

Xpert MTB/RIF for diagnosis of tubercular liver abscess. A case series

Roshan Agarwala¹, Sahajal Dhooria², Niranjan S. Khaire³, Shubhra Mishra¹, Samman Verma³, Jimil Shah¹, Harshal S. Mandavdhare¹, Savita Kumari³, Usha Dutta¹, Vishal Sharma¹

¹Department of Gastroenterology, Postgraduate Institute of Medical Education and Research, Chandigarh, India;

²Department of Pulmonary Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh, India;

³Department of Internal Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh, India

SUMMARY

Hepatic involvement is an infrequent manifestation of abdominal tuberculosis and could occur in form of granulomatous hepatitis, nodular involvement or abscess formation. Tubercular liver abscess (TLA) is uncommon, and diagnosing this entity is a challenge. Xpert MTB/RIF (Cepheid, Sunnyvale, CA, USA) assay has been widely used for diagnosing pulmonary tuberculosis (TB) and lymph nodal tuberculosis. Its utility in some forms of other extrapulmonary TB has also

been studied. The role of Xpert MTB/RIF for diagnosis of tubercular liver abscess is not known. Here we present a series of four cases of TLA, where the diagnosis was made on the basis of positive Xpert MTB/RIF assay tested on liver drained pus.

Keywords: tuberculosis, hepatic tuberculosis, liver abscess, AFB; gastrointestinal tuberculosis.

INTRODUCTION

Liver abscess is an important clinical entity in tropical countries like India, with amoebic liver abscess being the most common type [1, 2]. Liver is an uncommon organ for involvement in TB, being involved in 0.8-1.2% cases of TB [3, 4]. Hepatic TB can present either as a disseminated/miliary form, which is more common, or a localised/isolated form [5]. Tubercular liver abscess (TLA) is exceedingly rare; reported in literature only as case reports and case series [5-9]. Diagnosing it is difficult and the diagnosis is based on a strong clinical suspicion, confirmed by demonstrating acid fast bacilli or positive culture result in pus sample from the abscess. The suspicion of

tuberculosis as underlying cause should be entertained in patients who are immunosuppressed, have associated other organ involvement like lungs, or have a non-resolving liver abscess. Usually the diagnosis has been reported with the use of acid-fast bacilli smear and culture. However, since the pus culture is negative in many cases, there is a need for novel modalities for diagnosing TB liver abscess. Xpert MTB/RIF is being widely used for diagnosis of pulmonary TB [10]. Its utility in some forms of extrapulmonary TB has also been established [11-13]. The role of Xpert MTB/RIF for diagnosis of TLA is not known. Here we present a series of 4 cases of TLA where the diagnosis was made by Xpert MTB/RIF positivity. Xpert Mtb/Rif assay is a nucleic acid amplification test which uses a disposable cartridge system and is fully automated and provides a rapid method of diagnosis of Mycobacterium tuberculosis complex and also presence of rifampin resistance.

Corresponding author

Vishal Sharma

E-mail: docvishalsharma@gmail.com

Case 1

A 60-year old male, who was a known diabetic with poorly controlled glycaemic status (HbA1c-9.9) presented with history of right upper quadrant abdominal pain associated with fever, anorexia and weight loss of 2 weeks duration. On evaluation, he had anaemia (haemoglobin- 6.9 g/dL), leucocytosis (Total leucocyte count- 14100 cells/cubic mm), hypoalbuminemia (albumin- 1.96 g/dL) and raised alkaline phosphatase (ALP- 288 IU/L). Ultrasound abdomen showed a hypoechoic lesion in both segment VI and VII of liver. In suspicion of amoebic liver abscess, he was empirically started on metronidazole. Amoebic serology was negative. However, there was no response to therapy. Percutaneous drainage of liver abscess was done, to which also the patient was non responsive. Computed tomography of chest and abdomen showed multiple pulmonary lesions in both right and left lung and presence of the liver abscess. Sputum analysis could not be done as patient had mild cough which was non productive. The pus was sent for Xpert MTB/RIF and AFB staining. AFB culture and staining was negative, nonetheless, Xpert MTB/RIF turned out to be positive. No resistance to rifampicin was detected. Mantoux test was negative. Test for HIV was negative. He was started on antitubercular therapy (ATT), following which he responded. On follow up after 6 months of ATT, he had gained weight, was asymptomatic, and there was no residual abscess on ultrasonography.

