

Case Reports

Acute brucella meningomyeloencephalo – spondylosis in a teenage male

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ABSTRACT

Background

Brucellosis has been known from the time of Hippocrates. In 1885 Sir David Bruce isolated the causative organism from the spleens of soldiers who had died from “Malta disease” (now brucellosis). There are 4 species of brucella pathogenic to humans and each of them has a specific types of animal reservoir: *B. arbotus* (cattle, buffallos), *B. melitensis* (goats, sheep, camels), *B. suis* (pigs), *B. canis* (Dogs). Humans are infected when they are exposed to body fluids from an infected animal. The symptoms and signs of brucellosis are protean. Diagnosis is usually dependent on clinical features and serology or culture.

Objectives

To describe a case of neurobrucellosis , raise awareness about the existence of the disease in Uganda and Africa in general and share our experiences in its diagnosis and management.

Methods

A male teenager was admitted with symptoms and signs of an acute meningo-encephalitis. He underwent clinical , laboratory and basic radiological evaluation.

Results

The un-incubated brucella titer was significantly reactive(1:160).Oblique-view cervical x-rays showed early osteophyte formation with encroachment on the vertebral foramina on the left hand side.

A diagnosis of acute brucella meningomyeloencephalo-spondylosis was made and the patient was successfully treated using conventional therapy for brucellosis (oral doxycycline for 6weeks and IM streptomycin for 2 weeks).

Conclusions

Neurobrucellosis though said to be rare, is a reality in our health units should be considered in the differential diagnosis of neurological and psychiatric illnesses. The good news is that it is curable and is responsive to drugs used for other forms of brucellosis.

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INTRODUCTION

History

Brucellosis is a primarily zoonotic infectious disease found in both domestic and wild animals. It has been known since the time of Hippocrates as a disease of fever with a long duration ¹. It has been known by many names: Mediterranean fever, Malta fever, gastric remittent fever and undulant fever. In 1885,Sir David Bruce described “a disease of long duration clinically characterized by fever, profuse perspiration, splenomegally, frequent relapses, rheumatoid or neuralgic pain, swelling of the joints and orchitis”.He isolated the organism from the

spleens of soldiers who died as a consequence of “Malta disease”^{1,2}

Microbiology

Brucella are small, coccoid or rodlike, aerobic, gram-negative bacteria of 0.5 to 1.5 microns in length, immotile and sporeless. There are six species than can be identified by their oxidative utilization and sensitivity to bacteriophages, namely: *B. Melitensis* (in goats, sheep, camels), *B. Arbotus* (in cattle, waterbuffallos, horses, camels, yaks), *B. Suis* (pigs, caribou), *B. canis* (dogs), *B. Ovis* (in sheep) and *B. neotomac* (in desert wood rats).Only the first four are known to cause disease in humans.Brucella have a substantial capacity to survive in especially chronic carriers and infected secretions such as milk,urine,fetal membranes,placentae.Organisms can last in soil for up to 10 weeks, in liquid manure up to 2 years, in goat cheese

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Picture 1



up to 180 days at 4-8 degrees centigrade and in tap water up to 60 days. They are very sensitive to heat, ionizing radiation and are killed by pasteurization.¹

Pathophysiology

Brucella species are facultative anaerobes that are capable of surviving and replicating within the phagocytic cells of the host. On entry into the body, they are ingested by polymorphonuclear leucocytes. Polymorphs have only a limited capability to kill the bacteria within themselves. Copper-Zinc superoxide dismutase, the O polysaccharide and nucleotide-like substances are among the factors that protect brucellae from being killed by polymorphs. The brucellae not killed by polymorphs are ingested by macrophages and become localized within organs of the reticulo-endothelial system and multiply in the macrophages and monocytes. However, any organ system can become involved by brucellosis e.g. central nervous system, cardiovascular, gastrointestinal tract, musculoskeletal, genitourinary, pulmonary, hematological and even the skin. Humoral antibodies against the brucella cell wall antigens (mostly endotoxic lipopolysaccharides) are produced soon after infection. Development of cell mediated immunity is the principle mechanism of recovery.^{2,3}

