Clinical Case Reports: Open Access

Yumed Text
OPEN ACCESS JOURNALS

Case Report | Vol 6 Iss 1
ISSN: 2582-5038
https://dx.doi.org/10.46527/2582-5038.245

Hepatopathy and Febrile Syndrome of Unclear Origin in a Young Woman: Case Report

Dos Santos MP[1*], Soares CB[1], Klöckner E[1], de Oliveira VHMS[1], Alves CH[1], Maestri IT[1], Treviso CA[1], Gomes LP[1], de Maman RS[1], de Lima BA[1], Merten FB[1], da Costa BEP[2], Caron-Lienert RS[3] and Baron MV[4]

[1]Medical student at the School of Medicine of the Pontifical Catholic University of Rio Grande do Sul, PUCRS, Brazil
[2]PhD in Cellular and Molecular Biology, Professor and Researcher at the Graduate Program in Medicine and Health Sciences
[3]Adjunct Professor in the Nutrition Undergraduate Course at the School of Health and Life Sciences at PUCRS, Brazil
[4]PhD in the Postgraduate Program in Medicine and Health Sciences of the Pontifical Catholic University of Rio Grande do Sul, PUCRS, Brazil

[*]**Corresponding author:** Michele Paula dos Santos, Medical student at the School of Medicine, Pontifical Catholic University of Rio Grande do Sul, PUCRS, 500 Marcone Street, apartament 402, Porto Alegre, Brazil, Tel: +5551981894844; E-mail: michelepaula123@gmail.com

Received: January 28, 2023; **Accepted:** February 13, 2023; **Published:** February 22, 2023

Abstract

Acute liver failure results from liver damage and may have drug and viral etiology. In addition, acute kidney injury is a common clinical syndrome in the hospital environment and is often associated with pulmonary manifestations, such as pleural effusion. This is a case report of a female patient with a past medical history of thyroid tumor resection 5 years ago, associated with hypothyroidism and depression. In August 2019, she was hospitalized for myalgia and fever, associated with right upper quadrant abdominal pain and choluria. The patient had a series of complications, such as liver and kidney dysfunction, which will be reported below.

Keywords: ***Hepatitis; Acute Kidney Injuries; Fevers***

1. Abbreviations

ICU: Intensive Care Units; AKI: Acute kidney injury; INR: International Normalized Ratio; ESG: Globular sedimentation velocity; EBV: Epstein-Barr virus; CMV: Cytomegalovirus.

2. Introduction

Acute liver failure is not considered a frequent disease; however, it carries with it a high mortality rate during hospitalization. Treated as a systemic disorder due to failure of the largest gland in the human body, liver failure can lead to disastrous consequences for the body's homeostasis. Its etiology varies and can be attributed to different causes, such as drug use, viruses, metabolic etiologies, and idiopathic causes [1]. The implications of liver failure can be pleural effusion, coagulopathy, renal failure, respiratory failure, cerebral edema and hepatic encephalopathy.

Key parameters for suspecting acute injury to hepatocytes are elevated prothrombin time, since liver dysfunction affects the production of coagulation factors; and hepatic encephalopathy, which occurs due to toxins accumulation in the organism due to the failure of the main organ responsible for the detoxification of metabolic residues [2]. Thus, some symptoms can be observed, such as lethargy, fatigue, malaise, nausea, vomiting, anorexia, right upper quadrant pain, abdominal distention due to ascites, pruritus, and jaundice [3]. Overall, survival rates in patients treated for acute liver failure are greater than 60% [4,5]. About 55% will survive without the need for a liver transplant [4]. However, all cases of acute liver failure deserve hospital care, including the need for Intensive Care Units (ICU).

Acute kidney injury (AKI) can occur in approximately 30% to 70% of patients with acute liver failure [6,7]. The pathogenesis of renal injury in patients with hepatic dysfunction is still not understood, but it may be related to systemic and intrarenal hemodynamic alterations similar to those observed in hepatorenal syndrome, with renal vasoconstrictor action and low cardiac output [8]. Faced with such a picture, one can observe a progressive increase in the creatinine level, low sodium excretion rate and oliguria, depending on the severity [8,9].

