Chronic Liver Disease Association with Extrapulmonary Tuberculosis: Clinical and Histopathological Presentation- A Case Report

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ABSTRACT

Chronic liver disease (CLD) is a result of progressive deterioration of liver functionality over a period of more than six months. There has been an increase in the burden of the disease in the Sub-Saharan region by 57% in the past 20 years. Zambia is estimated to have a chronic liver disease death rate of approximately 26.02 per 100,000 population. One of the established etiological factors in CLD are infections and there is an association between chronic liver disease and tuberculosis infection. Extrapulmonary tuberculosis (EPTB) has of recent times been increasing due to the increased prevalence of AIDS and immunosuppressive therapies.

We report a case of a 34year old HIV-negative woman who presented with a history of progressive abdominal distension, abdominal fullness and generalized abdominal pain, anorexia, weight loss, night sweats, and a history of drinking alcohol with no significant past medical history. Abdominal ultrasound showed hyper-echogenicity of the liver parenchyma. Inguinal lymph node biopsy showed caseating granulomatous inflammation and Langerhans giant cells but no malignant cells. A histological diagnosis of tuberculosis (TB) was made and after initiation of ATT the patient responded well.

Making the correct diagnosis of chronic liver disease in the TB abdomen may be challenging. Physicians therefore must be aware of the disease and its behavior especially in high-risk patients and of the current diagnostic limitation. A combination of the high level of suspicion, microbiologic, radiologic and histopathological examinations help achieve diagnostic accuracy and prevent a delay in treatment which is associated with increased mortality and morbidity in patients with this disease.

Keywords: Extrapulmonary Tuberculosis, TB-abdomen, Chronic Liver Disease, Ascites, Anti-tuberculosis Treatment.

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Introduction

Chronic liver disease (CLD) is a result of progressive deterioration of liver functionality over a period of more than six months. These functions include synthesis of some proteins, detoxification of harmful products of metabolism, synthesis of clotting factors, and excretion of bile.[1] The etiological

spectrum for chronic liver disease is broad and some of the most important include alcohol abuse over a prolonged period of time, toxins, infections, metabolic conditions, autoimmune diseases, and genetics. Signs and symptoms common in liver disease include vomiting, nausea, abdominal pain usually in the right upper quadrant, jaundice, abdominal distention, fatigue, and weight loss.

There is relatively little information patterning to the epidemiological picture of chronic liver disease in sub-Saharan Africa, there has been an increase in the burden of the disease in this region by 57% in the past 20 years. However, no correlation was made with respect to sex, age, racial differences, and region. A study done in 2018 showed that ranked 42nd in the world, and 22nd in Africa, Zambia is estimated to have a chronic liver disease death rate of approximately 26.02 per 100,000 population.[2]

Tuberculosis a disease caused by Mycobacterium tuberculosis is a systemic infection that can affect multiple organs and tissues, hence TB requires a high index of suspicion. The extrapulmonary form of TB has in recent times been increasing due to the increased prevalence of AIDS and immunosuppressive therapies targeting cancer treatment and other various medical conditions.[3] One of the established etiological factors in CLD are infections, and a study was done in Taiwan in 2014 established that there was an association between chronic liver disease and tuberculosis infection. The study, the multivariate stratified analysis demonstrated that chronic liver disease was associated with extra-pulmonary tuberculosis with adjusted ratios of 2.18 (95% CI: 1.86, 4.09; P<0.001) and 1.18 (95% CI: 1.02, 1.30; p< 0.001), respectively.[4]

Background of the patient: The patient was a 34-year-old female from a suburban locality who is a Christian of the Jehovah witness denomination, divorced, and not currently employed. She was encountered at the medical filter of the University Teaching Hospital.

Clinical assessments

History: The patient presented with complaints of progressive abdominal distension, abdominal fullness, and generalized abdominal pain all for 2 weeks. The patient also reported a history of appetite loss, weight loss, night sweats, and amenorrhea for 4 months, with a history of multiple skin sores. However, she had no fever, no jaundice, no constipation, no lower limb edema, and a history of contraceptive use. She reported no history of diabetes mellitus, epilepsy, asthma, tuberculosis, and hypertension.

Physical examination: On examination, the patient was lying supine in bed oriented to time, place, and person, appearing wasted with thin sparse hair, with moderate pallor, generalized solitary mobile non-tender lymphadenopathy, multiple skin infected sores, abdominal distension, and with a positive fluid thrill suggesting ascites. There was no jaundice, finger clubbing, linea nigra, and no lower limb edema. Her vitals were normal, with a BP of 134/79mmHg, temperature 36.7oC, respiratory rate 16bpm, and heart rate 83bpm.

Diagnostic focus: After a thorough history and physical examination, investigations conducted revealed; low Hb, leukocytosis with neutrophilia, reduced MCV, elevated AST and ALP, normal ALT, elevated direct

bilirubin, and low albumin, while biopsy results of inguinal lymph nodes revealed caseating granulomatous inflammation and Langerhans giant cells but no malignant cells. The ZN-stain results were not ready at the time. The HIV rapid test SD Bioline was non-reactive.

Abdominal u/s showed hyper-echogenicity of the liver parenchyma. The chest x-ray suggested no obvious lung pathology.

Therapeutic focus and outcome: On the day of presentation, paracentesis was performed on the patient with 2 liters tapped in 24 hours, and the patient was started on septrin 960mg per oral once daily for prophylaxis, Paracetamol 1g per oral three times daily for 3 days, and spironolactone 25mg once daily for two weeks.

