Etiological role of brucellosis in autoimmune hepatitis

Colakoglu Onder, Taskiran Bengur, Adnan Kirci, Tunakan Mine, Buyrac Zafer, Unsal Belkis, Aksoz Kadir, Yorukoglu Gazi

INTRODUCTION

Brucellosis can present with various manifestations and may involve any organ in the body. Hepatic pathology comprises noncalcified granulomas, suppurative abscesses, and mononuclear cell infiltration. Liver and spleen enlarge in 15-20% of cases. Elevated liver enzymes and bilirubin levels accompany these pathologies.

CASE REPORT

A woman, who was diagnosed with brucellosis by serological and clinical means three months ago, received a treatment regimen of doxycycline and streptomycin. She was admitted to hospital because of partially improved fatigue and elevated liver enzymes.

Biochemical tests yielded AST 140 IU/L, ALT 122 IU/L,
Table 1  AIH scoring system

| Category                        | Feature                     | Score | Patient |
|---------------------------------|-----------------------------|-------|---------|
| Gender                          | Female                      | +2    | +2      |
| ALP:AST (or ALT) ratio          | <1.5                        | +2    | -2      |
|                                 | 1.5-3.0                     | 0     |         |
|                                 | >3.0                        | -2    |         |
| Gamma globulin or Ig G levels over normal values | >2.0 | +3    | +3      |
|                                 | 1.5-2.0                     | +2    |         |
|                                 | 1.0-1.5                     | +1    |         |
|                                 | <1.0                        | 0     |         |
| ANA, SMA, or anti-LKM1 titer    | >1.80                       | +3    | +3      |
|                                 | 1.80                        | +2    |         |
|                                 | 1.40                        | +1    |         |
|                                 | <1.40                       | 0     |         |
| AMA                             | Positive                    | -4    | -4      |
| Viral markers                   | Positive                    | -3    | +3      |
|                                 | Negative                    | +3    |         |
| Drugs                           | Yes                         | -4    | -4      |
|                                 | No                          | +1    |         |
| Alcohol                         | <25 g/d                     | +2    | +2      |
|                                 | >60 g/d                     | -2    |         |
| HLA                             | DR3 or DR4                  | +1    |         |
| Immune disease                  | Thyroiditis, colitis,       | +2    | 0       |
|                                 | synovitis, others           |       |         |
| Other liver-related antibodies  | Anti-SLA/LP, anti-aktin,    | +2    | 0       |
|                                 | anti-IC, p-ANCA             |       |         |
| Histologic features             | Interface hepatitis         | +3    | +3      |
|                                 | Plasmocytes                 | +1    | +1      |
|                                 | Rosette formation           | +1    | 0       |
|                                 | None of the above           | -5    | 0       |
|                                 | Bilary changes              | -3    | -3      |
|                                 | Other features              | -3    | 0       |
| Response to therapy             | Complete                    | +2    | +2      |
|                                 | Relapse                     | +3    |         |
| Score before therapy           | >15                         | 6     |         |
| Absolute diagnosis              | >10                         | 10-15 |         |

Abbreviations: ALP, serum alkaline phosphatase level; AST, serum aspartate aminotransferase level; ALT, serum alanine aminotransferase level; ANA, anti-nuclear antibody; SMA, smooth muscle antikoru; anti-LKM1, antibody against liver/kidney type 1; AMA, anti-mitochondrial antibody; anti-SLA/LP, antibody against soluble liver antigen/liver pancreas; anti-LC1, antibody against liver cytosole type 1; p-ANCA, perinuclear anti-neutrophilic cytoplasmic antibody.

DISCUSSION

Liver involvement due to brucellosis recurrence and toxic hepatitis was suspected at admission. Microvesicular fatty infiltration, suggesting toxic hepatitis due to tetracycline and doxycycline, was not evident. Hence, histopathology did not support toxic hepatitis. Liver biopsy yielded bile duct injury, interface hepatitis, and plasmocyte infiltration. As a result we focused on AIH and evaluated immunologic markers of AIH, ANA positivity supported AIH. Increased gamma globulin levels, female gender, negative viral markers, and absence of alcohol usage also supported the diagnosis. Unfortunately anti-SLA/LP, anti-aktin, anti-IC, and HLA tests were unavailable.

AST and ALT levels (3.5 and 3.0 times UNL) in our case were not in the range of a typical AIH case (more than 5.0 times UNL). In most cases of AIH, AST and ALT are below 500 IU/L. Bile duct injury and increased ALP/AST and ALP/ALT ratio indicated cholestatic component. Absence of ductopenia, nondestructive nature of cholangitis, and periductal infiltration supported PBC in spite of PSC component. AMA positivity was also valid for PBC. As in PBC, ALP was predominantly elevated than AST and ALT.

The case was diagnosed with an overlap syndrome according to the AIH scoring system probably triggered by doxycycline. Clinical and biochemical response to steroid and UDCA therapy is achieved.

Liver involvement in brucellosis is not restricted to granulomatous hepatitis; nonspecific cell infiltration (mononuclear cell and plasmocyte) is evident in most cases. This finding suggests that hepatic involvement of brucellosis may contribute to hepatic injury in our case. Furthermore, an overlap syndrome triggered by brucellosis is also open to discussion. Whether brucellosis or doxycycline is a trigger of overlap syndrome is an important question waiting for an answer. We think that our case demands attention since there is only one case in the literature about hepatitis developed after brucellosis infection and doxycycline usage.
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