Acute Cholecystitis with Granulomatous Hepatitis as Atypical Clinic Presentation of Brucellosis: Case Report and Review of Literature

Brusellozisin Atipik Klinik Prezentasyonu Olarak Granülomatöz Hepatit ile Birlikte Akut Kolesistit: Olgu Sunumu ve Literatürün Gözden Geçirilmesi

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ABSTRACT Brucellosis is a zoonotic infection transmitted from animal to human. The infection is endemic in many countries, mainly in the Mediterranean basin, the Middle East, India, parts of south and central America and east and western Africa. Human brucellosis is a multisystemic infection caused by species of Brucella that produces a wide spectrum of clinical symptoms.The most common gastrointestinal complication is granulomatous hepatitis. Acute cholecystitis due to Brucella species is a very rare manifestation. Here we report the case of a 35-year-old male with acute cholecystitis and hepatic mass like granuloma caused by Brucella spp and a review of previously reported cases.

Key Words: Acute cholecystitis; brucella; biopsy

ÖZET Brusellozis hayvanlardan insanlara bulaşan bir zoonozdur. Enfeksiyon başlıca Akdeniz havzası, Orta Doğu, Hindistan güney ve Orta Amerika, Doğu ve Batı Afrika olmak üzere birçok ülkede endemiktir. İnsan brusellozisi geniş klinik semptomlar meydana getiren Brucella türlerinin etken olduğu, multisistemik bir enfeksiyondur. En yaygın gastrointestinal komplikasyon granülomatöz hepatittir. Brusella türlerinin sebep olduğu akut kolesistit çok nadir bir durumdur. Burada Brucella mikroorganizmasının neden olduğu akut kolesistit ve hepatik brucellomalı 35 yaşında erkek hastayı rapor ettik ve daha önce yayınlanmış derlemeleri gözden geçirdik.

Anahtar Kelimeler: Akut kolesistit; brusella; biyopsi

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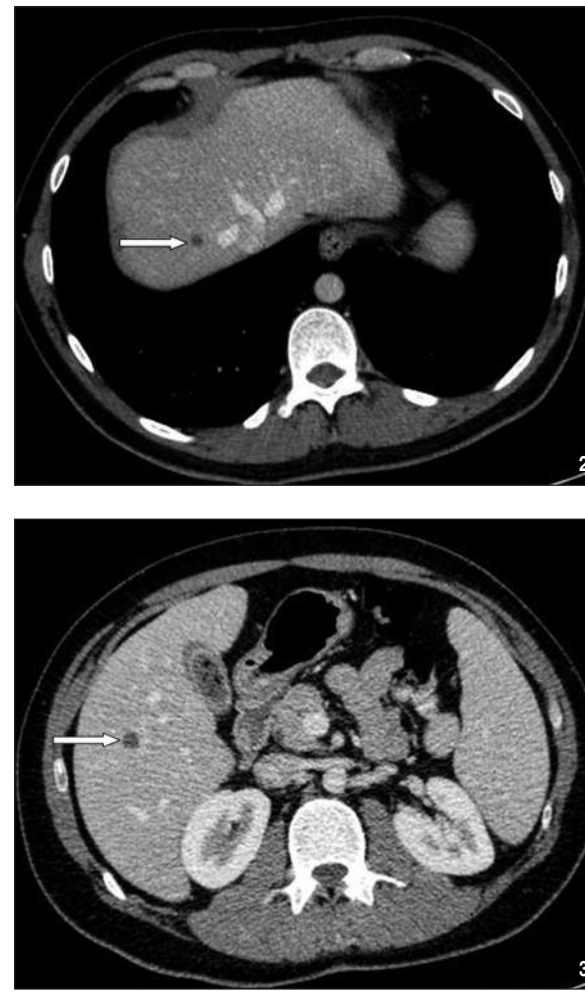
Bruceleosis is a zoonosis that is common worldwide, and highly endemic in the Mediterranean basin, Middle East, India, Mexico, and central and south America. Human brucellosis is a systemic infection, which is caused by Brucella species, and produces a wide spectrum of clinical symptoms. Complications can affect almost all organs and systems. Cholecystitis is a rare complication of brucellosis.[1-10] Here, we present a case report of a patient, whose first clinical symptom of brucellosis was acute cholecystitis with hepatic brucelloma as mass-like. We also reviewed previously reported cases of brucella cholecystitis. To the best of our knowledge, this is the first case reported in the English language medical literature.

