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Review Article

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BRUCELLOSIS OSTEOARTHRITIS: A LOOK AT THE PREVALENCE, DIAGNOSIS AND TREATMENT IN THE MODERN WORLD

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ABSTRACT

Brucellosis osteoarthritis is a prominent and debilitating manifestation of human brucellosis, a globally prevalent zoonotic infection caused by *Brucella* species. The condition primarily affects the musculoskeletal system, with the spine, sacroiliac joints, and large peripheral joints being the most commonly involved. In endemic regions, delayed diagnosis and inadequate treatment often contribute to high morbidity, chronic pain, and permanent joint damage. The disease remains underrecognized due to its non-specific clinical presentation and resemblance to other inflammatory or infectious arthropathies. Diagnosis of brucellosis osteoarthritis requires a multidisciplinary approach combining clinical assessment, serological testing, imaging, and microbial cultures. Serological assays such as the standard agglutination test and ELISA are crucial for early detection, while imaging modalities like MRI aid in evaluating the extent of joint and bone involvement. Culture confirmation remains the gold standard but is limited by low sensitivity and prolonged incubation times. In chronic or relapsing cases, histopathological analysis and advanced imaging are invaluable.

KEYWORDS: *Prevalence of brucellosis osteoarthritis, Diagnosis of brucellosis arthritis, Treatment of brucellosis arthritis.*

INTRODUCTION

Osteoarticular brucellosis is the most common presentation of human active disease although its prevalence varies widely. In 1884, the causative bacteria Brucella was first discovered in the spleen of a soldier who died from the infection.[1] The three most common forms of osteoarticular involvement are sacroiliitis, spondylitis, and peripheral arthritis. B. abortus induces bone damage through diverse mechanisms in which TNF-α and the receptor activator of nuclear factor kappa-B ligand (RANKL)-the natural modulator of bone homeostasis are involved.[2] Osteoarticular brucellosis is well documented as a major public health problem in several countries, particularly in the Middle East, the Mediterranean region and Central and South America, Arabic countries.[3] Bone damage can be attributed to the direct action of the bacteria or to an immunopathological process due to inflammation triggered by innate immunity.[2]

Aim

The aim of this review is to provide a comprehensive and up-to-date overview of brucellosis osteoarthritis, focusing on its global prevalence, clinical presentation, diagnostic challenges, and current treatment strategies.

MATERIALS AND METHODS

Search for Publications and Selection of studies

The information search algorithm was created in accordance with the requirements and guidelines for reporting systematic reviews and meta-analyses PRISMA in the Pubmed and Google Scholar database and included searching for studies using search terms, keywords and Boolean operators. Abstracts of reports, notes of meetings, books were not used. English has been set as the restricted language. Two authors independently reviewed the titles and abstracts of publications to determine whether they met the inclusion criteria, and any disagreements were resolved through negotiations. Key words in the PubMed database: (Brucellosis arthritis) AND (Prevalence) AND (Diagnosis) AND (Treatment). To search for information in the Google Scholar database, the following query was used: brucellosis arthritis, prevalence, diagnosis, treatment. Last search performed on December 1, 2024.

Inclusion and Exclusion criteria

Only those studies that adequately reported baseline data, including information on the prevalence, diagnosis and treatment of the disease, were included in the systematic review. A prerequisite for inclusion of a publication in

the meta-analysis was the availability of data on clinical outcomes. The age of the patients less than 18 years was a limitation of the study. Animal studies were not included. The number of patients included in the studies was not a determining factor for our selection.

Prevalence of brucellosis arthritis

47% of brucellosis patients experienced osteoarticular complications.[4] Osteoarticular involvement is the most common complication, with a prevalence of 2-77%, usually manifesting as spondylitis, sacroiliac arthritis and peripheral arthritis.[5]

Table 1: Prevalence of brucellosis arthritis in different clinical studies.

Authors	Year of edition	
Turan *et al*[4]	2011	47% of brucellosis patients experienced osteoarticular complications
Jin *et al.*[5]	2023	Prevalence of 2-77%, usually manifesting as spondylitis, sacroiliac arthritis and peripheral arthritis
Liu *et al.*[6]	2023	Present joint pain in 37.30% patients with Brucellosis
Qureshi et al.[7]	2023	Epidemiology, pathogenesis, diagnosis and treatment–a comprehensive review
Pappas *et al*[3]	2006	New global map of human brucellosis
Turan *et al.*[4]	2011	Osteoarticular involvement among brucellosis cases identified in Central Anatolia region of Turkey.
Galińska *et al.*[1]	2013	etiology, diagnostics, clinical forms.
Stroczyńska Sikorska *et al.*[8]	2004	Serologic examinations for brucellosis in human
Bilecki S. Bruceloza.[9]	2001	Logs of Agriculture and Environmental Medicine
Martes Rolnictwa[10]	1968	Regulations in the matter of brucellosis-control in animals,
Pritam M, Kumar[11]	2024	Vaccine Candidates, and Drug Targets for Human Brucellosis
Shi *et al.*[12]	2024	Clinical features of human brucellosis cases in China.
Pappas *et al*[13]	2005	SCIRP, The New England Journal of Medicine
Esmaeilnejad-Ganji and Esmaeilnejad-Ganji[14]	2019	manifestations of human brucellosis

