, 1964*]. Now, however, thorough research and solid pieces of evidence have allowed for the determination of the causative factor of the development of disequilibrium. characteristically in the form of ascites/ spontaneous bacterial peritonitis development. In three cases of cirrhotic individuals, acute brucellosis acted as the stimulus for fatal hepatic decompensation. This was either because of the pathogen's direct effects on the liver or because of the requisite antibiotic regimens' hepatotoxicity.

Brucellosis is one of the most prevalent zoonotic infectious illnesses in Armenia is. Disease is identified in the nation's capital (Yerevan) as well as in the rural areas. According to the National Institutes of Health's Annual Statistical Records, the number of cases with Brucellosis that were initially diagnosed in Armenia was 309 in 2015, 362 in 2017, and 201 in 2018 simultaneously no data for 2016 has been provided. Data collected from Infection Disease Hospitals in Yerevan showed that 265 people with Brucellosis were hospitalized in 2016, 16 of these patients were between the ages of 0 and 14, and 94% of these patients were male. Overall days spent in hospitals were 1798; the hospitals suffered economic losses worth an estimated AMD$36 million annually. According to clinical data, 71% of patients had acute Brucellosis, which was characterized by fever, arthralgia, and night sweats, while 29% had chronic Brucellosis, which had caused organ system damage [*Asoyan V et al., 2018*]. As Brucellosis is an endemic disease for Armenia, sometimes there can be co-infection of Brucellosis with other diseases. Management of such cases is difficult because of drag-drag interactions and hepatotoxicity of drags. The aim of the case report is to discuss the challenges of management of patient with Brucellosis and Hepatitis C Viral Infection.

CASE PRESENTATION

A 59-year-old man was admitted to the hospital, Intensive Care Unit with gastrointestinal bleeding with a primary diagnosis of liver encephalopathy.

The primary examination results: Icteric coloration of the skin and mucous membranes, chronic liver disease stigmas were found – telangiectasia in the upper arm region, splenomegaly, and ascites. Regional lymph nodes were not palpable. Swelling of the lower limb till the upper 1/3 of the calves.

Cardiovascular system: cardiac sounds by auscultation are clear, cardiac activity is rhythmic, pulse – 85*BM*, AP – 120/80 *mm Hg*.

Pulmonary system: coarse crackles from both sides by auscultation, percussion tone-resonance, oxygen saturation (SpO2) – 96% (at rest in-room air).

Gastrointestinal system: The tongue is wet and slightly white-coated. Abdominal palpation: the abdomen is soft, painful in the epigastric area, and

bloated due to ascites (positive shifting dullness sign), the peritonitis signs are negative. The liver and spleen are not palpable due to ascites. Noticeable umbilical hernia. Rectal exam shows melena. Normal bowel sounds by auscultation.

Urinary system: urination is normal, painless. Kidney percussion – negative from both sides.

Nervous system: clouding of consciousness, disorientated.

Based on the clinical and laboratory findings (Table) the patient was diagnosed with liver cirrhosis of mixed etiology (alcohol + Hepatitis C virus), Child-Pugh C class (decompensated disease) Meld-Na22, splenomegaly, grade 3 ascites, stage 3 liver encephalopathy.

Esophagogastroduodenoscopy was performed during the intensive care unit with the results of a duodenal ulcer approximately 2*cm*, with a visible vessel underneath, covered in hematin in the bulbar area; fungal esophagitis. A smear test was taken from the oral cavity for finding the etiology of fungal esophagitis, the results were positive for Candida Albicans. Based on an esophagogastroduodenoscopy and smear test results an antifungal treatment started, despite the fact that it was resistant to all the antifungal drugs, however, Fluconazole, 200*mg* for 20 days was the chosen final therapy. After 2 days spent in the intensive care unit (given medication also included: Rifaximin, Vitamin K, and enteral nutrition was performed), the patient then moved to the Gastroenterology Department. During the primary examination, the patient noted neuropathies and lower limb weakness. Based on the latest complaints, high markers of mean corpuscular volume (Table) and alcohol consumption of Vitamin B12, Vitamin B9, and Vitamin B1 were added to the existing therapy. The patient also tested positive for Hepatitis C virus (HCV) (Table) so including him in the national program for HCV treatment was performed.

