MANAGEMENT OF BRUCELLOSIS

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Summary :

Experiences with management of 140 (82 males and 58 females) patients of brucellosis is presented. The diagnostic criteria was based on clinical presentation (fever, joint pains) and high titre positive brucella agglutination test. Forty-four (31.4%) patients responded in 2-9 days as evidenced by high temperature coming to normal on receipt of adequate threapy by tetracycline alone or in combinatin with streptomycin or other drugs. Inappropriate antibiotic or appropriate antibiotic in inappropriate doses was given to 23 (16.4%) patients resulting in a slow response. More than half 73 (52%) were not treated as they did not attend for follow up for result of investigation or misdiagnosis. The complications were bone and joint involvement and endocarditis. To give adequate therapy and avoid complications any patient with pyrexia in Saudi Arabia should be investigated for brucelloosis.

Introduction :

Brecellosis is a disease of animals caused by Gram negative coccobacilli of genus Brucella. The other names of the disease are Undulant fever, Mediterranian fever or Malta fever. The disease may be transmitted to man directly or indirectly by handling infected cow, goat, sheep, camel or patient's exereta, drinking raw milk or meat of infected animals.

Brucellosis presents in one of the four forms, acute, subacute, local or chronic. The treatment of acute cases is easier than that of subacute or chronic forms.[2] The range of antibiotics for the treatment of brucellosis is limited. The result of treatment of brucellosis depends entirely on the drugs used in proper dose, frequency and duration of treatment. Complete cure should be obtained as incomplete treatement will result in replaps or complications. It seems to be a public health problem in the Kingdom of Saudi Arabia and probably in the neighbouring countries. Patients should be treated adequately and follow up maintained. The aim of this paper is to present the results of retrospective study of experiences with management of 140 cases of brucellosis attending Riyadh Alkharj Hospital Programme in Saudi Arabia.

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Methods and Results : Selection of Patients

The study period was from June, 1981 to January, 1983 There were 82 males and 58 females. There were 137 Saudis and three non-Saudis. The Patients who had symptoms suggestive of brucellosis such as pyrexia, joint pains, backache, headache, myalgia and sweating were investigated. The patients were selected on the basis of 1 : 160 or higher antibody titre to brucella abortus or melitensis in presence of clinical features. Microagglutination test was done using Wellcome reagents (Wellcome research laboratories, Backenham, B3 3BS, England). Doubling dilutions of patients' and control sera were made from 1 : 10 through 1 : 5120 and further dilutions done if the agglutination reaction was strong at a dilution of 1 : 5120. Positive and negative control sera were included for each batch of test. Clinical and therapeutic information were collected from clinical case notes. Titres of 1 : 160 or higher in presence of symptoms were considered diagnostic.[3,4] Successful treatment was considered as reduction of higher temperature to normal and relief of pain and other symptoms after therapy. Blood cultures for Brucella species or other organisms were done on 18 patients for upto six to eight weeks.

Clinical presentation : All but three of 140 patients were Saudi Arabians. All of them had fever, bodyaches, and lethergy. Twenty four patients had bony involvement. There were 11 pregnant patients with brucellosis, six of them had aborted. Six petients had epididymoorchitis due to brucellosis and two had endocarditis. Blood cultures were positive in five patients and Brucella melitensis was isolated. Agglutination titres are shown in table 1.

Table 1.
Agglutination titres obtained for brucella (abortus or melitensis) in 140 patients at the Riyadh Al Khari Hospital Programme.

Titre	Number of patients
160	31
320	16
640	11
1280	16
2560	21
5120	19
10240	10
20480	16
Total	140

Treatment schedule : There were no record of any treatment for brucellosis for 73 (52%) patients. Tetracycline by itself was given in 16 patients, tetracycline with streptomycin was given to 20 cases and tetracycline with other antibiotics was given in eight patients. Treatment was given in other hospitals or clinics to 16 (11.4%) patients but details were not available. Three patients had both brucellosis and tuberculosis at the same time and all these three patients responded to anti TB therapy with rifampicin, isoniazid and ethambutol. Cotrimoxazole was given to two pregnant patients with brucellosis. Two other patients were treated with cotrimoxazole. Treatment schedule is summarised in table 2.

Table 2. Antibiotics used in the treatment of Brucellosis.

