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Hepatic Tuberculoma – Diagnostic difficulty and challenges

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Abstract: *Hepatic Tuberculoma is a rarely diagnosed clinical entity. We present a case of 26 year old female who presented with high grade fever and loss of weight. Blood investigation showed raised alkaline phosphatase levels. Initial imaging showed a multisepatated cystic lesion with peripheral enhancement suggestive of abscess. Percutaneous drainage failed and started on empirical antibiotics. Patient continued to have fever and hence image guided biopsy was done twice which was not conclusive. Due to strong suspicion of non neoplastic etiology, third biopsy was done which showed granulomatous inflammation. Patient was started on Anti Tubercular Treatment ATT and she improved symptomatically. This case highlights the importance of repeated biopsy to confirm the nature of disease and hepatic Tuberculosis should be considered in differential diagnosis of space occupying lesion of liver . Isolated elevation of Alkaline phosphatase levels with SOL in liver, one should suspect hepatic tuberculoma.*

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I. Introduction

India accounts for about a quarter of the global Tuberculosis(TB) burden. Worldwide India is the country with the highest burden of TB[1]. Hepatic tuberculosis is rare in the absence of miliary tuberculosis. Primary hepatic tuberculosis is rare even in country like India with high prevalence of tuberculosis. Manifestations are varied ranging from right upper quadrant pain to non specific symptoms such as fever, anorexia, weight loss and rarely jaundice[2.] Common laboratory abnormalities were elevated alkaline phosphatase and gamma-glutamyl transferase[3.]Imaging findings depends on the type of hepatic tuberculosis. Honey comb appearance is characteristic of hepatic tuberculoma[4.] Final diagnosis depends on combination of clinical, imaging and pathological evidence of tuberculosis. Treatment is by ATT for a period of 12 months.

II. Case Report

26 year old female from Tamil Nadu , presented with 1 month history of persistent high grade fever and loss of weight of around 9 kilograms. Her appetite was normal.She was recently diagnosed to have diabetes for which she is on treatment with insulin. She was moderately built and nourished, anicteric. Abdomen examination was normal. Blood investigation showed leucocyte count of 9400 cells / cu mm. Blood tests for fever including WIDAL , Malarial parasite, Dengue IgM, MSAT for leptospirosis, blood culture and urine culture were negative. Liver function tests showed mild elevation of Alkaline phosphatase (ALP) levels 312U/L with normal bilirubin and Aspartate Transaminase (AST) and Alanine Transaminase (ALT) levels.

Ultrasonogram (USG) of abdomen showed 5.2*4.6 cm hypoechoic cystic mass with multiple small internal cystic lesion in segment 6&7 of right lobe of liver. In suspicion of liver abscess and to characterize lesion better contrast enhanced computed tomography (CECT) abdomen was performed which showed 6.5*5*4.3 cm cystic lesion in segment 7 with multiple internal septations and thick peripheral enhancement noted on post contrast study- possibility of inflammatory etiology Fig (1).With working diagnosis of Liver abscess we started on empirical course of antibiotics and attempted percutaneous drainage, but due to multiloculated nature , only few drops of pus could be aspirated, which on culture turned to be negative. Cytology of aspirate showed many pus cells and few RBCs & no organisms were seen.

Patient continued to have fever daily inspite of antibiotics during hospital stay. To rule out rare possibility of neoplasm in this young lady, we performed MRI abdomen and tumor markers . MRI abdomen showed 5.5*4.8 cm multiloculated cystic lesion with internal septations in segment 7 showing thick peripheral enhancement and diffusion restriction on diffusion weighted images (DWI)- suggestive of liver abscess Fig 2. AlphaFeto Protein (AFP) 2.14, carcino embryonic antigen (CEA) 1.1 ng/ml, carbohydrate antigen 19-9(Ca19-

9) 3.6 U/ml – all were within normal limits. S.chromogranin was 237.5 ng/ml (normal <108 ng/ml). Upper GI endoscopy and colonoscopy were normal. In view of raised S. Chromogranin and persisting symptoms, DOTA - PET CT was done to rule out rare possibility of Neuroendocrine tumor (NET) . DOTA PET CT - showed 6*5.6 cm lesion with minimal 68Ga DOTANOC avid lesion with areas of cystic changes in segment VII Fig (3). Also few epiphrenic, mediastinal and bilateral Hilar nodes were noted.