In this report, the case of a patient with liver disease that progressed to AKI and pleural effusion underlying the liver injury will be presented. The patient was recruited and accepted to participate in research carried out in the ICU with CAEE number: 91988318.6.0000.5336 - Brazil.

3. Case Presentation

Female patient, 41 years old, arrived at the hospital's emergency room complaining of myalgia and fever for a week, in addition to abdominal pain located in the right hypochondrium and choluria. The patient had a past medical history of a thyroid tumor resection 5 years ago, associated with hypothyroidism and depression, having previously used fluoxetine and levothyroxine. On physical examination, she was in regular general condition, lucid and jaundiced, with normal heart rate (80 bpm) and feverish. The patient's abdomen was flaccid, bowel sounds were present, but there was pain on palpation in the right upper quadrant and a negative Murphy's sign. The extremities were well perfused and without edema.

Laboratory tests showed creatine phosphokinase and hemoglobin below the lower reference limit, oxaloacetic and pyruvic transaminase enzymes (TGO and TGP, respectively), INR (International Normalized Ratio) and the globular sedimentation velocity (ESG) above, leading to the suspicion of liver dysfunction. In addition, leukocytosis with a left shift, elevated GT gamma and alkaline phosphatase was observed. A cholangioresonance was performed, which concluded that there was no choledochal dilatation or signs of cholecystitis. Markers for hepatitis A, B and C were non-reactive, as well as IgM for Epstein-

Barr virus (EBV). Thus, a picture of viral myalgia associated with elevated transaminases, bilirubins and increased INR was considered, suspecting acute hepatitis, empirical antibiotic treatment with Ampicillin - Sulbactam was started and laboratory control tests were requested (total bilirubin, transaminases, and INR).

Based on the infectology assessment, a chest CT scan without contrast was requested to rule out the possibility of bronchopneumonia at the base of the right lung, and two blood cultures were collected, with a new assessment of EBV and leptospirosis. In addition, the antibiotic (Cefitraxone) was maintained for suspected leptospirosis, and an examination for cytomegalovirus (CMV), toxoplasmosis and herpes was requested. HAV, HBV and HCV, EBV IgM, toxoplasmosis IgM and IgG markers were non-reactive and CMV IgM and IgG reagents. The patient's condition worsens, with intense myalgia, fever, polydipsia and reduced urinary volume. Control tests, transaminases, and INR, showed improvement with stable total bilirubin, but with worsening of renal function, leading to the suspicion of AKI. Thus, tests were requested and showed hyponatremia (128 mEq /L) and elevated creatinine (4.07 mg/ dL), with normal serum potassium.

The patient continued with clinical worsening, with oliguria, dyspnea, and hypotension. Laboratory tests showed worsening of renal function with increased creatinine (5.77 mg/ dL) and hyponatremia (120 mEq /L). An urgent chest X-ray showed moderate bilateral pleural effusion (greater on the left) and interlobular septal thickening, which, in association with the other findings, suggested congestion. Normal biliary and urinary tract. In addition to Cefitraxone, PipeTazo was associated and, due to the potential severity of the condition in a young patient in an acute context, ganciclovir was started, and the patient was transferred to the ICU bed for monitoring, without the need for intubation. The patient remained hemodynamically unstable, requiring vasoactive drugs (noradrenaline 7 mL/h). Physical examination showed reduced vesicular murmurs in both lung bases and crackling, but she was eupneic and without signs of ventilatory effort, painful abdomen on palpation and without signs of peritonism and visual acuity alteration. Thus, Cefitraxone was suspended and PipeTazo was adjusted according to renal function, and hemodialysis and Doxycycline (100 mg VO 12/12 h) were initiated for empirical coverage of Riktesia.

Due to the febrile syndrome of unclear etiology, markers for investigation of autoimmune liver disease, iron, ceruloplasmin, ANA, copper were requested, in addition to new serologies for Leptospirosis, Hantavirus, Riktisia and Brucellosis. The patient continued with myalgia, receiving Dipyrone and Tramadol, with slight improvement. Ganciclovir was suspended due to low probability of CMV.

The patient had two episodes of abrupt onset, with no prodrome, of spasms in the mouth with rhyme deviation to the right and clonias in the right upper limb lasting 15 seconds, keeping the gaze fixed, but without loss of consciousness. She did not present post-ictal drowsiness, paresis, paresthesias, speech disorders and headache. An electrolyte disturbance was suspected, due to the dialysis, but a magnetic resonance imaging of the skull was requested to evaluate the structural cause, which showed no alterations, Clobazam (20 mg at night) was prescribed and follow-up with neurology was maintained.

