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Review

Brucellosis: A perspective from physical therapy and rehabilitation specialist

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ABSTRACT

Muscle-joint pain is one of the most common symptoms of brucellosis, an endemic zoonotic disease in our country. To avoid morbidity in these patients, brucellosis should be considered in the differential diagnosis, and any necessary serological/microbiological tests should be requested. Difficult-to-diagnose cases should be referred to the Infectious Diseases branch. Sacroiliitis is the most common musculoskeletal findings of brucellosis, followed by peripheral arthritis/arthralgia, spondylitis, osteomyelitis, and bursitis. The aim of the review was to examine brucellosis from the perspective of a Physical Therapy and Rehabilitation specialist in the light of the literature.

Keywords: Brucellosis, muscle and joint pain, physical therapy and rehabilitation.

Brucellosis is a systemic zoonotic disease caused by bacteria of the *Brucella* spp., which are small, Gram-negative coccobacilli, and develops as a result of hematogenous spread. It has been reported that it is transmitted to humans through a variety of routes, including meat, milk, pregnancy, and maternal tissues, urine, body fluids and skin, respiratory, mucosa, conjunctival flora contact with infected animals, and consumption of unpasteurized milk and dairy products. It has a global geographical distribution, with a focus on countries in the Mediterranean and Central Asia.[1-4] It can cause different organ involvement in a variety of ways, and clinical manifestations vary. Diagnosis and treatment can be challenging at times, and disease management can be difficult in some cases due to complications. According to various studies on the prevalence of brucellosis in Turkey, seropositivity ranges from 1.8 to 6%, with a morbidity rate of 20.3/100,000.[5,6]

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Only 15 to 50% of patients can be diagnosed with *Brucella* spp. growth in bone marrow or blood culture. In the absence of bacteriological evidence, serological diagnosis can be used. An antibody titer greater than 1/160, a four-fold increase in antibody titer using a standard tube agglutination test, or an increase in titration using the Enzyme-Linked Immunosorbent Assay (ELISA) method are all useful for diagnosis.[1,3,4]

Weakness, fatigue, high fever, loss of appetite, joint pain, muscle pain, abdominal pain, headache, gastrointestinal symptoms, night sweats, and weight loss are the most common symptoms of the disease.[2,4] Joint and muscle pain are reported at a rate of 20-60%. The most common clinical findings in both adults and children have been reported to be fever and osteoarticular findings (back pain, arthritis, arthralgia, myalgia). According to studies conducted in our country, the most common symptom is high fever, which is followed by arthritis/arthralgia.[7-9] Antigen-specific T cell activation by the host immune response in Brucella infections; CD4, CD8 T cells are thought to play a role in the humoral immune response.[10] The main protective immune response, however, is cellular immunity, in which two types of

reactions play a role. Microorganisms are killed by T cell-derived cytokines, while infected cells are lysed by CD8 cytolytic T lymphocytes.[11] In a study conducted in our country by Avşar,[9] it was found that the level of interferon-gamma (IFN-γ), a T helper (Th1)-type cytokine, was significantly higher in the patient group compared to the control group, and tumor necrosis factor-alpha (TNF-α) levels were higher in patients with brucellosis compared to the non-complication group. Tumor necrosis factor-alpha levels were not increased in patients with acute brucellosis, according to Ahmed et al.,[12] but interleukin 12 (IL-12) and interferon-alpha (IFN-α) levels were. These findings indicate that Th1-type cytokines are induced during human brucellosis.[12]

In light of the literature, we aimed to evaluate this disease, which can be intertwined with the field of physical therapy and rehabilitation in a variety of ways.

OSTEOARTICULAR BRUCELLOSIS

The musculoskeletal system is the one most affected (40%) by brucellosis. Osteoarticular complications of brucellosis include peripheral arthritis, sacroiliitis, spondylitis, tenosynovitis, bursitis, and osteomyelitis.[13] The most common sites of involvement are large or medium-sized peripheral joints, sacroiliac joints, and the spinal region.[14] There is a suggestion that the development of osteoarticular complications in brucellosis may be linked to a genetic predisposition associated with the human leukocyte antigen (HLA)-B27 gene[15] Different radiological imaging methods are used to detect osteoarticular complications, but it is known that osteoarticular changes occur radiologically late. Joint findings are most common in the third and fourth weeks of the disease.[2,16] Sacroiliitis is the most common brucellosis musculoskeletal finding, followed by peripheral arthritis and arthralgia, spondylitis, osteomyelitis, and bursitis. The complaints diminish quickly and disappear once treatment is started. Complaints may reoccur if treatment is discontinued too soon or is not administered in sufficient doses.[2]

PERIPHERAL ARTHRITIS

Arthritis is frequently manifested as monoarthritis or asymmetric peripheral oligoarthritis. In most cases, the onset of arthritis is sudden and extremely painful, with redness, warmth, effusion, and restriction of movement in the affected joints.[17] Peripheral arthritis typically affects large, weight-bearing joints (for example, the knee and hip joints). However, it can occasionally involve atypical joints such as the sternoclavicular and temporomandibular joints.[18,19]

Peripheral joint arthritis can be septic or reactive. Peripheral arthritis responds to antibiotic therapy, but spontaneous relapses can occur. Septic and destructive arthritis are less common.

