A RARE EXTRAPULMONARY TUBERCULOSIS, HEPATIC TUBERCULOSIS

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ABSTRACT

Introduction:

Tuberculosis (TB) is an infectious disease caused by Mycobacterium tuberculosis, a disease that attacks the lung parenchyma and can infect other organs. Tuberculosis is a significant health problem and is highly prevalent in developing countries. Abdominal Tuberculosis (TB) is a rare variant of TB, and hepatic tuberculosis is the most infrequent manifestation of tuberculosis infections.

Case Illustration:

A 44-year-old female patient complained of abdominal pain since one year ago. Abdominal pain felt in the lower right abdomen, sometimes spreading to the back side. Abdominal pain felt intermittent, not affected by eating or defecation. There were no complaints of fever, cough, shortness of breath, chest pain, and palpitations. The patient denied weight loss, loss of appetite, night sweats, or fluctuating fever. There was no prior history of tuberculosis. These patients have normal liver function and elevated alkaline phosphatase. Multiple calcified hypodense lesions appear in segments VII-VIII of the liver in a Computed Tomography (CT) Scan. A liver biopsy showed clusters of epithelioid cells accompanied by multinucleated giant cells. There was also necrosis resembling caseous necrosis with negative Acid-Fast Bacteria staining. The histological conclusion was following granulomatous inflammation, the possibility of tuberculosis infection could not be ruled out, and no malignant tumor cells were found in the preparations. The stage of fibrosis is around F2-F3. The patient was then diagnosed with hepatic tuberculosis and received anti-tuberculosis therapy. Obtained resolution of abdominal pain improvement and assessment of liver function remained normal after this 2-week treatment.

Conclusion:

Hepatic TB is a manifestation of extrapulmonary TB, which is rarely found. Anamnesis, physical examination, and supporting examinations are carried out to diagnose hepatic TB. Investigations such as imaging and liver biopsy can help diagnose this type of TB. The treatment given for hepatic TB is given according to the same regimen as other extrapulmonary TB.

Keywords: Hepatic Tuberculosis, Extrapulmonary Tuberculosis, Diagnosis, Management

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How to cite this article :

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Background

Tuberculosis (TB) is an infectious disease caused by Mycobacterium tuberculosis, a disease that attacks the lung parenchyma and can also infect other organs.[1] Tuberculosis is a world health problem with a high prevalence reaching 95% in developing countries.[2] Other data shows the prevalence of TB has increased by 80% in 22 countries, 58% of new cases have jumped in the Southeast Asia and West Pacific regions where the highest rates occur in India as much as 23% and in 2014, Africa dominates 28% of total world cases.[3]

Abdominal Tuberculosis (TB) is a rare variant of TB, accounting for 3.5% of extrapulmonary TB, and hepatic tuberculosis is the most infrequent manifestation of tuberculosis infections. Hepatic tuberculosis commonly appears in Filipinos; the most likely cause is racial susceptibility to tuberculosis bacteria.[2]

Hepatic TB spreads most often via the hepatic artery from miliary TB and may also via the portal vein or lymph nodes in the gastrointestinal tract. The diagnosis of hepatic TB alone is quite complex, considering that the symptoms and radiological appearance are varied, so it is easy to be misdiagnosed and delay definitive therapy. Supporting examinations such as histopathology are needed, the gold standard for diagnosing hepatic TB.[3,4] In this case report, we will discuss hepatic tuberculosis further and explain how to diagnose it from the history, physical examination, and supporting examinations related to the findings obtained.