With persisting symptoms of fever and imaging findings of non neoplastic etiology, to arrive at definitive diagnosis we planned for USG guided FNAC from lesion. First aspirate was negative for inflammatory and neoplastic cells. Then second, trucut biopsy was done which showed feathery degeneration and regenerative changes, some nucleus showing clearing, spotty necrosis, portal areas widened with fibrosis and inflammatory infiltrate- aggregates of lymphocytes and plasma cells – possibility of lymphocytic infiltration and autoimmune hepatitis with fibrosis. Workup for auto immune etiology includes AMA- M2, M2-3E, Sp100, PML, Gp210, LKM-1, LC-1, SLA/LP, Ro-52, ANA, Anti smooth muscle Ab were Negative.

Persisting fever not responding to antibiotics and weight loss we thought of tuberculosis as differential diagnosis. We repeated Trucut biopsy for third time, which showed fibrocollagenous stroma with multifocal necrotizing granulomatous inflammation and fibroblastic reaction suggestive of Tuberculosis. Gene expert was negative.

With this, patient was started on Anti Tubercular Treatment (ATT) and patient started to feel better within one week of initiation of treatment. We followed up the patient after six months. Now she is asymptomatic, gained weight and appetite has improved. One year after follow-up after completing ATT, lesion has almost disappeared.Fig (4)

III. Discussion

Tuberculosis is very common in India. Hepatic involvement can occur either with or without pulmonary involvement. Miliary form of tuberculosis is the most common form of hepatic tuberculosis , accounting for approximately 80%. Miliary involvement occurs by spread through hepatic artery, whereas local hepatic involvement (tuberculoma, macronodular hepatic TB , pseudotumoral hepatic TB) occurs by spread through portal vein[5] . Here we have described a case of hepatic tuberculoma.

Clinical presentation of hepatic tuberculoma are varied. Patients can have right upper quadrant pain, fever, anorexia, loss of weight, loss of appetite, jaundice. Patients with malignancy also have similar symptoms posting diagnostic challenge.

Laboratory investigations show elevation of Alkaline phosphatase and gamma glutamyl transferase (GGT) levels. Hepatic TB patients often had an inverted albumin to globulin ratio (A/G), in which the serum globulin was reported to be 1.25-1.86 times higher than serum albumin[6]. Mild Transaminase elevation can occur, however higher elevations were seen in jaundiced patients[7]. Our patient had elevated Alkaline phosphatase levels with inverted albumin to globulin ratio.

Tubercular hepatic lesions that are more than 2 cm in size are referred to as macronodular or pseudotumoral tuberculosis. This form of hepatic tuberculosis is rare compared to the miliary variant and frequently manifests as solitary or multiple variable-sized hepatic masses. Often it may be difficult to distinguish these lesions from the more common neoplastic and other infective lesions. Depending on the stage of the hepatic granuloma, the imaging appearances can be quiet variable. CT imaging features of macronodular granuloma of the liver depends on the stage of the disease. Non-caseating granulomas appear hypodense on the unenhanced study and usually display no or minimal peripheral rim enhancement following intravenous contrast administration. Understandably, such a lesion if present in isolation can pose a diagnostic dilemma making it practically impossible to differentiate it from hepatic metastasis or other primary tumours. The lesion can in addition show punctuate or chunky internal calcifications on CT. Lesions with frank caseous necrosis result in tubercular abscesses whose imaging appearances vary depending upon the degree of internal liquefaction. The liquefaction can be multifocal or central . Tubercular abscesses can at times exhibit a “honeycomb” appearance with multiple enhancing septations and intermixed areas of necrosis. A conglomeration of these cystic lesions can give rise to the “cluster sign”, which is more often associated with pyogenic or cholangitic abscesses Occasionally, the lesions can display extensive necrosis thus mimicking cysts depicting no discernible peripheral enhancement[8]