Case 2

A 45 year-old man, reported previously, presented with complaint of pain in epigastrium and fever. Contrast enhanced computed tomography done for abdomen revealed an abscess in the liver with mural thickening of cecum. A possibility of amoebic colitis with amoebic liver abscess was kept. Colonoscopy was also done, which showed ulcers in the cecum and ascending colon. He was treated with metronidazole. Initially, there was equivocal response to therapy. However, he continued to have weight loss and severe abdominal pain. On repeat colonoscopy, there was persistence of colonic ulcers. On histopathology, non-caseating granuloma without AFB was seen. Upper gastrointestinal endoscopy revealed a fistula opening in the stomach with pus discharge in the region of the antrum and was noted to be origi-

nating from the left lobe liver abscess on imaging. The material was sent for Xpert MTB/RIF, and was reported positive. AFB smear was negative and culture was not done. Mantoux test was positive. Anti-tuberculosis therapy was started. Screening for diabetes and human immunodeficiency virus was negative. Following ATT, there was resolution in symptoms, weight gain, closure of gastric fistula and resolution of liver abscess.

Case 3

A 33 year old male was being evaluated in pulmonology department for chronic cough, fever and upper abdominal pain. Chest X-ray was unremarkable. His ultrasonography of the abdomen was suggestive of an abscess in the left lobe of the liver. Contrast enhanced computed tomography of chest and abdomen showed centrilobular nodules and tree in bud appearance in the lung field, and a hypodense lesion of size 6.1 X 4.2 cm in segment II and III of the liver (Figure 1). Mantoux test was positive. However, sputum for acid fast bacilli and Xpert MTB/RIF was negative. Amoebic serology was negative. Percutaneous drainage of liver abscess was done, and pus was drained. AFB stain and mycobacterial culture were negative, but the Xpert MTB/RIF turned out to be positive. No resistance to rifampicin was detected. Mantoux and HIV tests were negative. He was started on four drugs ATT, following which the patient responded with defervescence and weight gain. Full course was completed.

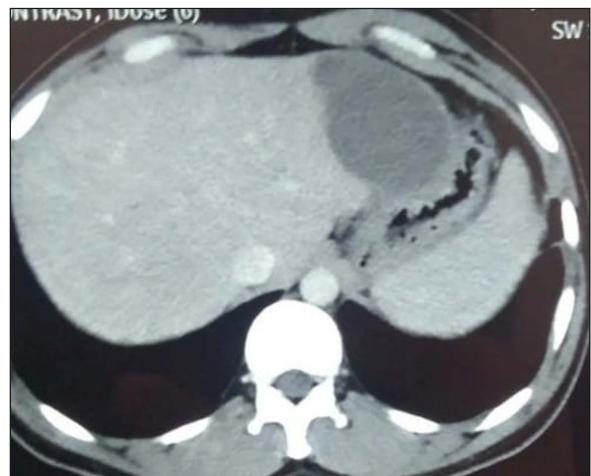


Figure 1 - Computed tomography showing hypodense lesion in left lobe of liver.

Case 4

The fourth case, a 27 year old male, was a diagnosed case of autoimmune hemolytic anemia for five years on steroids and azathioprine. He had history of right sided tubercular empyema thoracis two years back, for which he had been treated with four drug ATT regimen. He now presented to us with history of pain right upper abdomen and fever. On evaluation, he had an abscess in the left lobe of the liver. Amoebic serology was negative. The abscess was drained and pus was sent for analysis. Xpert MTB/RIF was positive for tuberculosis, and showed resistance to rifampicin. AFB was negative but culture was not done. He was started on Cycloserine, Ethionamide, Levofloxacin, Ethambutol, Pyrazinamide and injection Kanamycin. He had symptomatic improvement and was doing fine. However, after four months he was again admitted with acute hemolysis, skin lesions, fever, cough and hypotension. The liver abscess had resolved by this time. On evaluation he was found to have disseminated histoplasmosis. He was started on amphotericin B but eventually succumbed to sepsis related shock.

DISCUSSION

Hepatic tuberculosis is an uncommon entity which can present, occasionally, in the form of liver abscess. The present series reports four cases of TLA, wherein the diagnosis was clinched on by

Xpert MTB/RIF. Also, one case of rifampicin resistance was detected by Xpert MTB/RIF, and managed with second line ATT. Xpert MTB/RIF is a cartridge-based nucleic acid amplification test. It is automated, and can diagnose TB rapidly. It also detects rifampicin resistance status, and has a good sensitivity and specificity (10, 11). Use of Xpert MTB/RIF has not been reported for diagnosis of TLA although it has been used in other forms of abdominal tuberculosis [12, 13].

Hepatic involvement is uncommon in TB [3, 4]. Hepatic TB has been classified as military/disseminated type and localised/isolated type. Localised involvement can be in form of granulomatous hepatitis, nodular TB (pseudotumours) or abscess formation [14, 15]. Hepatic involvement as a part of disseminated TB is more common as compared to isolated hepatic TB. TLA has been reported in <1% cases of hepatic TB [3, 14].