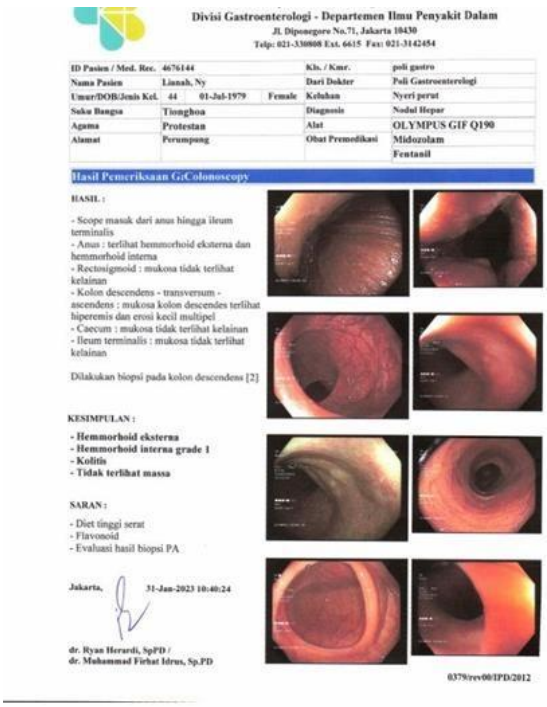
Case Illustration

A 44-year-old female patient complained of abdominal pain one year ago. Abdominal pain felt in the lower right abdomen, sometimes spreading to the back side. Abdominal pain felt intermittent, not affected by eating or defecation. There was no nausea or vomiting. There was no jaundice. Vomiting blood and bloody stools are denied. The patient admits that it is sometimes difficult to defecate, which tends to be hard, and the frequency of defecation is only2-3 times a week. The lump in the anus is small and painless. There were no complaints of fever, cough, or shortness of breath. There were no chest pain and palpitations. The patient denied weight loss, loss of appetite, night sweats, or fluctuating fever.

Because of this frequent abdominal pain, the patient went to the Hospital. Abdominal ultrasound showed a suspicion of a tumor in the liver, so the patient underwent a *Computer Tomography* (CT) scan. The CT results revealed a liver tumor in the right lobe, and then the doctor referred the patient to Cipto Mangunkusumo Hospital in November 2022. The patient was then subjected to further examination with a multiphase abdominal CT scan (January 2023), colonoscopy (January 2023), and liver biopsy (April 2023) to confirm the diagnosis.

The physical examination showed vital signs and a stable hemodynamic condition with functional status—*the Eastern Cooperative Oncology Group* (ECOG) 1. The right hepatic lobe was palpable two fingers below the arcus costae. The surface was not lumpy, and the edges were blunt. It was painful to press there. The spleen is not palpably enlarged.

From laboratory examinations, the patient had mild hypokalemia (3.3), normal transaminase (13/9), increased Alpha-Fetoprotein (AFP) value (1.71), normal albumin (4.3), and hepatitis markers HbsAg and AntiHCV are non-reactive. Anti-HIV is non-reactive. A colonoscopy examination in January 2023 showed external hemorrhoids, grade 1 internal hemorrhoids, and colitis. From the biopsy results, histology showed active chronic colitis with an ischemic impression. (Figure 1)



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ID Pasien / Med. Rec.	4676144			Kls. / Kmr.	poli gastro
Nama Pasien	Lianah, Ny			Dari Dokter	Poli Gastroenterologi
Umur/DOB/Jenis Kel.	44	01-Jul-1979	Female	Keluhan	Nyeri perut
Suku Bangsa	Tionghoa			Diagnosis	Nodul Hepar
Agama	Protestan			Alat	OLYMPUS GIF Q190
Alamat	Perumpung			Obat Premedikasi	Midozolam
					Fentanil

Hasil Pemeriksaan G:Colonoscopy

HASIL :

- Scope masuk dari anus hingga ileum terminalis
- Anus : terlihat hemmorhoid eksterna dan hemmorhoid interna
- Rectosigmoid : mukosa tidak terlihat kelainan
- Kolon descendens - transversum - ascendens : mukosa kolon descendes terlihat hiperemis dan erosi kecil multipel
- Caecum : mukosa tidak terlihat kelainan
- Ileum terminalis : mukosa tidak terlihat kelainan

Dilakukan biopsi pada kolon descendens [2]

KESIMPULAN :