Sofosbuvir and Velpatasvir was the chosen drug therapy for 3 months (despite the fact that treatment duration needs to be 6 months, another thing is the drug absorption is decreased, due to proton-pump inhibitor therapy, and the maximal amount of proton-pump inhibitors that can be used with antiviral therapy was 20 *mg* of Omeprazole or 40 *mg* Pantoprazole, 80 *mg* Pantoprazole was chosen. Ribavirin therapy for 3 months, was also an option, but unable to use it for this case because of the anemia presence.) After 8 days of hospitalization, the patient was discharged with sub-febrile temperature and significant improvement. Second esophagogastroduodenoscopy procedure was performed after 5 weeks with the results of esophageal varices, grade 3; portal hypertension gastropathy and duodenal

Table

Laboratory tests results

Feature	Results	Normal range
General blood test		
Hb	82	112-152*g/dl*
Red blood cells	3.62	3.5-5.6 10^6 *u/L*
Mean corpuscular volume	110	80-100
White blood cells	14	4.0-9.0 10^3 *u/L*
Neutrophils	70.7	45-72%
Eosinophils	0.4	1-5%
Lymphocytes	16.1	19-40%
Monocytes	12.7	3-11%
Platelets	185	180-400 10^9*u/L*
Blood biochemistry test		
Creatinine	97	44-100 *mmol/l*
Albumin	29.36	35-52 *g/l*
C-Reactive protein	52.52	0.00-5.00 *mg/l*
Alkaline phosphatase	91.4	35-120 *u/L*
Alanine transaminase	84.5	0.1-41 *u/L*
Aspartate aminotransferase	60.2	0.1-50 *u/L*
tTotal bilirubin	36.4	0.00-24 *mmol/l*
Gamma-glutamyl transferase	48.7	0.1-55 *u/L*
Electrolytes		
Sodium	137	135-155*mmol/L*
Potassium	3.7	3.4-5.3*mmol/L*
Calcium	2.42	2.1-2.6*mmol/L*
Coagulation tests		
Prothrombin time	27.5	12-16 *sec.*
Prothrombin index	36	80-120%
Fibrinogen	162	200-400*mg*%
International normalized ratio	2.12	0.9-1.5
Serology test		
hepatitis B surface antigen	negative	negative
human immunodeficiency virus antigen-antibody	negative	negative
hepatitis C antibody	positive	negative
hepatitis C virus polymerase chain reaction	positive	negative

ulcer. Fungal esophagitis was absent. Based on the fact that the ulcer was present despite the 80 *mg* of Pantoprazole treatment, and also the complaints of epigastric pain, the dosage of proton-pump inhibitors was doubled and changed into 160*mg* Pantoprazole, at the same time eradication of H. Pylori with Clarithromycin and Amoxicillin for 14 days were added to the therapy.

Two months after the first hospitalization the patient started to develop an increase in body temperature (up to 39°C), pain in the spine, neuropathies and paresthesia were present, despite the Vitamin B therapy, weakness in the lower extremities were increased to the point where the patient could only move with the help of a wheelchair. Magnetic resonance imaging of the spine was performed, which showed spondylodiscitis L2-L3, L4-L5, primary epiduritis, edema of the paravertebral tissue, osteochondrosis, spondylosis, spondylochondrosis. After the magnetic resonance imaging, a vertebrologist consultation has been done, who suggested denying tuberculosis. For which a consultation with a physiatrist has been done. The Mantoux tuberculin skin test, and QuantiFERON-TB Gold were negative, based on these test results current extrapulmonary tuberculosis was denied. Cooperative meeting with the doctors leads to performing the Wright-Hedelson test before an aspiration biopsy for denying vertebral brucellosis. Wright-Hedelson positive results (positive, 1:200 respectively), and positive serology results (high levels of IgG and IgM) are witnessing Brucellosis.