Epidemiology

Brucellosis exists worldwide and virtually all infections derive directly or indirectly from animal exposure. Infected animal body fluids e.g. urine,

Picture 2



faeces, saliva, blood and unpasteurised dairy products e.g. milk, cheese, ghee together with undercooked or underroasted meat are known media of transmission.^{1,2} Recent findings have identified sexual intercourse, breastfeeding and inhalation through aerosols e.g. in slaughter houses and laboratories as other routes of transmission.^{2,4,5} The disease is still endemic in the Mediterranean countries, the Arabian peninsula, western Asia, Africa and Latin America. Neurobrucellosis occurs in only 5% of patients with brucellosis.^{2,6}

Case history and examination findings

A 19 year old male student, who had been previously well, was admitted with a 7 day history of fever of sudden onset, headache and generalized convulsions. He had been rushed to a nearby private clinic where an initial diagnosis of suspected cerebral malaria was made. He received 8-hourly intravenous quinine in 5% dextrose for two days without registering any improvement. On re-examination, meningeal signs were noted and he was treated with high-dose intravenous crystalline penicillin and chloramphenicol six hourly for 5 days but still his condition continued to worsen. Consequently, he was referred to our hospital for further management.

On arrival at our unit, he was found to be toxic, febrile with an axillary temperature of 39 degrees Celsius and had a thick *Herpes labialis* lesion. There were no HIV stigmata. Neurological examination revealed a young man in semiconscious state. He was aphasic with a stiff neck, positive kernig's sign and left facial palsy. There was a right sided hemiplegia with upper motor neurone

signs on the same side. He also had lower motor neurone signs (flaccid paralysis and eventually wasting) of the left upper limb. Examination of the other systems was unremarkable. Noting the above clinical findings and history of having failed to improve on the above treatment, we suspected he probably had pyogenic meningitis complicated by cerebral and spinal abscess. Consequently, therapy was changed to IV ceftriaxone 2grams OD and IV metronidazole 500 mg 8 hourly for 10 days. (We were unable to do a diagnostic lumbar puncture because of the presence of several CNS localizing signs and lack of imaging facilities such as CT scan to reliably exclude presence of raised intracranial pressure.) The patient regained full consciousness but the right hemiplegia, the flaccid paralysis and wasting of the left arm remained. Examination of the cranial nerves (which was now possible after regaining full consciousness) revealed craniopathies of the left V, VII, IX, X, XI, and XII.

MATERIALS AND METHODS

Due to the unusual presentation of this case and the inaccessibility of advanced imaging facilities e.g. CT Scan, MRI, in our hospital, a search for the cause was started using serological tests and ordinary x-ray facilities. HIV serology (Abbott Determine) was negative twice. Rapid Plasma Reagin (RPR), Hexagon syphilis (a treponemal test for syphilis) and anti-double-stranded DNA anti body – a specific test for Systemic Lupus Erythematosus (SLE) - (Human Diagnostics, Wiesbaden, Germany) were non-reactive as well. The Brucella serum agglutination test (Cambridge Biotech, UK) was positive with a titre of 1:160 without incubation (a significant titre in our environment is taken as being 1:80 and above, without incubation.)⁷ The hemogram showed an Hb of 12g %, a macrocytic normochromic picture with toxic granulation of the neutrophils. Left oblique view cervical x-ray showed osteophytes encroaching on the foramina of the cervical spine (See picture 1). The antero-posterior and left lateral view cervical x-rays were normal (attachments)

Treatment was started with oral doxycycline 200mg OD for six weeks and IM streptomycin 1gm OD for two weeks. At the end of the 2 weeks many of the signs had cleared except for the residual weakness and wasting of the left arm, that eventually cleared after 1 month of treatment. Brucella titres were negative 10 weeks from the beginning of the treatment. The patient was able to go back to school

and continues to do well to this day.

