ACUTE BRUCELLOSIS PRESENTING AS FEVER OF UNKNOWN ORIGIN (FUO)

By

Z. Farid, B. Trabolsi, W. Yassin, R.H. Watten and G.I. Higashi

U. S. NAVAL MEDICAL RESEARCH UNIT NO. 3
(CAIRO, ARAB REPUBLIC OF EGYPT)
FPO NEW YORK 09527
Acute brucellosis presenting as fever of unknown origin (FUO)

Z. Farid, B. Trabosi, W. Yassin, R. H. Watten and G. I. Higashi
U.S. Naval Medical Research Unit No. 3 (NAMRU-3), and Abbassia Fever Hospital, Ministry of Health, Cairo, Egypt

Brucellosis ranks after salmonellosis and tuberculosis as the most important systemic infection causing fever of unknown origin (FUO) in Cairo (Hassan & Farid, 1974). The cause is nearly always *Brucella melitensis* (see Petschner et al., 1957) but owing to the widespread indiscriminate use of antibiotics in Egypt (Farid et al., 1975), it has become difficult to isolate the organism by blood culture and thus establish a definitive diagnosis. We summarize the clinical data of 16 patients with acute brucellosis developing over both lower limbs. He became afebrile after two weeks of antimicrobial therapy and appeared to improve clinically but died in congestive heart failure at the end of four weeks of treatment.

**Case 1:** A 37-year-old manual worker presented a history of recurrent attacks of fever accompanied by severe arthralgia of nine months' duration. He had been admitted three times to hospital and had received several courses of tetracycline, chloroquine and chloramphenicol. Physical examination showed a seriously ill male with pitting oedema and a diffuse petechial rash over both lower limbs. His temperature was 39.6°C and there was a high-pitched soft diastolic murmur over the aortic area; leucocyte count 4,800/mm³; ESR 43 mm/hr and *Brucella* agglutination 1:1260. Several blood cultures were reported negative but the *Brucella* agglutination was 1:1260. He started on oral tetracycline two grams and intramuscular streptomycin one gram daily. On the fifth hospital day the patient's condition deteriorated and a pathologic, high pitched, soft diastolic murmur was heard over the aortic area. He became very dyspnoeic and a diffuse haemorrhagic rash developed over both lower limbs. He became afibrile after two weeks of antimicrobial therapy and appeared to improve clinically but died in congestive heart failure at the end of four weeks of treatment.

**Case 2:** A 38-year-old engineer was admitted to hospital complaining of recurring episodes of fever, generalized musculoskeletal pains and night sweats of two years' duration. He had been treated with many antibiotics but three weeks before entry to hospital endocarditis was suspected and he was started on intramuscular crystalline penicillin. Physical examination showed a seriously ill male with 2 pitting oedema and a diffuse petechial rash over both lower limbs. His temperature was 38°C and there was a high-pitched soft diastolic murmur over the aortic area; leucocyte count 3,050/mm³; ESR 25 mm/hr, and *Brucella* agglutination 1:1260. Several blood cultures were reported negative but a bone marrow culture was positive for *Br. melitensis*. He responded to tetracycline and streptomycin and became afibrile after four weeks of treatment; but the heart murmur persisted due to the development of irreversible aortic insufficiency.

**Case 3:** A 42-year-old male clerk was admitted to hospital in July 1976 complaining of recurrent fever, night sweats, arthralgia and weight loss of 17 months' duration. He had been admitted three times to hospital and had received several courses of tetracycline, chloroquine and chloramphenicol. His temperature was 38°C; leucocyte count 4,800/mm³; ESR 43 mm/hr and *Brucella* agglutination 1:1260. Blood cultures were positive for *Br. melitensis* and he was treated with tetracycline and streptomycin. In April 1977 he relapsed and was retreated with tetracycline and streptomycin for another three weeks. During the next two years he had three further relapses; on each occasion blood cultures were positive for *Br. melitensis*. In August 1977 he was admitted complaining of fever and cough with haemoptysis. An X-ray of the chest showed bilateral...
Z. FARIĐ et al.

Fig. 1. Chest and cervical spine radiographs of Case 3.

- a. At third relapse in August 1977 bilateral basal opacities can be seen.

- b. In November 1978, there is marked anterior and posterior intervertebral disc space with destruction of adjacent vertebral bodies of C3 and C4.

Basal opacities (Fig.). He responded to six weeks' treatment with tetracycline and streptomycin. Seven months later he returned to hospital with severe neck pains. An X-ray of the cervical spine showed early spondylitis of C3-C4; his chest X-ray was clear. He treated for six weeks with tetracycline and streptomycin and went home much improved. In November 1978, he returned complaining of severe neck pains and recurrence of cough with haemoptysis. There was a diffuse petechial rash over the whole body. A chest X-ray showed patchy opacities of the right lower lung field, and an X-ray of the cervical spine showed osteomyelitis of C3 and C4 (Fig.). He discharged himself from hospital and died three weeks later in another hospital.

Brucella infection in these three patients had lasted nine to 24 months, yet all were seriously ill and all three had markedly elevated agglutination titres denoting an acute rather than a chronic process. During this period they had received many short courses of various antimicrobials, never adequate to cure but sufficient to suppress the fever and hint at the real nature of the infection.

