CASE REPORT OPEN ACCESS

Leptospirosis and Severe Malaria presenting in a Male with Fulminant Hepatic Failure from Wilson's Disease: A Case Report

Maham Kayani, Elma Khalil, Abdul Samad Khan

Resident Physician-Medicine Dept. Lady Reading Hospital

An unusual co-finding of two potentially life-threatening infections that is leptospirosis and malaria complicating to fulminant hepatic failure with an underlying Wilson's disease. As for from what we have learned and encountered in our clinical years, a co-existence of four fatal conditions has not been seen. An 18-year-old Asian male presented with fever, rigors, vomiting, jaundice, and behavioral changes. Following clinical and laboratory evaluation he was diagnosed with leptospirosis, complicated malaria, and fulminant hepatic failure. He received treatment for both infections and showed significant improvement. Furthermore, he was also diagnosed with Wilson's disease. Therefore, fulminant hepatic failure in a young adult should alarm the physician to suspect a primary liver pathology as Wilson's disease for the early diagnosis and prompt management.

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INTRODUCTION

Malaria is an acute febrile illness caused by Plasmodium parasites, which spreads by the bite of infected female Anopheles mosquitoes. There are five species of plasmodium causing malaria in humans with two of them that is plasmodium falciparum and plasmodium vivax carrying the

highest threat. P. falciparum is the most dangerous form of malaria and highly prevalent in Africa whereas, P. vivax is the dominant form common outside of sub-Saharan Africa [1]. Leptospirosis is caused by an organism, Leptospira interrogans which is a zoonosis causing protean and a spirochete. It is characterized by sudden onset of fever, rigors, myalgias, headache and occasionally nausea, vomiting, and diarrhea. Along the course of illness, it is mild-moderate in presentation but in some rare cases lead to liver failure [2]. Wilson's disease is a rare inherited disorder of copper metabolism, increased deposition of copper in various organs clinically manifest as neurological, hematological, renal and hepatic features, primarily affecting females between five and 40 years of age [3]. Fulminant hepatic failure (FHF) or acute liver failure (ALF) is rapid onset of liver damage with severe impairment of function and development of hepatic encephalopathy within 8 weeks of illness in a patient with no previous or underlying liver pathology [4].

CASE REPORT

An 18 years old male was admitted to the hospital following a twenty-day history of high-grade fever with associated rigors, chills, vomiting, fatigue, yellowish discoloration of the skin, and sclera of the eye. In addition, his family reported that he has shown a change in behavior to being more aggressive and irritable in the past three years. A local General Practitioner at the time, after evaluation, started him on anti-seizure and anti-psychotic medication to which no medical records were found. He is a resident of Mardan, a city in Khyber Pakhtunkhwa, Province of Pakistan. He reportedly never used alcohol or any recreational drugs but gave a history of swimming in a lake, near his house around 2–3-time in the last month. Furthermore, he has three fraternal cousins who had the same symptoms including anger outbursts, delayed milestones, and jaundice.

Upon examination, he had a temperature of 103 Fahrenheit (F) with rigors and moderate epigastric tenderness on palpation without any appreciable visceromegaly. Upon further assessment, no other signs of liver disease could be found other than jaundice. Slurring of speech, aggressive behavior, and confusion were evident on neurologic examination. On arrival, baseline investigations were sent, including a complete blood picture, coagulation profile, renal, and liver function tests, split bilirubin levels, and serum enzymes as shown in **Table 1**.

Table 1.

Investigations		**Result/units**	**Normal range**
White blood cell count		2.31x10.e3/ul ▼	4-11x10.e3/ul
Hemoglobin level		8.6 g/dL ▼	12-16g/dl
Platelet count		33x 10.e3/ul ▼	150-450 x 10.e3/ul
International normalized ratio (INR)		1.5 ▲	1
Serum Lactate dehydrogenase		1973 U/L ▲	91-180 U/L
Serum creatinine kinase		545U/L ▲	0-189 U/L
Alanine aminotransferase		138 IU/L ▲	5 to 40
Aspartate aminotransferase		328 IU/L ▲	5 to 37
Serum Bilirubin	Total	20.85mg/dL ▲	< 1mg/dl
	Direct	17.78mg/dL ▲	
	Indirect	3.7 mg/dL ▲	
Serum urea		195mg/dL ▲	5 – 20 mg/dL
Serum creatinine		3.9 mg/dL ▲	0.55-1.02mg/dl

