

CASE REPORT

## Diagnosing lepromatous leprosy by liver biopsy: A case of granulomatous hepatitis

NAIARA A. FRAGA BRAGHIROLI<sup>\*<sup>\*\*\*</sup></sup>, PEDRO  
D. OLIVEIRA<sup>\*<sup>\*\*\*</sup></sup>, MOYSES SADIGURSKY<sup>\*\*\*\*</sup> &  
PAULO R.L. MACHADO<sup>\*</sup>

<sup>\*</sup>*Universidade Federal da Bahia, Salvador, Bahia, Brazil*

<sup>\*\*</sup>*FIOCRUZ, Bahia, Brazil*

<sup>\*\*\*</sup>*Universidade Federal de Sergipe*

<sup>\*\*\*\*</sup>*Serviço de Imunologia – HUPES, Universidade Federal da Bahia, Salvador, Bahia, Brazil*

Accepted for publication 15 August 2018

*Summary* Hansen's disease (HD) is a chronic and contagious disease caused by *Mycobacterium leprae*. After the neurocutaneous system and the lymph nodes, the liver is the organ most commonly affected, secondary to hematogenous dissemination of the bacilli to the liver, immune-mediated inflammatory infiltrate in reactional states or due amyloid deposits may also be detected in the liver. The authors report on a patient with lepromatous HD whose initial symptoms and diagnosis relied in the presence of granulomatous hepatitis by liver biopsy. Although liver involvement in leprosy is more frequent than suspected, clinical manifestations resulting from its damage are uncommon. Therefore, when treating a patient with multibacillary HD, physicians should be aware that this is a multisystemic disease and that multiple organs may be affected. Furthermore this case also shows that the slow skin infiltration in lepromatous HD may be associated with lack of clinical diagnosis and favor a severe compromise in internal organs.

*Keywords:* Hansen's diseases, Leprosy, granulomatous hepatitis

### Introduction

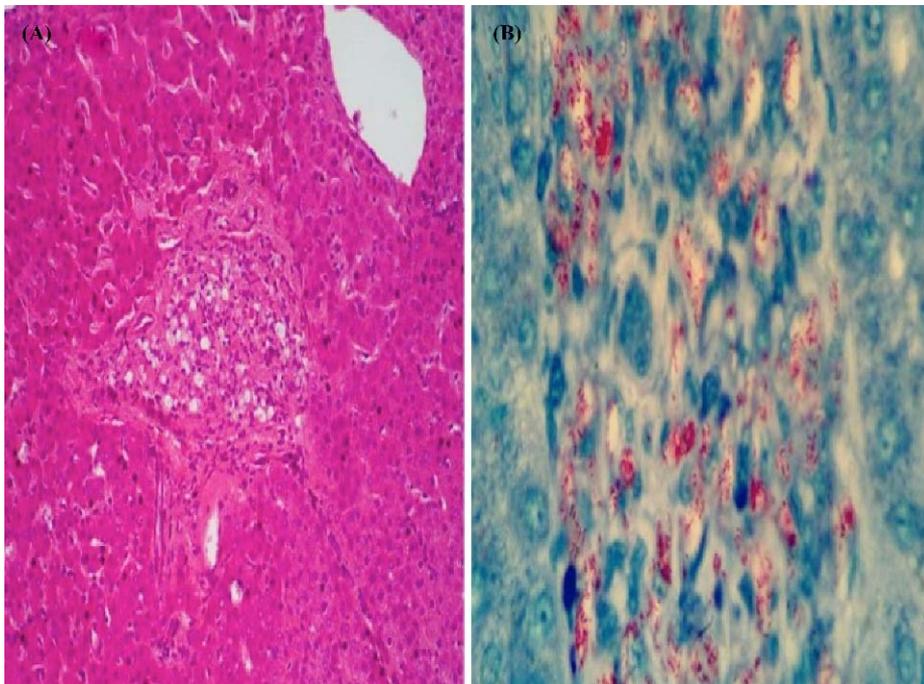
Leprosy or Hansen's disease (HD) caused by *Mycobacterium leprae* affects predominantly skin and peripheral nerves, but liver involvement can occur with high bacterial load. For instance, the incidence of liver involvement ranges from 4–100% in the multibacillary forms of the disease.<sup>1</sup> In addition to the granulomatous reaction that occurs after hematogenous

Correspondence to: Naiara Abreu Fraga-Braghiroli, MD, PhD, Rua Padre Feijó s/n Canela, Salvador, Bahia, Brazil (e-mail: nfraghiroli@gmail.com)

dissemination of the bacilli to the liver, immune-mediated inflammatory infiltrate in reactional states and amyloid deposits may also be detected.<sup>2-4</sup> The authors report a patient with lepromatous HD with granulomatous hepatitis. The aim of this study is to alert physicians about this multi-faceted disease. When treating a patient with multibacillary HD, physicians should be aware that this is a multi-systemic disease that may affect multiple organs.

### Case Report

A 58-year old male, farmer, originally from Feira de Santana, Bahia/Brazil, presented to the University Hospital in Salvador, Bahia/Brazil with a history of leg edema over the past 7 years, associated with epistaxis, choluria and erythematous nodules in the lower extremities. The patient has no significant co-morbidities and he did not take medications other than ibuprofen for arthritis. A physical examination showed lower extremities edema, hepatosplenomegaly, jaundice and erythematous subcutaneous nodules on his chest, back and legs. A complete metabolic panel showed elevated liver enzymes. Abdominal ultrasonography revealed hepatosplenomegaly and calculous cholecystitis. Magnetic resonance cholangiography showed cholelithiasis, choledocholithiasis and dilatation of the choledochus. The patient underwent an endoscopic retrograde cholangiopancreatography, revealing dilatation of the extrahepatic bile ducts with choledocholithiasis. Despite drainage



**Figure 1.** (A) Liver biopsy showed slightly enlarged portal spaces containing clusters of histiocytes with abundant microvacuolated cytoplasm and early granulation formation without giant cells or necrosis (H&E  $\times 100$ ). (B) Ziehl-Neelsen stain ( $\times 400$ ) detected multiple clusters of acid-fast bacilli.