DISCUSSION

Neuro-brucellosis is uncommon (occurring in only 3-5 % of all brucellosis cases) and the neurologic manifestations of Brucella are diverse. The clinical picture may be confused by the existence of two or more clinical syndromes in the same patient. These include acute toxic manifestations, psychosis, meningitis, encephalitis, myelitis, cerebellar abscesses, subarachnoid hemorrhage, cranial nerve palsies, paraplegia, hemiplegia, sciatica, peripheral neuropathy, radiculopathy, Guillain-Barre syndrome, papillitis, retrobulbar neuritis and optic atrophy. Others include arachnoiditis, ruptured basilar aneurysm, hemiparkinsonism and chorea. Brucella can even mimic a brain tumor requiring neuro surgery. In the chronic form (symptoms lasting more than 1 year-as defined by Spinks), brucellosis can present with depressive or chronic fatigue syndrome-like features.^{1,2,6,8,9,10} Actually recently, one of our patients, a 16 year old secondary school student who presented with features of 'hysteria', had this illness. A 15 year old boy who had dropped out of school 8 years earlier, due to 'mental deterioration' following a febrile illness, was found to have chronic brucella encephalitis.

Not all patients will have a history of direct contact with livestock¹¹ – our patient in this case never had any livestock at home but got the disease from eating under-roasted meat during a school tournament in a neighbouring town! (Mbarara). It is therefore wise to make the screening for brucellosis a routine investigation in our health units owing to the protean nature of this disease and the fact that it is still endemic in our continent-Africa and many other parts of the world. It has been said by some experts that neurobrucellosis can only be treated using rifampicin and third generation cephalosporins¹² but we have successfully used doxycycline and streptomycin in several other cases of neurobrucellosis in our hospital. Other manifestations of brucellosis include: osteoarticular, genitourinary tract (orchitis, endometritis, pyelonephritis etc), endocarditis, hepatitis, splenic abscess, thyroid abscess, pneumonitis, pleural empyema, uveitis, aneurysm of the aorta, aneurysm of the cerebral vessels and peritonitis among others.

The significant serological (Serum Agglutination Test) titre remains controversial especially in those areas with low prevalence of the disease e.g northern Europe. No single titer of brucella antibodies is always 'diagnostic'. In our experience we have found that a titre of 1:80 or higher without incubation is significant enough if there is adequate epidemiological and clinical evidence. In the chronic forms the titre may be low or even negative! (references 1,4). *Brucella canis* titration may be negative in

presence of the disease as the commonest reagent used for serology is made from *Brucella abortus* which shares the smooth O-polysaccharide with *B. melitensis* and *B. suis*. *B. canis* is a rough species lacking the smooth O-polysaccharide antigen therefore, it is necessary to use antigen prepared from *B. canis* or *B. ovis* to diagnose canine brucella. Also the titre may be negative owing to the prozone phenomenon-requiring dilutions up to 1:320 or more to get a positive result. Sometimes a false negative test occurs because of serum-blocking substances ('blocking antibodies'). If these antibodies are suspected, a Coombs test or blocking antibody assay is to detect them. False positive reactions can occur with sera containing antibodies to the organisms of cholera, tularemia and yersinia. The WBC count is usually normal or even low, thus misleading the clinician to think that there is no infectious process involved. The gold standard is isolation of the organism from bone marrow culture on special media e.g Bactec, Du Pont Isolator. The catch rate with these media varies from 15 to 75% and it may take 30 days or more before any bacteria are isolated.^{1,2,7} Even more, they are not readily available in most of our institutions in Africa.

The purpose of writing this article is to raise awareness about the many forms in which brucellosis can present in our population, the fact that it can be diagnosed even using simple laboratory procedures and the fact that it responds to ordinary drugs available even in rural, resource-poor health units.^{1,2,12,13,14}

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