Significant clinical improvement was observed, anicteric patient, stable vital signs, afebrile, well perfused and without edema and improvement in renal function. PipeTazo was suspended due to treatment time, Doxycycline and hemodialysis catheter was removed. Serologies for viral and autoimmune hepatitis were non-reagent, as well as EBV IgM, toxoplasmosis IgG and IgM, VDRL, FTA-ABS and anti-HIV; EBV IgG was reactive. False positive CMV IgG and IgM reagents are suspected. Patient

with febrile syndrome of unknown etiology, with cholestasis due to direct bilirubin, with no identified obstructive factor, with AKI. Infectious etiology is not characteristic of the patient's clinical evolution, characterizing an unusual case of liver disease. The patient was discharged after 16 days of hospitalization, with a return plan for evaluation within 15 days, but did not return.

4. Discussion

Acute liver failure is characterized by the development of encephalopathy and liver impairment in people without preexisting liver disease, resulting from liver damage, which may be caused by drugs and viruses, including HAV, HBV, HCV, Epsteins-Barr and CMV [2]. The dosage of bilirubin (high) and alkaline phosphatase (very low), in addition to serology for viral and autoimmune hepatitis are essential when thinking about acute liver failure [10]. In the case presented, serologies were requested, CMV IgM and IgG and EBV IgG reagents; however, contrary to expectations, the alkaline phosphatase dosage was elevated. Still, the elevation of transaminases, bilirubin and INR enlargement led to the suspicion of acute hepatitis. One review reported the prevalence of acute liver failure induced by CMV and EBV of 13% and 6%, respectively, being lower than that induced by hepatitis viruses, especially HEV [11].

Regarding liver dysfunction, it is characterized by loss of liver function, which can occur suddenly (acute) or gradually (chronic) [2]. The most common causes include routine and inappropriate use of medications, hepatitis, alcohol abuse and advanced fatty liver. The patient is usually jaundiced, with pain and edema in the abdomen. Patients with hepatic dysfunction may have metabolic abnormalities such as hypokalemia, hyponatremia, hypophosphatemia and hypoglycemia. Furthermore, these patients may develop complications such as hepatic encephalopathy, cerebral edema and acute renal dysfunction. The treatment consists of managing the symptoms and mainly the cause of the dysfunction [5-8].

AKI is characterized by a reduction in the glomerular filtration rate accompanied by oliguria adjacent to the increase in laboratory values of urea and creatinine, and is often accompanied by pulmonary complications, mainly in patients with hepatic dysfunction and hypoalbuminemia [9]. In the case presented, the patient had liver dysfunction and clinical worsening, with oliguria and increased creatinine, increasing the suspicion of AKI. In addition, the picture of congestion, with bilateral pleural effusion, reinforced this hypothesis. Renal impairment leads to a series of electrolyte changes, the most common of which are hyponatremia, hyperkalemia, hyperphosphatemia, hypocalcemia, and hyperuricemia. Hyperkalemia can cause cardiac arrhythmias, aggravated by metabolic acidosis, while hyponatremia is responsible for sensory alterations [12].

Hyponatremia is defined as a serum sodium concentration less than 135 mEq/L. It is usually a consequence of decreased renal water elimination, which may or may not be concomitant with excessive oral or parenteral water intake. The presence of this condition is associated with a series of unfavorable outcomes, such as increased length of hospital stay, need for intensive care, and is associated with higher mortality [13]. In the presence of hyponatremia, the extracellular fluid becomes hypotonic in relation to the intracellular fluid, thus, water enters the interior of the cells. Consequently, the main clinical manifestations of the decrease in serum sodium are related to neurological changes, since the bones of the skull prevent the expansion of brain parenchyma, causing cellular edema to cause hypertension. Because it has major hemodynamic repercussions, whenever possible, it is important to diagnose and treat the cause of hyponatremia to resolve the situation [13]. Thus, we can relate the finding of hyponatremia with some of its symptoms observed in this case. The patient had a serum sodium dosage of 120 mEq/L, being classified as having moderate to severe hyponatremia. In addition, the patient presented symptoms such as

episodes of abrupt onset, without prodrome, of spasms in the mouth with rhyme deviation to the right and clonias in the right upper limb without loss of consciousness, which are consistent with the picture.