**Table 1.** Laboratory values at admission and follow up.

Laboratory tests	At admission	At discharge from hospital	23 months later	Reference Values (men)
White blood cell count ( $10^3 \times \text{mm}^3$ )	5400	3600	5900	5000–10000
Segmented neutrophils/Lymphocytes ( $10^3 \times \text{mm}^3$ )	3618/1620	2376/1080	4012/1593	1800–7700/1000–4000
Hemoglobin (grams/dl)/ Hematocrit (%)	9.0/28.5	8.7/29.1	9.1/27.7	15 ( $\pm 2$ ) 35–45
Platelets ( $\text{mm}^3$ )	205,000	149,000	117,000	150000–400000
Prothrombin time (%) /IRN	90%/1.15	95%/1.01	100%/1.0	70–120%/0.9–1.26
AST/ALT (U/L)	65/81	81/92	36/41	16–37/30–65
Alkaline phosphatase (U/L)	1335	3246	1805	50–136
Gamma GT (U/L)	743	529	15	10–20
Bilirubins/Direct Bilirubin/Indirect Bilirubin (mg/dl)	1.6/1.2/0.4	1.52/0.66/0.86	0.72/0.38/0.34	< 1.1/< 0.8/< 0.3
Total proteins (grams/dl)	9.7	7.2	6.5	6.0–8.5
Albumin/globulin (grams/dl)	2.6/7.1	3.1/4.1	3.4/2.1	3.5–5.5/1.4–3.2
Serology for hepatitis B (HBsAg, Anti-HBc, Anti-HBs) and Hepatitis C (Anti HBC)	Non-reactive			Non-reactive

of the bile duct via a suprapapillary fistulotomy the liver enzymes remained elevated. Liver biopsy showed enlarged portal spaces containing clusters of histiocytes with abundant microvacuolated cytoplasm and early granulation formation (Figure 1A). Grocott's methenamine silver stain was negative for fungal elements and the Ziehl-Neelsen stain detected clusters of acid-fast bacilli (Figure 1B).

The final diagnosis was granulomatous hepatitis consequent to lepromatous leprosy. During this admission the bacillary index from a skin smear was 5.0. Tuberculosis was ruled out with a negative IFN gamma release assay and a normal chest radiography. Multidrug therapy (MDT) was initiated with rifampicin 600 mg monthly, clofazimine 300 mg monthly and 50 mg daily, and dapsone 100 mg daily. The patient's jaundice improved and the cutaneous nodules diminished in size. In the third month of MDT the patient progressed with hemolytic anemia. Dapsone was discontinued and ofloxacin 400 mg/day was initiated. Four months later, the patient experienced painful erythematous nodules on his arms, consistent with erythema nodosum leprosum (ENL), which regressed spontaneously. Three months later, thalidomide 100 mg/day was initiated due to the recurrence of the ENL/Type 2 reaction. The patient completed 24 doses of MDT and serum level of transaminases as well as bilirubin have returned to normal levels (Table 1) without recurrence of ENL.

## Discussion

Leprosy is a spectral disease in which the interaction of *M. leprae* and the cellular immune host response may lead to a localised and non-contagious form (tuberculoid pole), or to several borderline presentations with variable degrees of clinical manifestations and bacterial load, up to the lepromatous pole where a high bacillary load is reflected by cutaneous disseminated and infiltrating lesions in multiple visceral organs. Organ dysfunction varies with the degree of bacterial infiltration and acute inflammation during reactional episodes.<sup>1–4</sup>

Liver involvement in Hansen's disease is often asymptomatic. The incidence of hepatomegaly occurs in 30–40% of cases, especially during reactional episodes.<sup>2</sup> In the lepromatous form, alterations in liver function and enzymes may occur following damage to the hepatobiliary and muscular systems, respectively.<sup>5,6</sup> Other possible causes are immune complex deposits, drugs or other concomitant diseases.<sup>1,3</sup> Mild hepatomegaly may occur as a result of direct mycobacterial infiltration or from an immune complex-mediated reaction syndrome.<sup>7–10</sup> A more severe hepatic involvement was reported by Mendiratta *et al*, when he described a case of fulminant hepatitis in a 15-year old boy leading to cardiac death secondary to lepromatous hepatitis.<sup>11</sup>

In the present case, the Type 2 reaction and the choledocholithiasis were the main factors responsible for the increasing in the transaminases and canalicular enzymes levels. The reactional episode may also have contributed to the onset of jaundice due to the presence of inflammatory infiltrate extending up to the junctional ducts, bile retention, or involvement of the entire hepatic lobe due to the acute reactional inflammatory process.<sup>2</sup> The MDT was continued for 24 months due to the high pretreatment bacillary index (>4+) and internal organs involvement, factors associated with relapses.

When treating a patient with multibacillary HD, physicians should be aware that this is a multi-systemic disease that may affect multiple organs.<sup>2,3,6</sup> The slow skin infiltration in lepromatous HD may be associated with lack of clinical diagnosis and favour a severe compromise in internal organs.

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