An unusual detected cause of abnormal liver enzymes in an aircrew member periodical visit: case report

Abstract

Background: Hepatic tuberculosis (TB) is a rare entity, poorly described in the literature. It presents with nonspecific clinical manifestation and imaging findings mimicking other liver disease making diagnosis challenge. We report a case of isolated hepatic tuberculosis in asymptomatic cabin crew member diagnosed accidentally by investigating a liver chemistry test disorder.

Case report: a 28 year-old Moroccan cabin crew attendant came to the aeromedical expertise center to perform her periodical medical assessment. She had no medical history. Physical examination was unremarkable. Liver chemistry test values were elevated. Imaging studies of the liver suggested malignant disease. Histological examination showed isolated hepatic tuberculosis.

Discussion: isolated hepatic TB is very uncommon, lacks typical clinical manifestation and radiological features, but remains an important differential diagnosis of hepatic nodules especially in endemic areas. This observation highlights the benefit of liver chemistry test evaluation realized systematically for periodical aeromedical fitness to diagnose some pathology in asymptomatic stage avoiding complications. Hepatic TB is a cause of temporarily unfitness because it's not compatible with flight safety conditions. Aircrew with hepatic TB will need to be assessed for both complete disease control and full resolution of any iatrogenic side effect of anti-tubercular drugs before returning to fly under some restrictions.

Keywords: liver tuberculosis, extra pulmonary tuberculosis, flight safety, aptitude management.

Introduction:

Tuberculosis (TB) is a worldwide public health problem with considerable morbidity and mortality in both developed and developing countries [1]. In Morocco, it's still endemic with more than 30000 new cases per year [2]. Pulmonary involvement remains the most frequent form of TB with 80-90% of cases but there is an increasing interest in extrapulmonary forms of TB as its relative frequency increases [3].

Hepatic TB is a rare pattern, particularly in the absence of miliary TB; it is poorly described in the literature and represents less than 1% of all cases of TB [4]. Clinical symptoms vary widely; they are nonspecific like right upper quadrant pain, jaundice, ascites, nausea hepatosplenomegaly, fever, weight loss or night sweats, etc. [5]

Imaging findings are nonspecific and can mimic other liver diseases such as hepatic tumors or metastasis which lead to a diagnostic challenge [6]. Sometimes Hepatic TB may be asymptomatic leading directly to several complications like miliary, fulminant hepatic failure and death if not early diagnosed and properly managed [4-6].

We report a case of hepatic TB in a cabin crew member diagnosed accidentally by investigating perturbation of liver chemistry tests performed in a systematic aeromedical fitness. Through this case we reveal the interest of liver chemistry tests (realized for pilot and crew members every one and two years respectively) in leading to early diagnosis for some rare pathology, avoiding complications, and preserving life and flight safety.

The diagnosis of hepatic TB leads to unfitness to fly and requires rationally specific fitness assessments.

Case presentation:

We report a case of a 28-year-old woman Moroccan cabin crew member who came to the aeromedical expertise center at the military hospital of Rabat for her periodic medical assessment. She has no medical history, no smoking, and no alcohol or drug consumption. She was declared to be asymptomatic.

Physical examination was normal. Liver and spleen were not palpable with any jaundice and there was no palpable lymphadenopathy.

Chest X-ray was normal within opacities.

Systematic chemistry liver tests showed abnormalities: y-glutamyltransferase (up to three times the upper limit of normal (ULN)), the elevation of aminotransferases (up to two to three times the ULN) (cf. Table 1).

Erythrocytes sedimentation rate (ESR) was elevated at 50 mm in the first hour.

The complete blood count was normal (cf. table 2).

Abdominal ultrasonography revealed nodular hepatomegaly.

Abdominal CT showed low-density multiple liver nodules without bile duct dilatation (cf. figure1).

Liver MRI showed a well-defined liver round mass, with different size hypointense on T1 hyperintense on T2 moderated with intermediate B-value diffusion enhanced in portal time with late homogenization (cf. figure2).

This aspect was highly suspected of malignancy.

An ultrasonography-guided percutaneous liver biopsy was performed, and a histopathological examination of the specimen showed caseation granulomas with epithelioid histiocytes and giant cells. Acid-fast bacilli (AFB) were detected on a smear examination.

The diagnosis of isolated hepatic tuberculosis was confirmed after excluding other localization of tuberculosis and anti-tubercular drugs were prescribed for 9 months. The cabin crew was declared unfit to fly.

After 3 months of treatment without any adverse effects, chemist liver tests and ESR were normal with the total disappearance of liver lesions (cf. Figure 3). Therefore, the patient was declared fit to fly by derogation.