Based on the Clinical Practice Guidelines for the Diagnosis and Treatment of Native Vertebral Osteomyelitis in Adults, 2015 Infectious Diseases Society of America [*Berbari E et al., 2015*], which recommends performing an aspiration biopsy if the serology markers are negative, and don't perform if the serology markers are positive, which is what we did in our case. We thoroughly looked after all the aspects and came to the conclusion to start Ciprofloxacin monotherapy 500 *mg*, twice a day, for 4 weeks, until the HCV elimination will be finished. Such a big group of drugs are being used for the brucellosis treatments, such as Gentamycin, Trimethoprim-Sulfamethoxazole, Rifampicin, Doxycycline, and Streptomycin. Gentamycin and Streptomycin are contraindicated for patients with decompensated cirrhosis, due to its high nephrotoxicity, the patient was allergic to Sulfamethoxazole. Rifampicin, Doxycycline and Ciprofloxacin were left, but Rifampicin could not be used with Sofosbuvir. 1 month was left for the HCV elimination therapy, and during that month brucellosis treatment was performed with Ciprofloxacin. After the HCV elimination course, an HCV PCR test was taken, the result was negative. After this, the brucellosis treatment was performed with Rifampicin, Doxycycline and Ciprofloxacin combination (for 3 months). During these 3 months the patient has undergone regular check-ups. All of the mentioned complaints started to decrease, inflammatory tests were improved, HCV quantitative HCV tests were negative, and no HCV RNA was found. A sustained virological response was achieved.

Discussion

The treatment of concurrent brucellosis and hepatitis C can be challenging due to potential drug-drug interactions and contraindications. In this case, the patient required a careful evaluation of available treatment options to manage both conditions effectively. Let's delve into more detail about the drug interactions between the medications used to treat brucellosis and HCV:

1. Rifampicin:

- Rifampicin is a key component in the treatment of brucellosis, as it is one of the first-line antibiotics for this infection.
- However, rifampicin is known to induce the cytochrome P450 enzyme system, which can lead to reduced levels of some drugs, including those used in HCV therapy.
- The induction of the cytochrome P450 system can potentially decrease the effectiveness of direct-acting antivirals used to treat HCV, such as sofosbuvir and velpatasvir.

2. Doxycycline:

- Doxycycline is another antibiotic used in the treatment of brucellosis. It is often combined with rifampicin for better efficacy.
- While doxycycline itself does not have significant interactions with HCV medications, the combination with rifampicin should be considered for potential interactions, particularly in the context of altered liver function in patients with cirrhosis.

3.Ciprofloxacin:

- Ciprofloxacin is an alternative antibiotic option for brucellosis treatment, and it was chosen in this case due to concerns about the potential interactions between rifampicin and HCV therapy.
- Ciprofloxacin is generally better tolerated by patients with liver cirrhosis, but it may still require dosage adjustments in severe liver disease.
- Ciprofloxacin is not known to have significant interactions with HCV medications, which can make it a suitable choice in such complex cases.

4. HCV Medications (Sofosbuvir and Velpatasvir):

- Sofosbuvir and velpatasvir are direct-acting antivirals commonly used to treat HCV. These medications have specific absorption requirements and may be affected by changes in gastric pH and drug interactions.
- The concern in this case was that rifampicin, due to its enzyme-inducing properties, could potentially reduce the effectiveness of sofosbuvir and velpatasvir, leading to suboptimal HCV treatment outcomes.
- Therefore, choosing a different antibiotic like ciprofloxacin that does not significantly affect the metabolism of HCV medications became essential to ensure successful HCV therapy.

In complex cases involving concurrent infections and liver cirrhosis, close monitoring of liver function, therapeutic drug monitoring, and regular assessment of patient response are crucial. The decision to use ciprofloxacin and adapt the treatment plan was a well-considered approach to balance the management of both brucellosis and HCV, taking into account potential drug interactions. This illustrates the importance of individualized care and close collaboration between healthcare providers in managing patients with multiple medical conditions.

Conclusion

This case report highlights the complexity of managing a patient with decompensated liver cirrhosis, concurrent HCV infection, Brucellosis and multiple complications, including fungal esophagitis. The interdisciplinary approach, involving gastroenterologists, infectious disease specialists, and other healthcare professionals, played a crucial role in making the correct diagnoses and optimizing treatment strategies.

The successful management of this patient's multifaceted medical conditions underscores the importance of considering drug interactions and contraindications when planning treatment regimens for complex cases. Close monitoring, regular check-ups, and adjustments to therapy based on the patient's response were essential components of the successful outcome in this case.