- Hemmorhoid eksterna
- Hemmorhoid interna grade 1
- Kolitis
- Tidak terlihat massa

SARAN :

- Diet tinggi serat
- Flavonoid
- Evaluasi hasil biopsi PA

Jakarta, 31-Jan-2023 10:40:24

dr. Ryan Herardi, SpPD /
dr. Muhammad Firhat Idrus, Sp.PD

0379/rev00/IPD/2012

Figure 1: Colonoscopy shows external hemorrhoids, grade 1 internal hemorrhoids, and colitis. There was no mass

From the results of chest radiology, there were no radiological abnormalities in the heart and lungs. (Figure 2) The patient then underwent a *Computed Tomography Scan* of the multiphase upper abdomen; an image of the right lobe of the liver appears slightly smaller. Multiple calcified hypodense lesions appear in segments VII-VIII of the liver, not enlarged in the arterial and venous phases, and become isodense in the delayed phase; the lesion boundaries are not clear, the size of the lesion is approximately 7.8 x 8.2 x 7,1cm. (Figure 3) The hilar segment of the portal vein is seen with an abrupt appearance before branching into the right portal vein. The right branch portal vein was not visualized, and the anterior segment of the liver was bleeding from the left branch portal vein. Following granulomatous inflammation, the possibility of tuberculosis infection cannot be ruled out, and fibrosis stage was F2-F3. No malignant tumor cells were found in this preparation. The stains for acid-fast bacteria were negative.

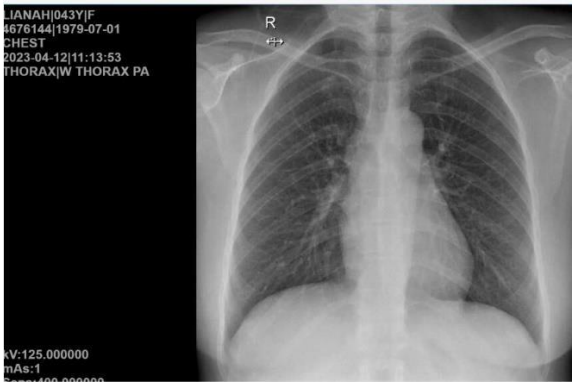

Figure 2: Chest radiology shows no radiological abnormalities in the heart and lungs.

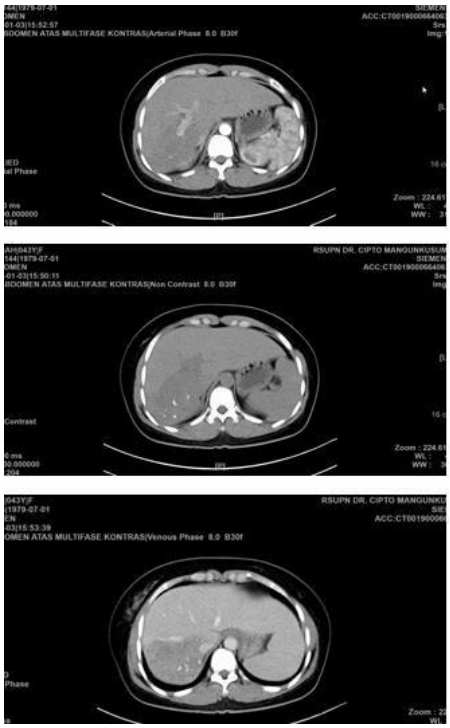

Figure 3: Multiple calcified hypodense lesions appear in segments VII-VIII of the liver

Based on physical examination and supporting examinations, the patient was diagnosed with hepatic TB at the beginning of July 2023. Finally, the anti-tuberculosis drug regimen Rifampicin (R), Isoniazid (H), Pyrazinamide (Z), and Ethambutol (E) started.

Discussion

Tuberculosis is a significant health problem; this case has a relatively high prevalence of 95% in developing countries. Cases increased significantly in the 1980-1990s due to population movement from countries with high majority, drug abuse, and HIV infection.