Discussion:

Several forms of hepatic involvement of TB are described in the literature, but the most common form is the miliary form. Hepatic involvement of TB in the absence of miliary or pulmonary/extrapulmonary TB is a rare entity and constitutes less than 1% of all cases [1, 4]. Because low oxygen tension in the liver is unfavorable for mycobacteria growth [7]. It is believed that the route of transmission is different in miliary TB from primary hepatic TB. In the miliary form of T,B the route of dissemination is similar to other forms of extrapulmonary TB which result from hematogenous dissemination of the infection through the hepatic artery [5]. While in primary hepatic TB, the tubercle bacillus reaches the liver through the portal vein from primary intestinal TB [8], the infection may also reach the liver by lymphatic spread [9].

A variety of diseases and conditions favor the development of active TB such as tobacco smoking, intravenous drug use, malnutrition, and severe underweight, diabetes, HIV infection, immunosuppressive treatment, chronic renal failure, silicosis, gastrectomy, and jejunoileal bypass. [10]. In the case presented, we don't recognize any risk factor presented by our flight attendant, she was HIV negative without a history of smoking or drug use.

The most frequently encountered clinical and laboratory findings described in literature are fever with chills, weight loss, abdominal pain, jaundice splenomegaly, hepatomegaly in 94-

100% of cases in nodular form simulating a cancer of the liver or tender form simulating liver abscess [1,4,7,9]. Liver enzymes are elevated in only 25% of patients [1]. In this case report, the patient was asymptomatic; no hepatomegaly was detected in physical examination with only an elevated aminotransferase and γ-glutamyltransferase level's.

Hepatic TB has no characteristic imaging features and can closely mimic primary liver malignancy or metastasis [4, 7, 9], or other liver diseases like sarcoidosis and lymphoma [9]. Computed tomography is superior to ultrasound scanning for identification of hepatic disease, it can shows intrahepatic hypodense lesions or liver calcifications and can be used to guide liver biopsies which is the most useful tool to confirm the diagnosis.

It is very difficult to differentially diagnose using imaging modalities primary hepatic TB from intrahepatic cholangiocarcinoma (iCCA). MRI of hepatic TB shows a hypointense nodule with a hypointense rim on T1-weighted imaging, a hypointense, isointense or hyperintense nodule with a less intense rim onT2-weighted imaging [8]. Hepatic TB also shows FDG-avidity on F-18 FDG PET/ CT similar to other malignant tumors [11]. F-18 FDG PET/CT is also less useful in differentiating hepatic TB from other hepatic necrotic masses because FDG-avidity can also been seen in necrotic tumors such as hepatocellular carcinoma, iCCA, and metastatic carcinoma [8].

Our patient had multiple nodules expanded to both lobes of the liver on CT-scan and MRI; this aspect was highly suspected of malignancy. PET /CT was not performed in our case.

Once the diagnosis of hepatic tuberculosis has been made and other localizations or a military were excluded, anti-tubercular therapy will be started for a minimum of 6 months, rifampicin and isoniazid for the duration of treatment with additional pyrazinamide and ethambutol during the induction. Some clinicians use an extended antibiotic course to reduce the risk of

relapse [5,9], although some recent publications indicate that at least 1 year of medical therapy is required [4,6]. Our patient was treated for 9 mounts.

The prognosis is usually good in most of cases after an early diagnosis and anti-tubercular treatment with a good clinical response (disappearance of symptoms, increases in appetite and weight gain) [6, 9].

The response to treatment in case of hepatic TB must be assessed by clinical findings, radiological and biological investigations. In our case, we had a normalization of liver chemistry tests after 3 mounts of treatment with total disappearance of liver nodules on CT-scan and MRI.

In aircrew, hepatic TB is considered as a cause of temporary disqualification because symptoms or excessive fatigue are incompatible with safe flying conditions. Moreover anti tubercular drug has a significant side effect [12] of aeromedical concern mainly in the induction phase where there is a high risk of hypersensitivity reaction especially to Isoniazid. There is also a risk of convulsion, peripheral neuropathy, arthralgia, and hyperuricemia with a risk of gout attack caused by Pyrazinamide. The most redoubtable and serious side effect is retrobulbar optic neuritis due to Ethambutol, it occurs within two months of starting medication and includes dyschromatopsia (red-green), decreased visual acuity, central scotoma, visual evoked potentials (VEP) alteration, and finally optic atrophy. This latest effect should be taken into account when resuming flying duties.

Hepatotoxicity must be periodically assessed for all duration of anti-tubercular treatment.

In addition to those side effects, there are other constraints which can make the aircrew unfit to fly. For instance, the long missions cause problems in anti-tubercular drug availability and biological monitoring hardness, besides the constraints due to jet lag in perturbing the schedules of drug taking.

