

Post Liver Transplant Granulomatous Hepatitis: Hepatic Tuberculosis Diagnosed By Synovial Aspirate of the Knee.

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Citation

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Abstract

Tuberculosis (TB) is a rare but serious opportunistic infection in transplant recipients, with an incidence in organ transplant recipients ranging from 0.35% in developed countries to 15% in endemic areas¹. It carries a mortality rate of as high as 40%. We report on a patient with granulomatous hepatitis on liver biopsy and negative tuberculosis culture of the biopsy. The correct diagnosis was made on clinical grounds and aspirate of a swollen knee.

CASE HISTORY

A 69 year old man underwent liver transplantation for end stage liver disease secondary to alcoholic liver disease. His post-transplant course was unremarkable apart from post transplant diabetes mellitus. Standard post transplant immunosuppression consisted of a tapering course corticosteroids, tacrolimus and mycophenolate mofetil.

Nine months post-transplant, he presented with fever, malaise, night sweats and weight loss of several weeks duration. There was no history of cough, dyspnoea, hemoptysis or abdominal pain. His pre-transplant work up was negative for TB as assessed by a skin Montoux test (PPD test) and a chest X-ray. His past medical history was significant for chronic obstructive pulmonary disease. His physical examination revealed a body temperature of 39 degrees Celsius with rigors but was otherwise unremarkable. His social history revealed that he was born in Italy during the Second World War. There was no history of street drug use or post-transplant alcohol use.

His presenting laboratory work up is depicted in table 1.

CT scan of the chest showed calcification could be associated with previous latent TB.

Figure 1

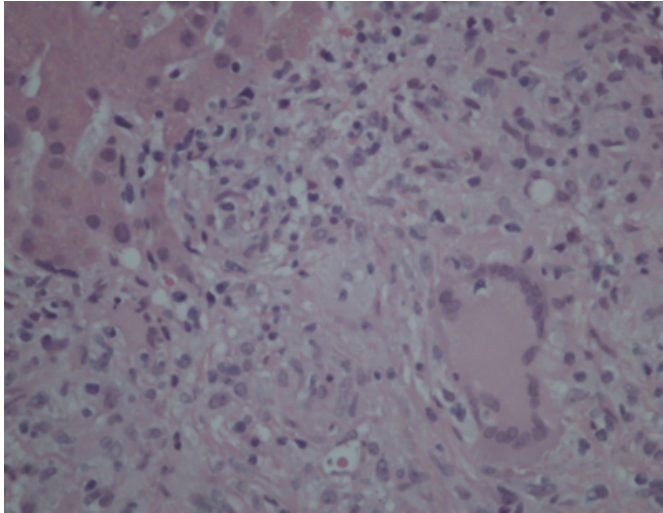
leukocytes	3.5 giga/L	Neutrophil count	0.9 giga/L	HbG	93 g/L
Platelets	130 giga/L	ENR	1.0	PTT	39 sec
K	19 µmol/L	Mg	0.76mmol/L	Serum Creatinine (normal < 88 umol/L)	126 µmol/L
ALT (normal < 55 U/L)	25 U/L	AST (normal < 38 U/L)	25 U/L	GGT (normal < 55 U/L)	332 U/L
ALP (normal < 120 U/L)	365 U/L	Total Bilirubin (normal < 22 µmol/L)	19 µmol/L	Albumin (normal 35-45)	32 g/L

The patient continued to spike of temperature on a daily basis despite empiric broad spectrum antibiotics and anti fungal agents. All cultures were negative. He developed a monoarthritis involving his left knee joint with significant effusion. He had ERCP (Endoscopic retrograde cholangio pancreatography) which did not reveal any abnormality. He underwent a liver biopsy which showed florid granulomatous inflammation (figure 1) but was reported negative for AFB and TB culture. His sputum was negative for AFB and culture for TB as well. A CT chest showed left upper lobe nodules which were consistent with previous TB. Repeated PPD test was negative Synovial fluid from left knee showed cell count of 17,500, the acid fast bacilli (AFB) stain was positive but negative culture. A synovial biopsy was also positive for AFB stain. Patient was started on empiric anti TB therapy consisting of (INH,RIFAMPIN,ETHAMBUTOL AND PYRIZINAMIDE) His fever and other symptoms subsided, he began re-gaining weight with normalization of liver

biochemistry.

Figure 2

Figure 1. Hepatic core needle biopsy, Haematoxylin and Eosin at 200X magnification showing a non-necrotizing granulomatous portal inflammatory cell infiltrate, expanding the portal tracts with some spillover into the adjacent lobule. Note the multinucleated giant cell.



DISCUSSION

Transplant recipients experiencing *M. tuberculosis* disease show high morbidity and mortality rates. The onset of tuberculosis can occur within 15 days to several years of solid organ transplantation (mean 9 months)^{1,2}. Reactivation of TB and, rarely, nosocomial acquisition or donor transmission are considered to be the most frequent modes of acquisition of TB. Among liver transplant recipients with tuberculosis, tubercular hepatitis was present in 48% of patients [1]. Rare presentations include focal/local tuberculoma or abscess.³ [1]

Other presenting sites included skin, muscle, bones or joints, central nervous system (meningitis or brain abscesses), gastrointestinal tract, genitourinary tract and lymph nodes^{2,3,4}.

Our patient's clinical presentation, with constitutional symptoms (ie. fever, night sweats, weight loss), granulomatous hepatitis on liver biopsy and epidemiologic

background (ie. born during the second World War in an endemic area) could be considered classic for post-transplant TB. The negative AFB stain and TB culture of the liver biopsy, however, initially caused clinical doubt on a diagnosis of post-transplant TB. The TB skin test was negative but this was not necessarily unusual in an elderly, immunosuppressed patient. The clinical diagnosis of TB was finally accepted based on the aspirate and synovial biopsy of the patient's knee which revealed a positive AFB stain, although the culture was again negative. The final clinical "proof" of post-transplant TB in the absence of positive cultures of liver biopsy and synovial fluid/biopsy, is the resolution of clinical symptoms and liver biochemistry with a course of TB treatment. Two years later, the patient remains free of symptoms and liver biochemical abnormality.

CONCLUSIONS

The case presented here illustrates the diagnostic and therapeutic challenges that a liver transplant recipient presenting with granulomatous hepatitis can present. In this case, despite negative TB cultures, the diagnosis was made on clinical, epidemiologic grounds and the aspirate of a swollen knee!.

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