

Breast Brucellosis in Taif, Saudi Arabia: cluster of six cases with emphasis on FNA evaluation

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Abstract

Background: Brucellosis is an endemic zoonosis seen in a variety of geographical locations such as the Middle East and Latin American and Mediterranean countries. Brucellosis is hyper- endemic in Saudi Arabia with an incidence of 5.4 per 1000 per year. Breast involvement very rarely occurs as a focal complication of brucellosis.

Methodology: We report six cases of breast brucellosis retrieved from the files of the patients. Fine needle aspiration (FNA) was performed on all patients. In all cases direct smears were made at the patient's side for assessment of sample quality. Cytospin and cell block preparation was done and Gram, periodic acid-Schiff and Ziel-Nelson stains were done on all samples. Microbiological analysis included routine fungal and bacterial culture for tuberculosis.

Results: Age range was 20 to 48 years with a median of 22 years. Two patients gave history of raw milk ingestion, one was lactating, and one patient was pregnant. Cytomorphologic features of brucellosis in the breast include an abscess-like background with granulomatous inflammation. Cytology of the patients presented with breast abscess showed predominant neutrophilic infiltrate compatible with acute pyogenic inflammation. Culture was positive for *B. melitensis* in all cases.

Conclusion: Brucellosis should be kept in mind in the differential diagnosis of breast abscess in endemic areas where ingestion of unpasteurized milk and milk products is common. Needle aspiration establishes a preliminary diagnosis and has the advantage of material submission for microbiologic cultures and provides focal treatment along with long-term combined antibacterial treatment for the control of systemic infection.

Key words: breast, abscess, brucellosis

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Introduction

Brucellosis is an endemic zoonosis seen in a number of geographical locations such as the Middle East and Latin American and Mediterranean countries. Brucellosis was first recognized as disease affecting humans on the island of Malta in the nineteenth and early twentieth centuries. It is also known as undulant fever, Malta fever, or Bangs disease.

The World Health Organization (WHO) classifies brucellosis as a Risk Group III Pathogen, meaning it poses a high risk to certain professions but a low risk to the community [1]. The disease usually presents as a systemic febrile illness. It is characterized by an acute bacteremic phase followed by a chronic stage that may involve many tissues; soft tissue localized infections due to *Brucella* are uncommon in humans [1]. Brucellosis is hyper-endemic in Saudi Arabia with an incidence of 5.4 per

1,000 per year [2]. Its prevalence has been variable in different regions of the country with values of 8.8-38% having been reported [2]. According to Memish *et al.* [3], more than 8,000 cases are reported per year to public health authorities. The mode of transmission is usually consumption of unpasteurized milk or infected dairy products or direct contact with livestock [4]. Breast involvement in animals is common, whereas in humans it is an extremely rare condition. The cytomorphologic features of brucellosis are not well described in the literature as patients are rarely subjected to fine needle aspiration cytology (FNAC) and the diagnosis is usually achieved by serologic tests. We present the largest series of culture-proven cases of breast brucellosis in Taif, Saudi Arabia, emphasizing the significance of FNAC evaluation and cytological features.

Table 1.

	Age (Yrs)	Laterality & Size (Cms)	Clinical presentation	Specific history	FNA findings	Culture	Treatment
Case 1	45	R (3x2.5) L (2x2)	Bilateral Breast Lumps With palpable axillary nodes. ?malignant	H/O Bloody nipple discharge for three weeks	Granulomas, Giant cells, numerous neutrophils. No Caseous necrosis	Positive for <i>B. melitensis</i>	Rifampicin & Tetracycline for 7 weeks with mass reduction.
Case 2	35	L(5x2.5)	Breast Abscess. S/S of systemic Brucellosis	H/O lactation. H/O raw milk ingestion	Neutrophilic infiltrate. No Caseous necrosis	Positive for <i>B. melitensis</i>	Surgical drainage & Antibiotics
Case 3	20	R (4x 3.5)	Breast Lump	H/O raw milk ingestion	Epithelioid cells, lymphocytes, neutrophils. No Caseous necrosis	Positive for <i>B. melitensis</i>	TMP / SMX for 2 months
Case 4	32	R (5x3) L(4x2.5)	Breast Abscess	H/O lactation	Neurtrophilic infiltrate.	Positive for <i>B. melitensis</i>	Surgical drainage & Antibiotics
Case 5	48	L (3x3)	Sub-areolar breast Lump	Pregnant	Epithelioid cells & neutrophils. No Caseous necrosis	Positive for <i>B. melitensis</i>	Doxycycline and Streptomycin
Case 6	32	L (4.5x 4)	Breast Lump ? malignant	None	Granulomas, dissociated giant cells, eutrophils. No Caseous necrosis	Positive for <i>B. melitensis</i>	Rifampicin & Tetracycline

Figure 1. Epithelioid granulomas with neutrophils in the Background (Papanicolaou, 200 X). B)