Clinical events

Brucellosis arthritis is usually seen as sacroiliitis, spondylitis, osteomyelitis, peripheral arthritis, bursitis and tenosynovitis.[14] The most characteristic symptoms of brucellosis are fever with large diurnal fluctuations, chills and sweating. Intoxication may be mild, so patients remain able to work for the first few days. Referral to a doctor is often associated with musculoskeletal, nervous system and genital lesions. Patients with brucellosis have arthralgias, arthritis, bursitis, synovitis, neuralgia and orchitis. Examination reveals polyadenitis, in the subcutaneous tissue - dense mobile formations - fibrositis. The liver and spleen are often enlarged. The blood shows leukopenia. High erythrocyte sedimentation rate, high C-reactive protein, high alanine aminotransferase and high aspartate aminotransferase are the most common laboratory findings.[11] The course of the disease can be acute, subacute or chronic.

Diagnostics of Brucellosis and Brucellosis Arthritis

Brucellosis is common in regions with developed livestock production. The source of the disease is small and large cattle and pigs. Infection occurs through the consumption of milk, dairy products, meat from diseased animals, as well as through the care, slaughter and processing of carcasses. Brucella is present worldwide, with only certain regions at high risk, including Asia, Africa, Eastern Europe, Mexico, South and Central America, the Caribbean, the Mediterranean Basin and the Middle East.[11] The disease is spread to humans mainly by the ingestion of infected meat or unpasteurized dairy products, by contact with infected animals or inhalation of infectious aerosolized particles.[13] The incubation period of brucellosis is one to three weeks. The diagnosis of brucellosis is confirmed by immunological tests as well as by intradermal allergy testing. Agglutination and its modifications, and complement fixation tests are still routinely applied, improved and supplemented by new tests, and remain a basis for laboratory diagnosis of brucellosis in humans and animals. Wright agglutination reactions with its valuable modification in the form of 2-mercaptoethanol (2-ME) test and complement fixation test (CFT) have served for decades (and still do), mainly for the detection of new cases of brucellosis.

Agglutination reaction (Wright reaction) with blood serum (AR) is applied in routine brucellosis diagnostics in humans. It may be carried out using tubes or plates. With the use of this reaction anti-Brucella agglutinins are detected. This reaction consists in the binding of Brucella to specific antibodies which are present in the sera examined. This results in the decrease in electric charge and change in the physical and chemical structure of bacterial cells. Their hydrophilic character changes into hydrophobic. This leads to the formation of clumps, which in the tube agglutination fall to the bottom of the test tube in the form of sediment. Agglutinating antibodies form mainly immunoglobulins of the IgM class. The time of their persistence in the body varies. They occur as early as in the first stage of the disease,

most frequently 6-7 days after infection. In acute and sub-acute forms of brucellosis in humans agglutination reaction gives positive results with high titres.

Bilecki emphasizes that the agglutination reaction may be positive in the course of other infectious diseases, such as tularemia, exanthematous typhus, tuberculosis, or in individuals vaccinated against cholera or typhoid fever. In addition, serologic cross-reactions may occur between Yersinia enterocolitica 03 and 09, and classical species of the genus Brucella. Negative results in the agglutination reaction may come -in infected individuals (when anti-Brucella agglutinins have not yet been produced); in individuals with chronic brucellosis (in whom the level of agglutinins reached zero value); in individuals with broken immunity. Complement fixation test (CFT)-apart from agglutination reaction (AR) is the second diagnostic test used in the diagnosis of brucellosis in humans. This test is sensitive and specific. This is the method for detection of the level of antibodies of the IgG class, which occur approximately on day 20 of the disease. High titres are observed during the first and second years of the disease, while several years after infection the results of studies may be seronegative.

Treatment strategy of brucellosis arthritis

Treatment of brucellosis arthritis should begin with the prescription of antibiotics. Adults and children over 8 years of age should be prescribed oral doxycycline (2 - 4 mg/kg, maximum 200 mg/day, in 2 divided doses) or oral tetracycline in combination with rifampin (15 -20 mg/kg, maximum 600-900 mg/day, in 1 or 2 divided doses) for a minimum of 6 weeks (gentamicin 5 mg/kg/day IM for 7 days may be used instead of rifampin). Children under 8 years of age should be prescribed oral trimethoprim 10 mg/kg per day, maximum 480 mg/day; and sulfamethoxazole, 50 mg/kg per day, maximum 2.4 g/day- divided in 2 doses for 4 to 6 weeks. Consider adding rifampin for combination therapy if not contraindicated.[15-16]

CONCLUSION

Brucellosis osteoarthritis remains a significant clinical entity within the spectrum of brucellosis-related complications, particularly in endemic regions. Its presentation can mimic various other infectious and inflammatory joint diseases, often leading to misdiagnosis and delayed treatment. As such, heightened clinical awareness, especially in patients with relevant occupational or dietary exposure, is essential for early identification. Accurate diagnosis hinges on a combination of serological, microbiological, and imaging techniques, with MRI playing a pivotal role in detecting early musculoskeletal changes. Prompt initiation of appropriate combination antibiotic therapy, guided by current clinical guidelines, is critical to halting disease progression, minimizing complications, and reducing relapse rates. In advanced or refractory cases, surgical intervention remains a valuable adjunct to medical therapy.

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