It is, however, a more severe form of Brucella arthritis and usually exhibits monoarticular involvement.[17] In general, destruction and permanent functional impairment are not seen in peripheral joint arthritis. Treatment has a good response rate, and relapse is uncommon.[16]

SPONDYLITIS, VERTEBRAL OSTEOMYELITIS, AND PARASPINAL ABSCESS

Spondylitis has been reported in 10-65% of brucellosis cases with musculoskeletal involvement. Spondylitis usually manifests itself within one or two months of the disease and is not accompanied by fever. Epidural abscesses (10-32%) may accompany this. Clinically, it is frequently confused with tuberculous spondylodiscitis or other vertebral diseases (pyogenic spinal osteomyelitis due to other bacteria, disc herniation, degenerative osteomyelitis, and vertebral metastatic lesions). In order of frequency, spondylitis is observed in the lumbar (71%), thoracolumbar (10%), lumbosacral (8%), cervical (7%), and thoracic (4%) regions. It has been reported that it is prevalently seen in elderly patients, with the majority of patients having a long history of disease prior to diagnosis. In addition to other systemic findings, these patients may exhibit low back and back pain. This pain can be gradual or sudden, spreading to the legs. Patients may complain of walking difficulties, myalgia, and night pain. Spinous process tenderness and the straight-leg-raising test were both positive in the affected vertebra during a clinical examination. Pain may cause a restriction in waist movements. Although spinal deformity

is rare, it is more common in cases where the diagnosis is delayed.[16,20-23] In 90% of cases, intervertebral space narrowing can be detected. Vertebral fusion may occur later in life.[23] Osteoporosis can be seen in the anterior upper corner of the vertebral body as a moth-eating appearance (Pedro Pons' sign), as well as osteophytes and syndesmophytes.[2,23]

a. Sacroiliitis: The most common clinical form of brucellosis is joint involvement, which has been reported at rates ranging from 11 to 72% in various studies. Sacroiliac involvement has been reported in 10-60% of arthritis cases.[16] Sacroiliitis can develop early in patients, either alone or associated with recurrent fever attacks.[23] Radiologically, the joint space may become dysregulated; this condition is known as coxalgia.[2,23,24] In 1-2% of pediatric brucellosis cases, pyogenic sacroiliitis has been reported.[25]

Sacroiliitis is usually unilateral and occurs in the young age group and during acute illness. In children, sacroiliac involvement is extremely rare. Sacroiliitis is characterized by the sudden onset of severe pain in the lower back and gluteal region. The source of the pain is difficult to identify. When the patient stands up or walks, the complaints become more severe. The typical pain and findings of sacroiliitis may dominate the clinical presentation, or it may mimic acute lumbar spasm or lumbar disc herniation. As a result, differential diagnosis can be challenging.[16,26]

b. Reactive arthritis: Brucellosis is a relatively rare cause of reactive arthritis. It could be caused by immune-mediated mechanisms directed against Brucella-infected cells. In this case, arthritis may develop the following infection at a site distant from the joint. More than half of arthritis seen in the course of brucellosis has been reported to be reactive. In brucellosis, spontaneous relapse arthritis is usually reactive arthritis. Migratory and multi-joint involvement are common features of sterile reactive arthritis.[16,27]

Diagnosis

The isolation of Brucella from blood and tissues is the gold standard in the diagnosis of brucellosis, and it can be diagnosed with serological examinations in addition to clinical findings that suggest brucellosis in cases where the factor cannot be isolated.[2] In practice, a titer of more than 1/160 and clinical findings in the most frequently used Brucella serum agglutination test (SAT) are diagnostic for acute brucellosis.[1,2] However, false-negative SAT can occur in the presence of incomplete antibodies or low serum dilutions in the early disease period, as well as in a condition known as prozone (antibody excess) when high antibody titers are found in the serum.[2,17] Serological examinations are generally helpful in diagnosis; however, it should not be forgotten that culture growth is helpful in the definitive diagnosis in seronegative cases. In two cases where serological examinations failed to diagnose brucellosis, the definitive diagnosis was made by isolating the agent in tissue culture and blood culture, as reported by Çelik et al.[10,28]

Treatment

The World Health Organization recommends doxycycline 200 mg/day and rifampicin 600-900 mg/day for the treatment of brucellosis; in oral/parenteral therapy, streptomycin 15 mg/kg/day (first 2-3 weeks) in combination with rifampicin for at least six weeks. Streptomycin 10.75-1 g intramuscular (IM) and doxycycline 2100 mg for 2-3 weeks is the standard treatment for osteoarticular brucellosis, followed by a combination of rifampicin 1600 mg and doxycycline 2100 mg. In complicated brucellosis, 12 weeks of triple therapy was associated with a lower relapse rate than a four-week combination of streptomycin or gentamicin + rifampicin/doxycycline.[29] The duration of treatment in patients with spondylodiscitis, paravertebral abscess, epidural abscess, or psoas abscess may need to be extended with clinical, laboratory, and radiological follow-up (3-9 months).[30,31]

Conclusion

In endemic regions such as our country, a microbiological examination for brucellosis should be requested in patients presenting with joint and musculoskeletal complaints. Consultations with relevant branch physicians should be requested in cases of undiagnosed high clinical suspicion.

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