

### **Brucellosis with Spondylitis**

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**We are reporting what we think is probably the first case of brucellosis in a Bahraini patient. Our patient was a 54 year old Bahraini who presented with a history of fever of three weeks and back pain. He has elevated liver enzymes, highly positive brucella serology and his spinal MRI revealed multilevel spondylitis. He was diagnosed as having Brucellar spondylitis and was treated with two courses of antibiotics over a period of 8 months. He improved dramatically and was discharged from the hospital in March 2007 and since then he had no recurrence.**

#### ***Bahrain Med Bull 2007; 29(4):***

Brucellosis is a severe public health and socioeconomic problem in many countries throughout the world<sup>1</sup>. In countries of the Middle East, brucellosis was reported in almost all domestic animals, particularly cattle, sheep and goats. It has been reported in racing camels in the United Arab Emirates. In Egypt, brucellosis was reported in buffaloes, equines and swine.

*Brucella melitensis* biovar 3 is the most commonly isolated species from animals in Egypt, Jordan, Israel, Tunisia and Turkey. *B. melitensis* biovar 2 was reported in Turkey and Saudi Arabia, and *B. melitensis* biovar 1 in Libya, Oman and Israel. *B. abortus* biovar 1 was reported in Egypt, biovar 2 in Iran, biovar 3 in Iran and Turkey, and biovar 6 in Sudan. The countries with the highest incidence of human brucellosis are Saudi Arabia, Iran, Palestinian Authority dominated area, Syria, Jordan and Oman<sup>2</sup>.

The reported incidence in Bahrain is zero; where as in Saudi Arabia it is a major public health problem. In a study done in Tabuk province in Saudi Arabia, 137 cases were diagnosed in 1997. The incidence rate was 34 /100,000. The most common infecting agents were *Brucella melitensis*, *B. abortus* and *B. Sui*. Splenomegaly and hepatomegaly were detected in 25.5% and 22.6% of cases respectively<sup>3</sup>.

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The aim of this paper was to report a rare case of brucellosis in a Bahraini patient, which we believe is the first case to be reported in Bahrain.

## **THE CASE**

We believe that this is the first case of brucellosis to be reported in Bahrain. Since it is uncommon and the clinical presentation is non-specific, diagnosis can therefore be difficult unless a high index of suspicion is maintained.

A fifty- four years old Bahraini male, a retired civil engineer who was previously healthy except for well controlled hypertension; presented on 23/7/05 with history of fever for three weeks and low back pain for one week. His fever started as a low grade for the first week then increased to a maximum temperature of 40°C over the following two weeks. The fever was associated with chills, rigors and profuse sweating; it subsided with antipyretics. His back pain was localized to the lumbar spine, with limited forward spinal flexion. There was no specific aggravating factor but it was relieved by sitting or lying down. The patient gave a history of drinking unpasteurized goat's milk on regular basis.

Family history and social history were not significant. His physical examination was unremarkable, except for tenderness over the lumbar spine with a spasm of the para spinal muscles.

His initial laboratory findings were normal except for Liver function tests: alkaline phosphatase 177 u/l, Alanine Aminotransferase 225 u/l and Gamma glutamyl transferase 290 u/l.

His Brucella titers were strongly positive and they were as follows Brucella Abortus 1/320 and Brucella Melitensis 1/640.

His chest x-rays, plain radiograph of the spine, CT chest and abdomen were normal. His spinal MRI (as shown in figure 1) revealed the following: Multilevel spondylitis at D10, L4 and L5 with spondylodiscitis at L4/5 level associated with posterior subligamentous phlegmon causing pressure over the anterior and right lateral aspect of the thecal sac at L4/5 level.



**Figure 1: Sagittal T2FS. Initial MRI shows abnormal high signal intensity at T10, T11 L4 and L5 with end plate irregularity and mild narrowing of the intervening disc**

The patient was diagnosed with Brucella spondylitis and started on doxycycline and rifampicin. He showed significant improvement and became afebrile and relief of his back pain. His repeated Brucella titers were negative after four weeks of treatment with a normal liver function test after two weeks of treatment. He received antibiotics for six weeks.

After 8 months of completing the antibiotics course the patient presented with a relapse and worsening of his MRI findings as shown in figure 2. The patient was treated with three antibiotics including doxycycline, rifampicin and gentamicin for six weeks and showed a significant clinical improvement.