Abdominal tuberculosis, especially hepatic TB, is very rare. Hepatic TB is common in Asian countries andusually occurs in Filipinos. It is believed this happens due to racial susceptibility to this bacterium.[2,5] Hepatic tuberculosis is also more common in men than women, with a ratio of 2:1; there is no specific age that describes the incidence of hepatic TB.[2]

Hepatic TB can be transmitted prenatally, perinatally, and postnatally. Prenatal and perinatal can be transmitted via the umbilical cord and maternal tuberculosis. These TB bacteria reach the liver via hematogenous or lymphatic spread, more commonly via hematogenous. Hematogenous spread in miliary TB occurs due to pulmonary TB infection (active or inactive) via the hepatic artery, whereas via the portal vein in focal hepatic TB or complex primary TB. The occurrence of primary TB in the liver itself is pretty rare.[2,5–7] Furthermore, the liver will respond with the formation of both caseous and non-caseous granulomas. In miliary TB, multiple small TB shows central caseation and fibroid necrosis. Peripherally, coronal epithelioid cells of varying diameters are found where *Langhans* cells are located.[2]

The clinical symptoms that occur in hepatic TB are pretty varied. Complaints of right upper abdominal pain or non-specific abdominal pain are the most common symptoms. Clinically, jaundice can be found in 20-35% of patients, indicating the possibility of biliary involvement due to hepatic nodules causing biliary compression or to pericolangitis, enlarged lymph nodes causing biliary compression, direct involvement of the biliary epithelium, or rupture of the tuberculous granuloma into the bile duct.[2,8] Other symptoms that can be found are fever with no clear cause, anorexia, and weight loss in 55-90% of patients.[2] Hepatomegaly is the most common physical examination that can be found, and it is reported that the majority occur in 94-100% of cases of hepatic TB. This finding is usually considered a liver tumor or abscess. Splenomegaly is also occasionally found, occurring in 25-57% of cases.[7] TB nodules can sometimes penetrate the bile duct and cause cholangitis TB with bile duct stricture. Portal hypertension can also occur due to portal vein compression by lymphatic TB.[2,5] Pain occurs not influenced by activity or eating. There was no jaundice, which indicates no biliary involvement. There were no symptoms such as fever, anorexia, or weight loss. The patient had no previous history of tuberculosis and no family history of it. There is a hepatomegaly in this patient, two fingers below arcus costae, and no splenomegaly.

Markers indicating the presence of hepatic TB are non-specific. Increases in liver functions such as alanine transaminase, aspartate transaminase, alkaline phosphatase, gamma-glutamyl peptide, decreased albumin, and increased globulin are commonly found in 30-80% of patients.[2,7] Liver function can reflect the location of hepatic TB, such as TB affects the liver parenchyma. There will be an increase in the transaminase enzyme compared to alkaline phosphatase, while TB affecting the portal or duct will show a higher alkaline phosphatase compared to transaminase. Laboratory markers related to infectious processes, such as white blood cells and CRP, are often elevated.[7] These patients have normal liver function and elevated alkaline phosphatase. (1.71)

Approximately 75% of patients with hepatic TB have a chest x-ray appearance of pulmonary TB. In this patient, no abnormalities were found in the heart and lungs. Calcification in the hepatic region on abdominal X-ray indicates local hepatic TB, which can be seen in 50% of cases. These liver calcifications usually involve both lobes and, in 98% of cases, are 8-12 mm in size, small, separate, and scattered.[2,5]