In addition to CBC findings a peripheral smear was advised, that showed microcytic hypochromic red blood cells alongside target cells with direct and indirect COOMB test conducted to rule out any hemolytic anemias, but both came negative. The Radiological test included, an ultrasound abdomen showing a spleen of 12cm and liver span of 17.5cm with normal texture, echogenicity, and no focal lesion. Moreover, tests done for viral causes I.e., hepatitis (A to E) and Dengue virus performed via Polymerase chain reaction (PCR) were performed and turned out negative. Malaria by thick and thin films was done, and came back positive with Plasmodium falciparum detected. Moreover, a Serologic test for Leptospira interrogans was also sent, which turned out positive (IgM 1.38). Urine cultures and blood cultures were obtained at admission, the former showed no growth whereas the blood cultures were inconclusive.

Patient was given oral Doxycycline (100 milligram every 12 hours) injectable penicillin (1.5 million units every 6 hours intravenously), and ceftriaxone 1 gram daily intravenously along with an add-on injectable antimalarials for 7 days [6]. Since our patient had low hemoglobin at presentation with deranged coagulation, he received a transfusion of five pints of whole blood, eight pints of fresh frozen plasma, and a single injection of vitamin K. Our patient appeared to have fulminant hepatic failure (FHF) secondary to two infectious diseases. After 2 weeks of hospital stay, he showed significant biochemical and physical improvement on day-to-day basics that lead us to further evaluate his case and seek out less likely causes after the common were excluded.

In this young patient, the combination of neurological, psychological, non-autoimmune hemolytic anemia, and elevated liver enzymes with family members of similar symptoms, provides high suspicion of Wilson's disease. According to the American Association for the Study of Liver Diseases (AASLD) [7] patients in whom Wilson's disease is suspected should undergo screening with serum ceruloplasmin, 24-hour basal urinary copper, and slit-lamp examination for Kayser-Fleischer rings. In this case, serum ceruloplasmin levels were 12mg/dL, and 24-hour urinary copper excretion was 740.68 mcg/day (normal values ≤ 40 mcg) [7] with a positive finding of Kayser-Fleischer rings on Slit-lamp examination provided us with the basis of finding the underlying liver problem. Therefore, he was started on a dual therapy with zinc that blocks the

intestinal absorption of copper, and penicillamine, which served as a chelator for copper. Our patient showed gradual signs of improvement over the next few days.

DISCUSSION

This case focused on suspecting underlying liver pathologies as rare as Wilson's disease in a young male adult who presented with fulminant hepatic failure which was initially thought to be a consequence of two severe infections. During his stay at the hospital, there was a constant decline in his clinical and biochemical findings till the end of first week. However, once both infective foci were addressed there was a significant improvement in the patient's appearance and lab findings by the second week. Despite the efforts, the patient remained confused and had recurrent anger outbursts that led us to believe that there may be another factor that could had worsen the patient to FHF after the viral, toxin, or immunologic disease were excluded. The presence of neuropsychiatric features, family history, and age under 35 years that was found in our patient intrigued us to carry out the diagnostic test for Wilson's disease, that is Slit-lamp examination for Kayser-Fleischer (KF) rings, serum ceruloplasmin levels below 20 mg/dL and 24-hour urinary copper above 40 mcg [7]. Since our patient satisfied the criteria of Wilson's disease I.e., positive KF rings, high urinary copper, and low ceruloplasmin, we believe that underlying Wilson's disease could be the underlying cause that intensified the outcome of malaria and leptospirosis to fulminant hepatic failure. So, treating the root cause, that is Wilson disease in this case leads to overall improvement.

CONCLUSION

To conclude, whenever an individual presents with features of acute liver failure with no previously diagnosed liver pathology secondary to infections such as leptospirosis or severe malaria should urge one to seek primary liver pathologies after excluding viral, toxin and immune causes. Most importantly, the purpose of this case is to encourage clinicians to suspect Wilson diseases when managing fulminant hepatic failure.

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