Concerning our patient, she's a cabin crew member and she must be in good health to do her expected duties in managing the aircraft cabin during the trip she must be able to take action if an in-flight or on-ground emergency occurs. During her periodical aeromedical fitness, we discovered liver chemistry abnormalities related to hepatic TB in an asymptomatic phase. The anti-tubercular drug was started for 9 months after excluding other prevalent localizations of TB and she was declared unfit to fly.

After 3months of treatment, normalization of liver chemistry values, and liver MRI imaging, allow our flight attendant to get her flight duties through a waiver delivered by the Moroccan expert committee of aerospace medicine, with some restrictions such as a quarterly control and unfitness for long haul flight until total recovery and end of her treatment.

Conclusion:

Hepatic TB is a rare entity and lacks typical symptoms, signs, and laboratory data. Imagining features are various and nonspecific making the diagnosis challenging. But it should be suspected especially in endemic areas for TB.

Through this case we highlighted the role of hepatic chemistry test monitoring during the periodical medical exam to diagnose some diseases in the initial stage before symptoms appear, avoiding complications and preserving life and flight safety.

Hepatic TB isn't a permanent bar of flying, anti-tubercular treatment while effective, requires a period of grounding due to adverse events with some probable potential aeromedical implications as described previously. Aircrew with hepatic TB will need to be assessed for both complete disease control and full resolution of any iatrogenic side effect of anti-tubercular drugs when resuming flying duties.

Ethical Approval:

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

Consent

As per international standard or university standard, patient(s) written consent has been collected and preserved by the author(s).

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chemistry liver tests	value	Limit normal
GGT(y-glutamyltransferase)	**101** U/L	< 32 U/L
Aspartate aminotransferase(AST)	**84** UI/L	<35UI/L
Alanine transaminase(ALT)	**68** UI/L	<40UI/L

Table1: Chemistry liver tests abnormalities.

Data	**Value**	**Normal value**
White blood cells	$8,0x10^3$/ µl	(4,0-10,0)
Lymphocytes	2,9	(1,5-4,0)
Neutrophils	4,3	(1,5-7,5)
Monocytes	0,6	(0,1-0,8)
Eosinophils	0,2	(0,0-0,5)
Basophils	00	(0,0-0,1)
Red blood cells	$4,64x10^6$	(3,9-5,5)
Hemoglobin	14,4 g/dl	(12-16)
hematocrit	41,5%	(36,0-47,0)
Platelets	$302x10^3$/µl	(150-450)

Table2: Data of complete blood count test.

Figure1: CT-scan showing multiple liver low-density nodules without enhancement.