CASE REPORT

A 35 year-old male was admitted to our hospital, presenting abdominal pain, chills, fever and night sweats. The onset of epigastric pain, fatigue, fever and anorexia was one week prior to his admittance. The abdominal pain started in epigastric area and became localized to the right upper quadrant. On physical examination, the patient exhibited febrile and right upper quadrant tenderness. Abdominal examination showed a positive Murphy's sing. A preliminary diagnosis of acute cholecystitis was made. Laboratory findings were as follows: alkaline phosphatase 99 U/L, hemoglobin; 8.9 g/dL, MCV: 92.3 fl, leukocyte 16 000/mm^3, trombocyte: 137 000/mm^3, MPV: 7.1 Fl, total protein: 6.2 g/dL, gamaglutamyl transferase: 28 u/L, aspartate amino transferase: 46 u/L, alanine amino transferase: 27 u/L, C-reactive protein: 176 mg/dL, sedimentation: 70 mm/hour. Ultrasound scan (US) and computed tomography (CT-scan) showed a thickened gall bladder wall with echogenic bile containing multiple stones, consistent with acute calculus cholecystitis. Also US and CT-scan revealed multiple hipoechocoic and heterogen masses with maximum diameter of 16 mm in right lobe and mild splenomegaly (Figures 1-3). Initially radiologic manifestations of the masses could mimic haemangioma or metastasis. US-guided multiple core needle biopsies of the liver were performed to rule out malignite. Empiric antibiotherapy was started. Liver biopsy revealed coalescing granuloma with caseous necrosis but no malignite features could be obtained (Figure 4). A cholecystectomy was

FIGURE 1: Sonogram of the right lobe of the liver shows a hypoechoic lesion (arrow).



FIGURES 2,3: Contrast enhanced computed tomography shows a low density lesion (arrow).

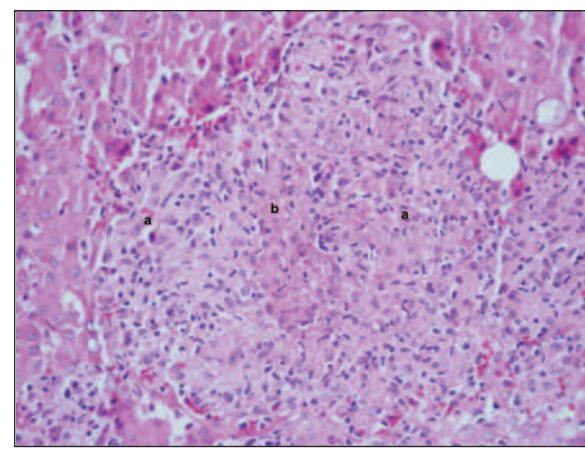


FIGURE 4: Histopathological examination of the liver core biopsy showing epitheloid cell granuloma (a) caseification necrosis (b) and liver parenchyma (H&E; x400).

TABLE 1: Characteristics of reported cases of brucella cholecystitis.

Author (Ref)	Year	Age/Sex	Risk factor	Symptom	Spleno-megaly	Hepato-megaly	Gall Stones	Gall bladder removed	Blood culture	Bile culture	SAT titre	Histo-pathology	Treatment
Shaheen[1]	1989	42/F	No	Right upper quadrant pain, fever, repeated vomiting	No	No	Present	Yes	B. melitensis	B. melitensis	1/650	Acute and chronic inflammation	Tetracycline +streptomycine
Colmenero[2]	1996	58/M	Shepherd	Fever, chills, sweating, right upper quadrant pain	NR	Yes	Present	Yes	B. melitensis	Negative	1/160	Granulom+chronic cholecystitis	Doxycycline+ rifampin
Fasquelle[3]	1999	72/F	Contaminated milk or dairy products	Abdominal pain, fever	NR	NR	Present	Yes	B. melitensis	B. melitensis	1/80	Acute and chronic inflammation	Doxycycline+ rifampin
Ashley[4]	2000	6/ M	No	Abdominal pain, fever, fatigue, loss appetite	Yes	No	Absent	No	B. melitensis	NA	NA	-	TMP/SMZ+ rifampin
Miranda[5]	2000	34/M	Contact with sheep and goat several year before	Cramp type abdominal pain, fever, nausea, vomiting	NR	NR	Present	Yes	Negative	B. melitensis	1/2560	Acute and chronic inflammation	Doxycycline+ rifampin
Andriopoulos[6]	2003	72/M	Shepherd	Abdominal pain, low back pain, fever, arthralgias	NR	NR	Absent	Yes	B. melitensis	B. melitensis	1/160	Granulom+acute and chronic cholecystitis	Doxycycline+ streptomycine
Kanafani[7]	2005	55/M	No	Epigastric and right upper quadrant pain, vomiting	NR	NR	Present	Yes	B.spp	B.spp	1/160	Acute and chronic inflammation	Doxycycline+ rifampin
Kanafani[7]	2005	29/F	No	Epigastric and right upper quadrant tenderness	NR	NR	Present	Yes	Negative	B.spp	1/640	Acute and chronic inflammation	Doxycycline+ rifampin
Gunal[8]	2008	64/F	Eat homemade cheese	Abdominal pain, chills, malaise, arthralgia	NR	Yes	Absent	No	B. melitensis	NA	1/320	-	Doxycycline+ rifampin+ streptomycin
Starakis[9]	2008	54/M	Eat unpasteurized dairy product	Fever, rigors and night sweats	Mild	Yes	Absent	Yes	B. melitensis	Negative	NR	Chronic inflammation	Doxycycline+ rifampin
Al-Otaibi[10]	2010	45/M	Drink raw Milk	Cramp type abdominal pain, fever	NR	NR	Absent	No	B. melitensis	NA	1/2560	-	Doxycycline+ streptomycin
Haltas*	2011	35/M	Eat homemade cheese	Abdominal pain, chills, fever, night sweats	Mild	No	Present	Yes	B.spp	NA	1/160	Chronic inflammation	Rifampin+ tetracyclin