Ultrasonography (USG) also shows hypoechoic lesions and complex masses, either multiple or solitary, sometimes difficult to distinguish from malignant processes. Tuberculoma is described as a hypoechoic mass that represents the caseation phase.[2,7] *Computed tomography* (CT) *Scan* and *Magnetic Resonance Imaging* (MRI) can help with the possible diagnosis of tuberculoma or hepatic TB abscess. On CT scanning, hepatic

tuberculoma appears as a low- density lesion, central to caseous necrosis, but it is also seen in necrotic tumors such as hepatoma or metastatic carcinoma. Liver calcifications are also occasionally seen on CT scans. In cases of multiple tuberculomas, the density of the lesions may vary and affect the stage of the disease; the tuberculomas conglomerate and form multiloculated masses such as a honeycomb appearance. TB portal vein and portal hypertension are rare but have been reportedin hepatic TB patients.[2,7]

MRI can also be used to evaluate tuberculoma, appearing as hypointense nodules withhypointense rims on T1-weighted images, but appearing as iso or hyperintense lesions on T2- weighted, sometimes also appearing as low-intensity lesions due to increased free radicals.[7] Military hepatic TB is difficult to detect on PET/CT. Still, PET may be the only clue in diagnosing hepatic TB because other modalities sometimes fail to find abnormalities other than non-specific hepatomegaly.[7] Abdominal CT scan of the 3-phase showed multiple calcified hypodense lesions in segments VII-VIII with indeterminate lesions with size 7.8x8.2x7.1cm.

The gold standard examination of hepatic TB is enforced histopathologically with the appearance of caseous granulomas or Acid Fast Bacilli (AFB) from smears, cultures, or biopsy specimens.[2] The histological identification of caseous granulomas is significant for diagnosing TB, although this picture is also present in Crohn's disease, sarcoidosis, and histoplasmosis.[3] A liver biopsy is the gold standard, especially when malignancy causes must be excluded. AFB examination with Ziehl Neelsen stain was positive in 40% of cases. Tuberculosis PCR has a sensitivity of 82% and can be performed to confirm the diagnosis.[9] The patient's liver biopsy examination showed clusters of epithelioid cells accompanied by multinucleated giant cells. There was also necrosis resembling caseous necrosis with negative Acid-Fast Bacteria staining. The histological conclusion was following granulomatous inflammation, the possibility of tuberculosis infection could not be ruled out, and no malignant tumor cells were found in the preparations. The stage of fibrosis is around F2-F3.

The patient also underwent a colonoscopy to look for other causes of the patient's abdominal pain symptoms, found external hemorrhoids, grade 1 internal hemorrhoids, and colitis, and nomass was seen.

The patient was finally given antituberculosis drug therapy based on these results. Treatment for hepatic TB is the same as for other extrapulmonary TB, using four anti-TB drugs consisting of rifampicin, isoniazid, pyrazinamide, ethambutol for two months, followed by rifampicin and isoniazid therapy for 6-12 months. This regimen can cure tuberculosis in more than 90% of patients.[2,9] The patient started treatment at the beginning of July 2023 with this regimen while undergoing periodic liver function evaluations. Obtained resolution of abdominal pain improvement and assessment of liver function remained normal in this 2-week treatment.

Based on *the American Thoracic Society*, drugs that induce liver damage, such as isoniazid OAT, must be monitored periodically. Based on the study of Alvarez et al., with anti- tuberculosis drugs, there was a 67% resolution of symptoms of abdominal pain, fever, weight gain, and reduced liver mass. The cumulative mortality rate for hepatic TB is 15-42%. Approximately 50% of case studies in the Philippines were associated with respiratory failure and the presence of ruptured esophageal variceal associated with cirrhosis. Other factors that may worsen the prognosis include miliary TB, steroid therapy, age less than 20 years, cachexia,HIV, cirrhosis, and liver failure.[2]

CONCLUSION

Tuberculosis is a significant health problem that is highly prevalent in developing countries; hepatic TB is a manifestation of extrapulmonary TB, which is rarely found. Anamnesis, physical examination, and supporting examinations are carried out to diagnose hepatic TB. There are various signs and symptoms regarding the history and

physical examination of hepatic TB. Investigations such as imaging and liver biopsy can help diagnose this type of TB. The treatment given for hepatic TB is given according to the same regimen as other extrapulmonary TB.

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