The increase in body temperature above 38.3°C that persists for more than three weeks with difficulty in identifying the cause within one week of hospitalization is defined as fever of unknown origin, and can be classified as infection, inflammatory disease, oncological process, and other conditions [14]. In order to identify the cause of the fever, invasive and non-invasive procedures can be used, with structural imaging techniques such as ultrasound, magnetic resonance imaging and computed tomography frequently used to identify inflammatory and infectious foci [15], which were the main suspect in this case.

Thus, imaging tests, such as MRI and CT, and investigation markers for autoimmune liver disease, iron, ceruloplasmin, ANA, copper, were requested, seeking to clarify the etiology of the patient's fever. In addition, in this case, in which the blood cultures were negative, an extended culture for Brucella spp. was requested, considering that slow-growing bacteria are common etiological agents [16], as well as serology was requested for investigation of Leptospirosis, Hantavirus and Riktisia, considering an infectious cause for the patient's fever, despite the non-characteristic clinical evolution.

5. Conclusion

In the presented report, it is possible to observe the difficulty of clarifying the diagnosis and the clinical complications of a patient with a febrile syndrome. The high mortality rate associated with liver failure, in addition to the implications it develops, such as AKI and pleural effusion, must be carefully evaluated, especially in a young patient without risk factors, as in this case.

REFERENCES

1. Grek A, Arasi L. Acute Liver Failure. AACN Adv Crit Care. 2016;27(4):420-9.
2. European Association for the Study of the Liver. EASL Clinical Practical Guidelines on the management of acute (fulminant) liver failure. J Hepatol. 2017;66(5):1047-81.
3. Lee WM. Acute liver failure. N Engl J Med. 1993;329(25):1862.
4. Reuben A, Tillman H, Fontana RJ, et al. Outcomes in adults with acute liver failure between 1998 and 2013: an observational cohort study. Ann Intern Med. 2016;164(11):724-32.
5. Ostapowicz G, Fontana RJ, Schiødt FV, et al. Results of a prospective study of acute liver failure at 17 tertiary centers in the United States. Ann Intern. 2002;137(12):947-54.
6. Munoz SJ. Difficult management problems in fulminant liver failure. Semi Liver Dis. 1993;13(4):395-413.
7. Tujios SR, Hynan LS, Vazquez MA, et al. Risk factors and outcomes of acute kidney injury in patients with acute liver failure. Clin Gastroenterol Hepatol. 2015;13(2):352-9.
8. Wadei HM, Mai ML, Ahsan N, et al. Hepatorenal syndrome: pathophysiology and treatment. Clin J Am Soc Nephrol 2006;1(5):1066-79.
9. Ginès P, Guevara M, Arroyo V, et al. Hepatorenal syndrome. Lancet. 2003;362(9398):1819-27.
10. Lee WM, Stravitz RT, Larson AM. Introduction to the revised American Association for the Study of Liver Diseases Position Paper on acute liver failure 2011. Hepatology. 2012;55(3):965-7.
11. Patterson J, Hussey HS, Silal S, et al. Systematic review of the global epidemiology of viral-induced acute liver failure. BMJ Open. 2020;10(7):e037473 .

12. Yu L, Santos BFC, Burdmann EA, et al. Acute Renal Failure. J Bras Nephrol. 2007.
13. Rocha PN. Hyponatremia: basic concepts and practical approach. J Bras Nefrol. 2011;33(2):248-60.
14. Fernandez C, Beeching NJ. Pyrexia of unknown origin. Clin Med (Lond). 2018;18(2):170-4.
15. García JR. Febrile syndrome of unknown origin: Indications for 18 F-FDG PET/CT in inflammatory and infectious processes. Radiology. 2017;59(3):253-63.
16. Gould FK, Denning DW, Elliott TS, et al. Guidelines for the diagnosis and antibiotic treatment of endocarditis in adults: a report of the Working Party of the British Society for Antimicrobial Chemotherapy. J Antimicrob Chemother. 2012;67(2):269-89.