The two patients with infective endocarditis gave no history of previous heart lesions, instead the first developed a heart murmur after 16 months of illness, only a few weeks before being referred to hospital because his clinical condition had suddenly deteriorated. Brucellosis was undoubtedly the cause of aortie valve disease in both patients. The third patient continued to relapse over a period of observation of 28 months. He developed lung and cervical spine complications although lumbar spine complications are common in *Br. melitensis* septicemia. FARIĐ & MAHF, 1967; certainly cervical spine lesions are uncommon despite adequate antimicrobial therapy. Detailed immunological studies performed in November 1978 showed this patient to have a defect in cell-mediated immunity which may explain his recurring brucella septicemia. The defect appears to have been acquired since a tuberculin test was positive on initial admission but turned negative subsequently. Delayed hyper-sensitivity skin tests in November 1978 with recall microbial antigens (Candida albicans, streptokinase-streptodornase) were also negative. In vitro microculture lymphocyte blast transformation assays were also uniformly suppressed 40 to 70% lower than normal responses. The patient's lymphocytes were tested against the three antigens above as well as to staphylocoecal lysate antigen and to the mitogens, phytohaemagglutinin, concanavalin A, and pokeweed mitogen. 10 autologous plasma further diminished the mitogenic responses by 50%, suggesting that the suppression observed results from both suppressor cells and soluble plasma factors.
Acknowledgements

Supported by ONR Contract No. N00014-70-C-0193, Fever of Undetermined Origin.

The opinions and assertions contained herein are the private ones of the authors and are not to be construed as official or as reflecting the views of the Department of the Navy or the Egyptian Ministry of Health.

References

Accepted for publication 7th August, 1979.

Comparison of IHA test for amoebiasis on serum and filter paper specimens

HENRY M. MATHEWS, HARRISON C. SPENCER and GEORGE R. HEALY
Bureau of Laboratories and Bureau of Tropical Diseases, Center for Disease Control, Public Health Service, U.S. Department of Health, Education and Welfare, Atlanta, Georgia 30333, USA

Specimens of blood collected and dried on filter paper have been useful in seroepidemiological studies for detection of diseases such as malaria (Lobel et al., 1976) and Chagas’s disease (Goldsmith et al., 1978). We have compared indirect haemagglutination titres to Entamoeba histolytica on serum and filter paper specimens collected simultaneously from the same person. The study population from El Salvador included patients with proven E. histolytica infection, their immediate families and neighbour controls. A total of 110 paired specimens was obtained.

Materials and Methods

Venous blood was collected in vacuum tubes and allowed to clot; serum was recovered by the usual methods. Serum was frozen at -20 °C until thawed for testing. For the filter paper specimens, blood was collected in heparinized microhaematocrit tubes (approximately 75 μl) by finger prick or from the vacuum tube before it clotted, and was transferred immediately to a 12-mm circle imprinted on a 2.5 x 5 cm rectangle of ROPACOF 1023-03G filter paper. James River Rochester, Inc., Rochester, Michigan 48063, USA. The blood was allowed to dry at ambient temperature and then was frozen at -20 °C. Serum and filter paper blood specimens were transported on dry ice to the Center for Disease Control, Atlanta, Georgia, USA, for processing.

The entire blood spot was cut from the filter paper and transferred to a well of a flat-bottomed tissue culture tray.* Flow Laboratories, Catalog No. 76-000-05, and 0.4 ml of phosphate buffered saline (PBS, pH 7.2) was added. The tray was covered with an acetate sheet, and the material was eluted from the papers at room temperature 25 °C. After two hours the paper was removed from the well, residual fluid was squeezed out with blunt nosed pliers, and the paper was discarded. Approximately 0.3 ml of dark brown eluate was thus recovered.

* Use of trade names is for identification only and does not constitute endorsement by the Public Health Service or by the U.S. Department of Health, Education and Welfare.
**Title:** Acute Brucellosis Presenting as Fever of Unknown Origin (FUO).

**Author(s):** Z. Farid, B. Trabolsi, W. Yassin, R.H. Watten, G.I. Higashi

**Performing Organization Name and Address:**
U.S. Naval Medical Research Unit No. 3
FPO New York 09527/0007

**Controlling Office Name and Address:**
Naval Medical Research and Development Command
National Naval Medical Center
Bethesda, Maryland 20014

**Summary:**
Brucellosis ranks after salmonellosis and tuberculosis as the most important systemic infection causing fever of unknown origin (FUO) in Cairo. The cause is nearly always Brucella melitensis but owing to the widespread indiscriminate use of antibiotics in Egypt, it has become difficult to isolate the organism by blood culture and thus establish a definitive diagnosis. We summarize the clinical data of 16 patients with acute brucellosis presenting with FUO between January 1971 and December 1977. Four of these patients were from the 1972-1973 epidemic in Egypt.
were women and 12 men, ages ranged from 15 to 54 years, three were farmers constantly in contact with cattle; the others lived in Cairo and presumably acquired the infection through drinking raw milk. Three of these 16 patients developed severe complications; all the others responded to treatment with tetracycline and streptomycin and were cured. Oral tetracycline was given in a dose of two grams daily and streptomycin in a dose of one gram intramuscularly daily; both drugs were given for a minimum of three weeks.