	No. of patients	Percentage
Untreated	73	52.14
Therapy given but unknown	15	10.7
Tet. + Strepto.	20	14.28
Tet. alone	16	11.47
Contrimoxazole alone	4	2.85
Anti TB therapy including Rif.	3	2.14
Tet. + Contrimoxazole	2	1.42
Tet. + Rif.	2	1.42
Tet. + Gent.	2	1.42
Tet. + Amp.	1	0.71
Erythromycin	1	0.71
Tet. + Gent alternating with Strepto.	1	0.71
Total	140	99.97

Key

Tet. = Tetracycline
Strepto.= Streptomycin
TB = Tuberculosis
Rif. = Rifampicin
Amp. = Amicillin
Gent. = Gentamicin.

Forty four inpatients including two with endocarditis, 24 with bone involvement and six with epididymoorchitis received tetracycline or tetracycline and streptomycin combination in adequate doses for at least three weeks. Other patients particularly out patients received inadequate doses or the correct dose for less than three weeks.

Therapeutic Response : The highest temparature recorded was 40°C. Temperature came to normal (37°C) and patients felt better, joint pains improved in 2-9 days after strating therapy with tetracycline 500 mg orally six hourly plus streptomycin 1 Gm IM or 0.75 Gm IM daily and got better if this treatment continued for three weeks. Slower response was obtained by tetracycline 250 mg six hourly with streptomycin 0.75 Gm IM daily. The oriteria of successful treatment was taken as reduction of higher temperature to normal. Rapid response was observed in patients with high agglutination titre when adequate doses of appropriate antibiotics were used.

Discussion :

A study of 140 patients with brucellosis managed at Riyadh Alkharj hospital programme is presented. One hundred and six patients were seen in Riyadh and 34 patients were seen at Alkharj (87 Kilometres south of Riyadh) armed forces hospitals. Although undesirable, an outstanding finding in this study was that more than half 73 (52%) the patients either did not attend for follow up or doctors missed the diagnosis. The patients with symptoms suggestive of brucellosis with high titre brucella agglutination test could have nomadic or bedouin style of life, in patients who are dependents, transfered elsewhere or paying patients who ere no more eligible by the time diagnosis is made. This is one of the problems of developing countries as highlighted from Saudi Arabia.[5,6] The patients who received treatment had ten types

either single or combination therapy. Medical audit and health education will improve the follow up of patients for treatment. Oral administration of tetracycline 500 mg six hourly for three to six weeks and one Gm of streptomycin IM for the first three weeks gave the best response. Coming down of temperature to normal and feeling of wellbeing in two to nine days to starting treatment was considered as best response. The newer tetracyclines such as doxycycline and vibramycin gave similar results. The above regime is that most commonly used and recommended by other authors[7,8] but it has a relapes rate of 6-9%.[8] Tetracycline alone was used in 16 (11.5%) cases and tetracycline with one or more drugs was used in 28 (20%) cases which are effective regimes of therapy in uncomplicated cases of brucellosis with a relapse rate or 1-10%.8 Tetracycline is effective because it penetrates the inside of cells where brucella organisms thrive. In this study it was also noticed that combination or tetracycline with streptomycin give dramatic response than any other combination. Three patients with brucellosis were on antituberculous therepy with drugs including rifampicin and tetracycline also responded well. Two other patients who were treated with rifampicin and tetracycline also responded well. This is because rifampicin is a promissing drug for brucellosis[3,10] because of its intracellar action. Rifampicin is bactericidal.[11] Llorens-Terol and Basquets[9] used rifampicin successfully in 15 children with brucellosis.

Cotrimoxazole was used in four pregnant patients and in two other patients in combination with tertracycline. This alternative combination was used by several authors[2,11,12,13] who achieved good results in some cases and replapses occured in others. Hence it is recommanded that at least two effective drugs should be used in the treatment of brucellosis. Inadequate or incomplete treatment may lead the patient to a state of chronic brucellosis and treatment should be repeated where necessary.

Patients should be followed for assessment of cure by means of the 2 - Mercapto-ethanol (2 - ME) test.[14] A cure is considered to have been effected when the 2 - Mercaptoethanol titre is down to less than 1 : 80. If the 2 - Me titre is higher than 1 : 80, two to three months after treatment then the treatment should be considered incomplete and repeated. Any patient with an agglutination titre of 1 : 80 and low 2 - ME titre should be considered as cured. So no further treatment is necessary unless reinfection occurs. This has not been carried out for the present study but should be considered in future studies. One should bear in mind that preventive measures are more important than curative procedure.

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A bee after stinging leaves its sting in the wound.

The breast of the chicken is the most easily digested meat known.

The normal weight of the brain is from 40 to 50 ounces. It is slightly heavier in men than in women.