TLA is a diagnostic challenge, as manifestation can be nonspecific or mimic amoebic liver abscess. At times, it can also mimic pyogenic abscess. It should be suspected in the setting of an immunocompromised patient, failure to respond to amoebicidal drugs and antibiotics, or coexistent TB elsewhere in the body. Clinical suspicion is the key to diagnosis. It should be considered in patients with non-resolving liver abscess, hepatic involvement with tuberculosis at other sites and may present with abdominal pain and fever. Even in patients with clinical suspicion, clinching the

Table 1 - Summary of cases with tubercular liver abscess.

	Case 1	Case 2	Case 3	Case 4
AFB smear	Negative	Negative	Negative	Negative
AFB Culture	Negative	Not done	Negative	Not done
Amoebic serology	Negative	Negative	Negative	Negative
Bacteriology	Sterile	Sterile	Sterile	Sterile
Mantoux test	Negative	Positive	Positive	Negative
Organs Involved	Liver Abscess, lung lesions	Liver abscess, Cecal ulcers, Gastric fistula	Lung lesions, liver abscess	Empyema thoracis, Liver abscess
Xpert MTB/RIF	Positive	Positive	Positive	Positive
Drug Resistance-XpertMTB/RIF	No	No	No	Resistance to rifampicin
Comorbidity	Diabetes Mellitus	None	None	Autoimmune hemolytic anemia on immunosuppressants
Response to ATT	Yes	Yes	Yes	?Yes

diagnosis is remarkably difficult due to low yield of conventional tests. Yield of AFB stain has been only 25% in liver biopsies, and expected to be even lower in pus from TLA. The sensitivity of mycobacterial culture is also low for hepatic TB [5]. Mantoux test has its own limitations. It cannot differentiate between tubercular infection and disease and has high false negative rate in immunocompromised patients. Interferon gamma release assay (IGRA) overcomes some of limitations of Mantoux test with its increased specificity, but it cannot differentiate between tubercular infection and disease.

TLA, being a rare entity has been reported in literature only as case reports and case series. Carrara et al reported a case of TLA in a patient with HIV infection who improved with ATT. The diagnosis in this case was made with positive AFB smear [7]. Mourad et al reported a case series of 3 cases of primary hepatic tuberculosis [6]. Diagnosis in those cases was clinched with a histology, which was suggestive of necrotising granulomatous inflammation. In one of the cases culture for Mycobacterium tuberculosis was found to be positive. A case of TLA rupturing into pleural cavity was reported in a young girl [16]. All work up for TB was negative, and finally the diagnosis was established by polymerase chain reaction positivity for Mycobacterium tuberculosis in pleural fluid. Another interesting case was reported by Kumar et al. [17]. The patient presented with ruptured TLA into the chest wall causing a subcutaneous swelling. Diagnosis was presumed by histology showing granulomatous inflammation without AFB positivity, and confirmed by a positive response to ATT.

In the last decade Xpert MTB/RIF has revolutionised the diagnosis of TB, mainly pulmonary TB. There is also evidence of its role in extrapulmonary TB like pleural, meningeal and lymph nodal TB [11-13]. However, its role in hepatic TB has not been studied. We diagnosed all four of our cases using cartridge based nucleic acid amplification test (Xpert MTB/RIF). In these cases all the conventional tests were negative. Also, one case of rifampicin resistance was detected with Xpert MTB/RIF. However, Xpert Mtb/Rif assay is well recognised to report both false positive and inconclusive results for rifampin resistance. Therefore these results must be confirmed using culture based testing and drug sensitivity testing [18].

Xpert Mtb/Rif can detect low numbers of bacilli (131 per ml) in sputum and therefore may provide better sensitivity for diagnosis of tuberculosis than traditional smear which is positive only if numbers are as high as 10^4 and 10^5 bacilli per ml. Genexpert Ultra is reported to be even more sensitive with a detection limit as low as 16 bacilli per ml. Unfortunately there is no comparative data on performance in hepatic abscess sample [19]. The Xpert Mtb/Rif assay has been recognised to detect additional cases (over culture positive cases) in extrapulmonary samples [20]. Although, we diagnosed all these cases based on Xpert MTB/RIF positivity and the diagnosis was confirmed with a positive response to ATT, the sensitivity and specificity of this test for diagnosis of TLA is not known. TLA, being an entity difficult to diagnose, we suggest considering the use of Xpert MTB/RIF testing as an ancillary test in all cases where there is suspicion of TB as an etiology for liver abscess.