Definitive diagnosis of hepatic tuberculosis can be made with liver biopsy. A liver biopsy is indicated in any person with a constellation of clinical, laboratory, and radiographic suspicion of hepatic TB. These may include, but are not limited to, hepatomegaly of unknown origin, fever of unknown origin, and abnormal liver enzymes in any patient from a TB-endemic region. It should be done under image guidance with adequate precautions. Biopsy specimen is sent for microbiological, histological and PCR assessment. Microbiological evidence includes smear positive for Acid Fast Bacilli(AFB), and positive culture for mycobacterium tuberculosis. However, sensitivity for detection by microbiological methods are low, with AFB smear 25%

sensitivity and for culture <10% sensitivity. In our case both smear for AFB and culture were negative. Histological evidence of granuloma provides non specific evidence of hepatic TB with sensitivity ranging from 14-100%. A diagnosis of hepatic TB based on hepatic granulomas may be supported by TB detected elsewhere in the patient. In TB-endemic regions, the presence of a hepatic granuloma on biopsy should suggest a TB etiology, and may warrant a course of anti-TB therapy

Anti Tubercular Treatment ATT should be initiated in patients with hepatic TB and in patients with high suspicion of hepatic TB. Amarapurkar et al from India, in his study showed that thirty eight hepatic TB patients were treated with for drug regimen containing Isoniazid, Rifampicin, Pyrazinamide and Ethambutol for two months, followed by Isoniazid and Rifampicin for ten months. After a period of 12 months all patients were improved[9]. All patients on ATT should be monitored for drug induced liver injury (DILI). Patients show symptomatic improvement within weeks of starting ATT , as in our case.

IV. Conclusion

Hepatic Tuberculoma is a rare form of extrapulmonary tuberculosis. With clinical findings and isolated elevation of Alkaline phosphatase levels, inverted albumin and globulin ratio and imaging findings of characteristic 'honeycomb' appearance on CT, one can strongly suspect tuberculosis. For defenitive evidence, biopsy and PCR is most sensitive followed by histopathology for granuloma is needed. Treatment is with 4 drug anti Tubercular regimen for total period of 1 year.

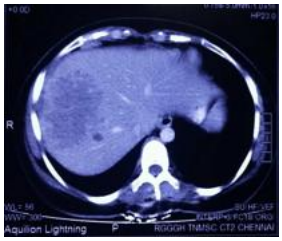

Fig (1) CECT

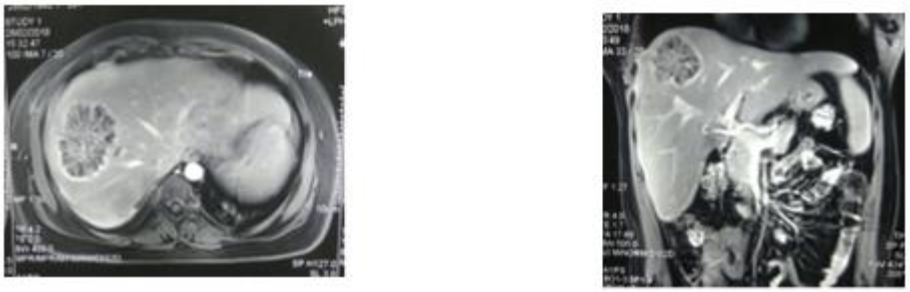

Fig (2) Honeycomb appearance of Tuberculoma in MRI

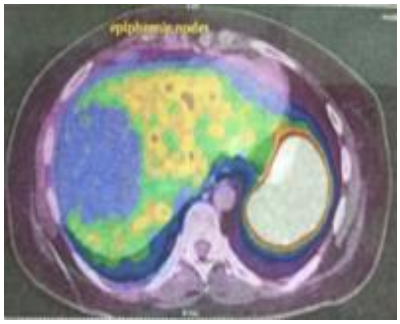

Fig (3) PET CT

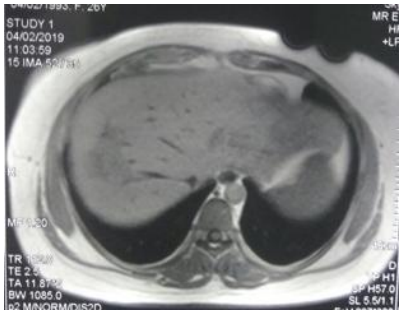

Fig (4) – complete resolution of tuberculoma

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