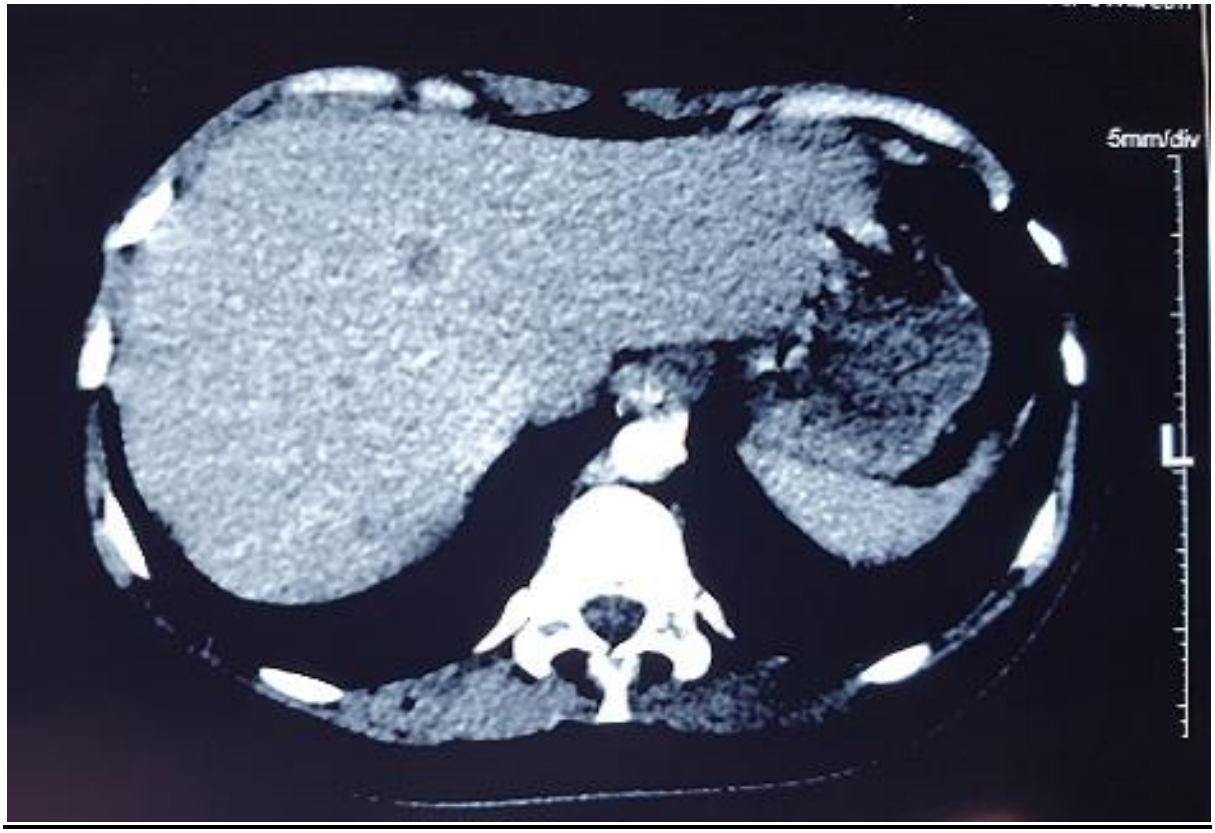

Figure2: MRI T2 weighted sequence showing multiple hyper signal nodules.

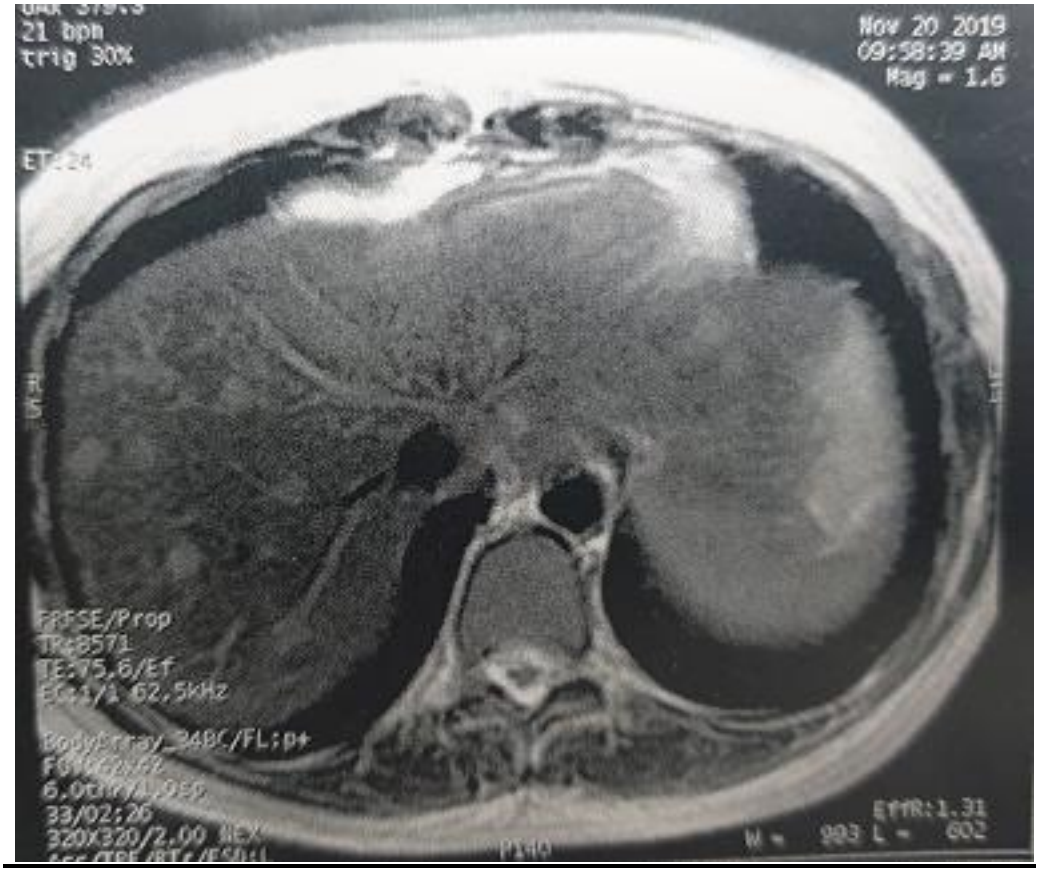

Figure3: Follow-up CT-scan of the abdomen 3 months under anti-tubercular drug, showing complete regression of the liver nodule.