This case serves as a reminder of the importance of a comprehensive and individualized approach to patient care, particularly in the context of complex, comorbid medical conditions. Collaboration among healthcare providers and meticulous attention to detail in treatment planning and execution are critical for the successful management of such patients.

REFERENCES

1. *Asoyan V, Hovhannisyan A, Mkrtchyan A, Davidyants M, Apresyan H., et al (2018).* Evaluating the burden of brucellosis in hospitalized patients in Armenia, 2016. Online J Public Health Inform. 10(1): e118 DOI: 10.5210/ojphi.v10i1.8891
2. *Berbari EF, Kanj SS, Kowalski TJ, Darouiche RO, Widmer AF., et al (2015).* Infectious Diseases Society of America (IDSA) Clinical Practice Guidelines for the Diagnosis and Treatment of Native Vertebral Osteomyelitis in Adults. Clin Infect Dis. 61(6): e26-46 DOI: 10.1093/cid/civ482
3. *Corbel MJ (2006).* Brucellosis in humans and animals. World Health Organization. 102p https://iris.who.int/bitstream/handle/10665/43597/WHO_CDS_EPR_2006.7_eng.pdf?sequence=1
4. *Doganay M, Aygen B (2003).* Human Brucellosis: An overview. Int J Infect Dis. 7: 173-182 https://www.ijidonline.com/article/S1201-9712%2803%2990049-X/pdf
5. *Giambartolomei G, Delpino M (2019).* Immunopathogenesis of Hepatic Brucellosis. Frontiers in Cellular and Infection Microbiology. 9: DOI: 10.3389/fcimb.2019.00423

6. *González-Espinoza G, Gorvel VA, ylvie Mémet S, Gorvel JP (2021).* Brucella: Reservoirs and Niches in Animals and Humans. Pathogens. 10(2): 186 DOI: 10.3390/pathogens10020186
7. *Hasanjani Roushan MR, Ebrahimpour S (2015).* Human brucellosis: An overview. Caspian J Intern Med. 6(1): PMC4478120
8. *Jiang W, Chen J, Li Q, Jiang L, Huang Y., et al (2019).* Epidemiological characteristics, clinical manifestations and laboratory findings in 850 patients with brucellosis in Heilongjiang Province, China. BMC Infectious Diseases. 19(439) DOI: 10.1186/s12879-019-4081-5
9. *Ljubas D, Lalovac M, Vince A, Papic N (2020).* Brucellosis, a forgotten cause of hepatitis in travellers. Journal of Travel Medicine. 28(3): DOI: 10.1093/jtm/taaa218
10. *Qasim SS, Alshuwaier K, Alosaimi MQ, Alghafees MA, Alrasheed A., et al (2020).* Brucellosis in Saudi children: Presentation, Complications, and treatment outcome. Cureus. 12(11): e11289 DOI: 10.7759/cureus.11289
11. *Shi QN, Qin HJ, Lu QS, Li S, Tao ZF (2024).* Incidence and warning signs for complications of human brucellosis: a multi-center observational study from China. Infect Dis Poverty. 13: 18 DOI: 10.1186/s40249-024-01186-4
12. *Spink WW (1964).* Host-Parasite Relationship in Human Brucellosis with Prolonged Illness due to Suppuration of the Liver and Spleen: Report of Six Cases. Trans Am Clin Climatol Assoc. 75: 1-12 PMCID: PMC2279347
13. *Sun GQ, Li MT, Zhang J, Zhang W, Pei X, Jin Z (2020).* Transmission dynamics of brucellosis: Mathematical modelling and applications in China. Computational and Structural Biotechnology Journal. 18: 3843-3860 DOI: 10.1016/j.csbj.2020.11.014
14. *Unuvar GK, Kilic AU, Doganay M (2019).* Current therapeutic strategy in osteoarticular brucellosis. Northern Clinics of Istanbul. 6(4): 415-420 DOI: 10.14744/nci.2019.05658
15. *Yildirim A, Kurt C, Çetinkol Y (2022).* Brucellosis with rare complications and review of diagnostic tests: A case report. Journal of Medical Case Reports. 16(1): DOI: 10.1186/s13256-022-03702-2

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CONTENTS