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Informed consent

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Conflict of interest

None

REFERENCES

- [1] [Lardière-Deguelte S, Ragot E, Amroun K, et al. Hepatic abscess: Diagnosis and management. *J Visc Surg.* 2015; 152: 231-43.
- [2] Jha AK, Das A, Chowdhury F, Biswas MR, Prasad SK, Chattopadhyay S. Clinicopathological study and management of liver abscess in a tertiary care center. *J Nat Sci Biol Med.* 2015; 6, 71-5.
- [3] Essop AR, Posen JA, Hodkinson JH, Segal I. Tuberculosis hepatitis: a clinical review of 96 cases. *Q J Med* 1984; 53, 465-77.
- [4] Tai W-C, Kuo CH, Lee C, et al. Liver Tuberculosis in Southern Taiwan: 15-years Clinical Experience. *Journal Int Med Taiwan* 2008; 19 (5), 410-17
- [5] Hickey AJ, Gounder L, Moosa M-YS, Drain PK. A systematic review of hepatic tuberculosis with considerations in human immunodeficiency virus co-infection. *BMC Infect Dis.* 2015; 15. 209.
- [6] Mourad MM, Lioussis C, Algarni A, Kumar S, Bramhall SR. Primary hepatic tuberculosis in immunocompetent adults: a UK case series. *Oxf Med Case Rep.* 2014; 2014, 148-50.

- [7] Carrara E, Brunetti E, Di Matteo A, Ravetta V, Minoli L, Youkee D. Tubercular liver abscess: an uncommon presentation of disseminated tuberculosis. *Infection*. 2015; 43, 237-40.
- [8] Köksal D, Köksal AS, Köklü S, Çiçek B, Altıparmak E, Sahin B. Primary tuberculous liver abscess: a case report and review of the literature. *South Med J*. 2006; 99, 393-5.
- [9] Meena M, Gupta N, Kewlani J, Kumararesan SH. Hepatic abscess as a paradoxical response to antituberculous chemotherapy for tubercular lymphadenitis. *BMJ Case Rep*. 2015; 2015:bcr2015211936.
- [10] Drobniowski F, Cooke M, Jordan J, et al. Systematic review, meta-analysis and economic modelling of molecular diagnostic tests for antibiotic resistance in tuberculosis. *Health Technol Assess*. 2015; 19 (34), 1-188.
- [11] Denkinger CM, Schumacher SG, Boehme CC, Dendukuri N, Pai M, Steingart KR. Xpert MTB/RIF assay for the diagnosis of extrapulmonary tuberculosis: a systematic review and meta-analysis. *Eur Respir J*. 2014; 44 (2), 435-46.
- [12] Bellam BL, Mandavdhare HS, Sharma K, et al. Utility of tissue Xpert-Mtb/Rif for the diagnosis of intestinal tuberculosis in patients with ileocolonic ulcers. *Ther Adv Infect Dis*. 2019; 6:2049936119863939
- [13] Kohli M, Schiller I, Dendukuri Net al. Xpert(®) MTB/RIF assay for extrapulmonary tuberculosis and rifampicin resistance. *Cochrane Database Syst Rev*. 2018; 8: CD012768.
- [14] Alvarez SZ, Carpio R. Hepatobiliary tuberculosis. *Dig Dis Sci* 1983; 28(3): 193-200.
- [15] Chien RN, Liaw YF, Lin PY. Hepatic tuberculosis: Comparison of miliary and local form. *Infection*. 1995; 23 (1), 5-8.
- [16] Bansal M, Dalal P, Kadian Y, Malik N. Tubercular liver abscess rupturing into the pleural cavity: a rare complication. *Trop Doct*. 2019; 49 (4), 320-2.
- [17] Kumar P, Taneja S, Gupta K, Duseja A, Dhiman RK, Chawla YK. Unusual presentation of tubercular liver abscess in an immune-competent adult. *J Clin Exp Hepatol*. 2017; 7 (1), 77-9.
- [18] Lawn SD, Mwaba P, Bates M, et al. Advances in tuberculosis diagnostics: the Xpert MTB/RIF assay and future prospects for a point-of-care test. *Lancet Infect Dis*. 2013; 13 (4), 349-61.
- [19] Chakravorty S, Simmons AM, Rowneki M, et al. The New Xpert MTB/RIF Ultra: improving detection of *Mycobacterium tuberculosis* and resistance to rifampin in an assay suitable for point-of-care testing. *mBio*. 2017; 8 (4), e00812-7.
- [20] Mazzola E, Arosio M, Nava A, et al. Performance of real-time PCR Xpert®MTB/RIF in diagnosing extrapulmonary tuberculosis. *Infez Med*. 2016; 4, 304-9.