**Figure 2: 8 months later; there is significant increase in the signal abnormality of the vertebra with destruction of the endplates and adjacent discs especially at L4/5. New foci of infection appear at L2 and L3 which were very subtle in the initial study**

## DISCUSSION

Human Brucellosis is a systemic infection which may involve any organ of the body. In addition to the forms characterized by the multitude of somatic non-specific complaints, such as fever, sweats, anorexia, fatigue, weight loss, symptoms and signs related to a single system occasionally predominate, when the disease is localized<sup>1</sup>. The most commonly localized form of human brucellosis is osteoarticular form.

Osteoarticular brucellosis was documented by Marston in 1861 at a time when this disease had not been diagnosed as a separate entity. In the following decades, Martson's observation was supported by Bruce and Hughes. It is an important entity because of its high prevalence and associated functional sequel<sup>4</sup>.

Brucellar spinal infection is still common public health problem in many parts of the world including the Middle East, South America and the Mediterranean Basin. The causative agent of brucellosis is hosted by domestic animals: *Brucella melitensis* in goats, *B. abortus* in cattle, *B. suis* in swine, and *B. canis* in dogs<sup>5</sup>.

The organism is transmitted to humans by consuming contaminated milk products or handling infected animals and may persist for many years<sup>6</sup>. The onset can be insidious or acute, generally beginning within 2 to 4 weeks after inoculation. An "undulant" fever pattern is apparent in patients who are untreated for long periods of time. Mild lymphadenopathy is reported in 10% to 20%, and splenomegaly or hepatomegaly in 20% to 30% of cases<sup>6</sup>.

Clinically, back pain is the most common complaint in patients with spinal involvement, as the case with our patient, due to invasion of the richly innervated periosteum<sup>5</sup>. The reported prevalence of brucellar spondylitis ranges from 2.9 to 65%. Spondylitis was most frequent in older patients and in patients with longer history before establishing the diagnosis<sup>1</sup>.

Complications due to indolent infection of the osteoarticular system are very common and result in a high morbidity in brucellosis<sup>5</sup>. Brucellar involvement of the spine can be focal or diffuse and occurs in 10-80 % of patients with chronic brucellosis. The lumbosacral region is most frequently involved in spondylodiscitis, followed by the thoracic and cervical segments<sup>7,8,9</sup>. In our patient the spinal involvement was diffuse and it was involving mainly the thoraco-lumbar area.

Because the symptoms of brucellosis are non-specific, it is important to obtain a detailed history which includes occupation, vacations, travel to endemic areas, and ingestion of high-risk foods, such as unpasteurized dairy products. The white blood cell count is often normal or low and the erythrocyte sedimentation rate is variable<sup>9</sup>.

The diagnosis is made with certainty when brucella is recovered from blood, bone marrow, or other tissues. The rate of isolation ranges from 15% to more than 90% depending on the methods used. Most laboratories now use continuous-monitoring

automated blood culture systems (e.g., BACTEC or BacT/Alert) that have improved the time to isolation and have obviated the need for biphasic media techniques<sup>9</sup>.

*Brucella* is isolated most often from blood and bone marrow; however, in selected cases, urine, CSF, synovial fluid, liver biopsies, lymph nodes, and other tissues can be successful<sup>9</sup>. Polymerase chain reaction (PCR), employing random or selected primers have been used widely in veterinary medicine and to differentiate *Brucella* species. PCR appears to be highly sensitive and specific when used on peripheral blood or other tissues<sup>9</sup>.

In the absence of bacteriologic confirmation, as it is the case with our patient, a presumptive diagnosis can be made by demonstrating high or rising titers of specific antibodies in the serum. A variety of tests have been applied to the serologic diagnosis of brucellosis, of which the serum agglutination test (SAT) is the most widely used. Rose Bengal and a new dipstick test are useful for screening; however, positive results should be confirmed by SAT. The brucella enzyme-linked immunosorbent assay (ELISA) is the most sensitive and specific serologic assay, and it may be positive when other tests are negative regardless of the assay used, no single titer is *always* diagnostic; however, most cases of active infection have titers of 1:160 or higher<sup>9</sup>. In our patient, both titers to brucella Abortus and *Brucella Melitensis* were above 1/160.

Radiological examination, although not a sensitive diagnostic test for extraspinal localization, remains an important tool for determining osteoarticular brucellosis. These examinations are supplemented with a radionuclide bone scan, despite the fact that it has low specificity, it is not a good modality to show soft tissue abnormality, and it is not useful in determining the course of the illness because abnormal uptake persists for a long time<sup>1</sup>. Computed tomography is especially useful for detecting joint destruction, vertebral osteomyelitis, and paraspinal abscess.