Based on the results of the inguinal lymph node histopathology and pus m/c/s for the ulcers, suggesting extrapulmonary TB and staphylococcus aureus skin infection respectively, the patient was immediately put on anti-tuberculosis treatment (ATT) comprising the intensive phase of rifampicin, isoniazid (INH), ethambutol and pyrazinamide for two months and the continuation phase of rifampicin and isoniazid for ten months. Pyridoxine (vitamin B6) 50mg once daily was given along with the ATT as prophylaxis against the INH induced peripheral neuropathy, 2 units of fresh frozen plasma was given and the patient was put on folic acid 5mg once daily per oral and ferrous sulphate 200mg three times daily per oral for two weeks. chloramphenicol 500mg QID for the sores after sensitivity tests.

The patient showed improvement since the initiation of the above treatment as the ulcers on the body had started to heal and the abdominal tapping relieved her symptoms.

The unit consultant advised the patient to visit the TB clinic and cautious weekly paracentesis to be done at the hospital. He further advised monthly follow-up and monitoring for possible drug side effects and resistance and dose adjustment of the ATT according to the weight of the patient.

Discussion: The liver is one of the rare sites for extrapulmonary tuberculosis and often results from the reactivation of latent foci that stems from hematogenous dissemination of primary infection in the lungs. However, this is not always the case as can be seen in our patient who had no overt prior history of pulmonary tuberculosis.[5] The clinical manifestations are usually non-specific with hepatomegaly, fever, abdominal pain, weight loss, ascites, and jaundice being among the most common symptoms. Abdominal TB is said to be more common among HIV-infected individuals compared to non-HIV-infected individuals. In a study conducted by Sinkala E et al in Zambia, medical inpatients presenting with fever, weight loss, and clinical features suggestive of abdominal pathology were recruited and subjected to further evaluations. Out of 140 HIV seropositive patients with the features of interest, 31 patients underwent full evaluation and 22 (71%) had definite or probable abdominal TB. The study revealed that the commonest presenting abdominal features were ascites and persistent tenderness while the commonest ultrasound findings were ascites, para-aortic lymphadenopathy (over 1 cm in size), and hepatomegaly. It was further

revealed that abdominal TB was associated with CD4 cell counts over a wide range though 76% had CD4 counts <100 cells/μL. The study concludes that patients with fever, weight loss, abdominal tenderness, abdominal lymphadenopathy, ascites, and/or hepatomegaly in Zambia have a high probability of abdominal TB, irrespective of CD4 cell count.[6]

Our patient presented with progressive ascites, abdominal fullness, and generalized abdominal pain, associated with loss of appetite, weight loss, night sweats, and amenorrhea for 4 months, with a history of multiple skin sores. On examination, she appeared wasted with physical findings of thin sparse hair, pallor +2, generalized solitary mobile non-tender lymphadenopathy, multiple skin infected sores, right upper quadrant tenderness, and ascites with no guarding. But she tested negative for HIV.

Although much has been done to educate the community and the local clinics on the signs and symptoms of pulmonary tuberculosis, the same cannot be said about extrapulmonary tuberculosis. Extrapulmonary tuberculosis continues to be a source of concern as can be demonstrated by the revelation that of the 6.3 million new cases of tuberculosis recorded by WHO in 2017, 16 % were extrapulmonary tuberculosis.[7]

This case was therefore presented to highlight the importance of early diagnosis of extrapulmonary tuberculosis and sensitization of the community and clinicians on the early signs of extrapulmonary tuberculosis.

In TB-endemic areas, a high index of clinical suspicion is required to make a diagnosis of abdominal TB in both HIV-infected and non-HIV-infected patients. In this regard, abdominal TB should be considered from the outset in all patients who present with any combination of chronic right upper quadrant pain, fever, hepatomegaly, weight loss, and ascites, even without any history of pulmonary TB.

Laboratory findings such as elevated ALP and GGT as well as inverted albumin/ globulin ratio should further solidify a clinical diagnosis of abdominal TB. In addition to clinical presentation, laboratory tests, and radiographic studies biopsy can be conducted on the lymph nodes as well as liver tissue to ascertain liver involvement in TB rather than due to other causes such as alcohol. This underscores the need for a gastroenterologist's input toward definitive work-ups.

Although a contrast-enhanced abdominal CT scan is the optimal radiographic test for diagnosis of abdominal TB, ultrasound and a plain radiograph are the most widely available and first to be done especially in resource-limited settings but lack any diagnostic specificity. For this reason, the value of ultrasound and plain radiographs in investigating patients with suspected abdominal TB should be to prompt further investigation as well as to identify the appropriate site for percutaneous liver biopsy for microbiology (AFB & culture) and histopathology.[8]

Conclusion: Ascites constitute the most common form of presentation of abdominal TB and since there are more common causes

of ascites, making the correct diagnosis of abdominal TB may be challenging. Physicians therefore must be aware of the disease and its behavior especially in high-risk patients and of the current diagnostic limitation. A combination of a high level of suspicion in endemic TB areas, microbiologic, radiologic and histopathological examinations help achieve diagnostic accuracy and prevent a delay in treatment which is associated with increased mortality and morbidity in patients with this disease.

Consent: Formal consent was obtained from the patient and the parent.

Author Contributions: All authors contributed to devising the theme and content and the ultimate write-up of the manuscript.

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