NR: Not reported; NA: Not applicable. *Present report.
TMP/SMZ: Tetracycline-Streptomisin-Doxycycline-Ripampin-Kotrimoksazol; SAT: Standart agglutination test.

performed and liver biopsy was taken from an area with normal appearance. After operation, Brucella spp. was isolated from blood culture. Gall bladder biopsy revealed chronic calculous cholecystitis and liver biopsy revealed granulomatous hepatitis consistent with brucella. Granulomas were not observed in wall of the gall bladder. The patient's medical history revealed that the consumed homemade raw cheese and his father was treated for brucella previously. He was diagnosed as having brucella related cholesystitis and hepatic brucelloma. The patient was discharged and was prescribed tetracycline with rifampisin for 3 months. The patient had an uneventful recovery. Informed consent was obtained from the patient.

DISCUSSION

Brucella infection is a systemic disease, but the microorganism rarely causes infection in the gastrointestinal system. Cholecystitis is a very rare complication of brucella with few reported cases.[1-10] Hepatic brucelloma (pseudo-tumoral hepatic brucellar caseous necrotizing granuloma) rarely manifest itself first clinically and is most often latent. The involvement of the liver by brucellosis is almost constant and is asymptomatic. Sometimes the clinical manifestation of hepatic brucelloma can mimic malignant liver tumors, metastasis and other tumors. To the best of our knowledge calculus cholecystitis with hepatic brucelloma with presentation of multiple masses hasn't been described previously.

In a review of English language literature (Medline 1898-2010), only 11 cases about acute cholecystitis by brucella have been reported previously, excluding this case. Table 1 shows the characteristics of reported cases of brucella cholecystitis (Table 1). The mean age of patients is 47 (range 6-72 y) and there were 8 male and 4 female patients. All patients had complaints and clinical symptoms which suggested acute cholecystitis. Seven patients had a brucellosis risk factor. One patient had history of contact with sheep and goat several years before. Two patients were shepherds. In four cases reported by Fasquelle, Gunal, Starakis and Al Otaibi,[10] brucellosis was linked to unpasteurized contaminated milk and dairy products.[3,8-10] Our patient stated homemade cheese consumption in his medical history and he said that his father was treated for brucellosis before. Gallstones were present in 6 cases.[1-3,5,7] Gall stones were detected in our Brucella Cholecystitis patient also. Eight patients underwent cholecystectomy. Histopathological examination of gall bladders showed chronic inflammation in one case and acute and chronic inflammation in six patients. Only two cases showed the presence of granuloma. In our case chronic inflammation was detected while granuloma wasn't observed in gall bladder wall. In six patients, Brucella spp. was isolated in the bile culture. In ten cases, brucella spp. was isolated in blood cultures. Six patients had B. melitensis and one had B. abortus isolated in the blood.

Brucella species are usually associated with bacteremia and systemic infection. Brucella spp. may reach the gall bladder and liver either by lymphatic vessels or via blood. There were no reports on chronic carriage of brucella in the gall bladder. But it may cause latent infection which only produces clinical symptoms months or years after its onset. Localized brucellosis may result as complication of bacteremia or may be the only manifestation of chronic infection. In this case, brucellosis resulted in acute cholecystitis associated with localized infection (hepatic brucelloma).

Different antimicrobial drug regimens have been used in the treatment of brucellosis including the following in various combinations; TMP/SMZ, rifampicin, doxycycline, ciprofloxacin, gentamycin, streptomycin. Currently recommended treatment regimens include tetracycline or doxycycline with rifampin.

CONCLUSION

Brucella is still a common public health problem in many parts of the world. Surgeons, physicians, radiologists and pathologists should be alerted to the atypical surgical presentation of the disease in endemic regions.

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