The diagnosis of osteoarticular brucellosis in our case was based on the clinical history, high brucella titer and the radiological findings. The radiological findings gave us a differential diagnosis of either tuberculosis or brucellosis. His PPD test was negative and he had no history of exposure to tuberculosis. So based on the above criteria and great response to the treatment of brucellosis with normalization of his liver function test and converting his brucella serology to negative, we were certain about the diagnosis.

Large weight-bearing joints (e.g., hips, knees, ankles) are involved more often than small joints, and when effusions are present, they contain a preponderance of lymphocytes, but brucella are isolated in fewer than half of the cases. A post-infectious spondyloarthritis, bursitis, tenosynovitis, and infection of joint prostheses have also been reported.

Magnetic resonance imaging is a sensitive method for detecting spinal brucellosis and the extent of infection throughout paravertebral structure<sup>10</sup>. MR imaging shows decreased signal intensity in the intervertebral disc, whereas the adjacent vertebral bodies are hypointense on T1 weighted images and hyperintense on T2- weighted images<sup>11</sup>.

The mainstay of treatment for brucellosis is antibiotic treatment. Intracellular localization of the brucella is believed to offer some protection against antimicrobials, and drugs with good penetration of the cells are thought to be necessary for cure.

The best results have been obtained with different agents such as streptomycin, rifampicin, tetracycline, doxycycline, and ofloxacin<sup>8</sup>. The World Health Organization (WHO) recommends a regimen of doxycycline (200 mg/day) plus rifampin (600 to 900 mg/day) given for 6 weeks, as this has the advantage of oral administration.

The eradication of infection from the bone is difficult and relapse may occur especially if only short term treatment is given as it happened in our patient<sup>8</sup>. Therefore, long-term anti-brucellar antibiotic treatment should be prescribed immediately after the diagnosis.

If the treatment is extended for longer than previously recommended (6 weeks), it would result in an incidence of relapse significantly lower than that for shorter courses of treatment<sup>12</sup>.

Brucella antibody titers have been recommended to assess the therapeutic response and the resolution of the disease<sup>7,8,9</sup>. As a rule, surgical intervention is rarely needed<sup>8</sup>.

Unfortunately, there is no consensus about the best antimicrobial combination and treatment duration. Surgical intervention is the last resort in the management of spinal brucellosis and it is advised only when there is persistence or progression of neurological deficits caused by soft tissues masses, progressive vertebral collapse, spinal instability, or when there is no response to prolonged antibiotic treatment<sup>1</sup>.

Recurrence of symptoms following therapy may or may not be associated with relapse of the disease. Bacteriologic relapse generally occurs within 3 to 6 months after discontinuing therapy and is usually not caused by antibiotic resistance<sup>13</sup>.

Chronic brucellosis is usually caused by persistent foci of infection in tissues, such as bone, spleen, liver, and other organs.

In chronic brucellosis, symptoms can recur over long periods and are associated with objective signs, such as fever. An important laboratory finding is the persistence of high titers of IgG antibodies<sup>14</sup>.

In contrast, some patients experience delayed convalescence, with persistent non-specific complaints, but without objective signs of illness or elevated titers of antibodies.

The cause of delayed convalescence is poorly understood, but some believe that it may represent preexisting psychoneurosis exacerbated by the infection<sup>15</sup>.

Moderate and severe sequelae are rare events in the osteoarticular brucellosis and mortality is an exceptional one<sup>1</sup>.

Concerning control of brucellosis in animals, there is a controversy on the choice of policy. In some countries, the test and slaughter policy and the vaccination of young females of potential carriers are adopted, in others, particularly with regard to sheep and goats; mass vaccination has recently been started. The most commonly used vaccines are *B. abortus* S19 and *B. melitensis* Rev.1 vaccines. *B. abortus* RB51 vaccine is used in some countries on a small scale. Vaccination is limited to cattle and small ruminants<sup>2</sup>.

Despite its control in many developed countries the disease remains endemic in Saudi Arabia where the national seroprevalence of the disease is 15%. In Saudi Arabia, the disease is introduced through uncontrolled importation of animals that are poorly screened for the disease. Every year the Kingdom imports a few million heads of sheep and goats for sacrifice during Hajj from Africa, India, and Australia. *Brucella melitensis* remains the principle cause of human brucellosis in Saudi Arabia, causing 88-93% of the cases. Recent national statistics indicate that the disease incidence in humans is close to 40 cases per 100,000<sup>16</sup>.

## CONCLUSION

**Brucellosis is not endemic in the Kingdom of Bahrain, but still has to be suspected in the differential diagnosis of fever of unknown origin. The spinal form of brucellosis should be considered in the differential diagnosis of patients presenting with back pain and a history of exposure to brucellosis. The patient presented in the paper had a typical history and a diagnostic titer.**

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