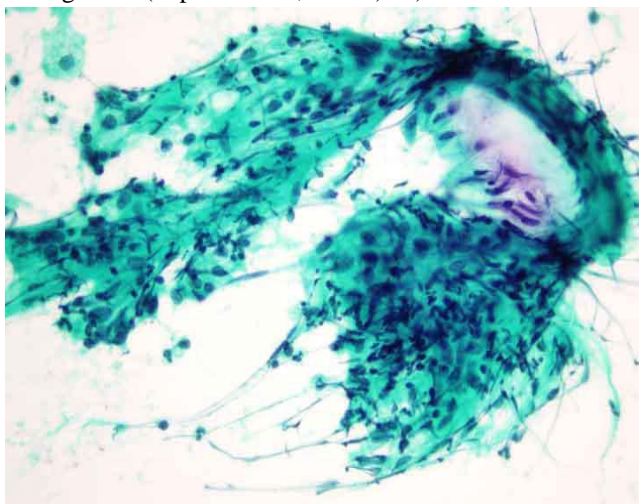
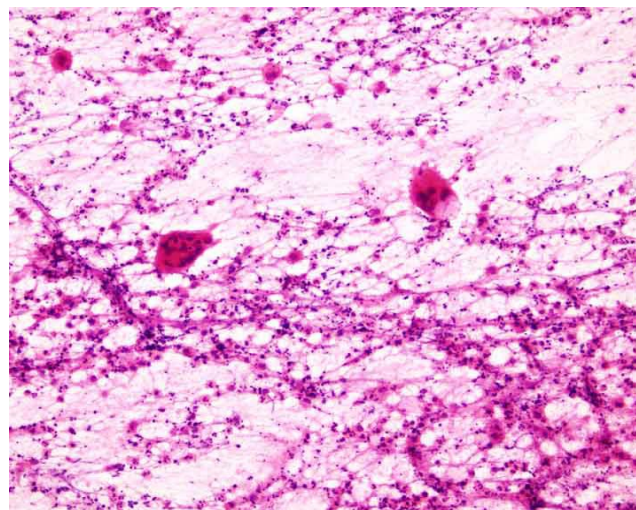


Figure 2. Numerous neutrophils and multinucleated giant cells in a case of breast brucellosis (H & E, 200 X)



Material and Methods

This study included a total number of six female patients. Files of the patients were reviewed. Fine needle aspiration was performed on all patients and surgical drainage was done in two patients. Needles with 25 5/8 G needles were used with 10 ml syringes. Direct smears were made and stained by Diff Quick stain at each patient's side for assessment of sample adequacy. Cytospin and cell block preparation was done in all cases. Gram, periodic acid-Schiff and Ziel-Nelson stains were done on all samples. The aspirates were identified as granulomatous based on the presence of granulomas with/without caseous necrosis and/or scattered discrete epithelioid cells. Multinucleated giant cells and presence of other inflammatory cells in the background including lymphocytes, plasma cells, neutrophils and eosinophils was also evaluated. Microbiological analysis included routine fungal and bacterial culture for tuberculosis. The aspirated material was inoculated on *Brucella* agar. The plates were incubated at 37°C in a CO₂ incubator. Colonies were observed after incubation.

Results

This study included total number of six female patients aged 20 to 48 years with a median age of 22 years. Two patients gave history of raw milk ingestion, one was lactating, and one patient was pregnant. Two patients had bilateral breast masses while three had left and one had right breast lumps. Two patients presented with clinical suspicion of malignancy and two had clinical diagnosis of breast abscess. One patient had signs and symptoms of systemic brucellosis in addition to the breast lump while the physical and systemic examination findings of rest of the patients were unremarkable. Cytology of the patients presenting with breast abscess showed predominant neutrophilic infiltrate compatible with acute pyogenic inflammation (Figure 1). FNAC of two patients showed granulomatous inflammation with poorly formed granulomas (Figure 2). Multinucleated giant cells were also seen. Two patients showed discrete scattered epithelioid cells in a background infiltrate of neutrophils (Figure 3 & 4). None showed caseous necrosis. Gram Stain, periodic acid-Schiff and Ziel-Nelson stains were done on all cases which were negative. Microbiological analysis included routine fungal and bacterial culture for tuberculosis. Culture was positive for *B. melitensis* in all cases. Small colonies measuring between 1-2 mm were observed during the second to the fifth day of

incubation. Gram staining revealed Gram negative cocco-bacilli that were catalase and urease positive. Prolonged incubation period of 11 days was required in one case. Serology was positive in all cases. All patients received combined anti-bacterial treatment for variable periods. Two patients with breast abscess had surgical drainage in addition to drug treatment.

The results are summarized in Table 1.

Discussion

Brucellosis is caused by members of the genus *Brucella*, which consists of six recognized species based on pathogenicity and host preferences: *Brucella abortus* (cattle), *Brucella canis* (dogs), *Brucella melitensis* (goats or sheep), *Brucella suis* (swine), *Brucella ovis* (rams), and *Brucella neotomae* (desert rats), as well as recently identified strains from marine mammals. *Brucellae* are intracellular facultative Gram negative cocco-bacilli that infect many organs and soft tissues. Systemic brucellosis is the most common clinical form of the disease but hematogenous spread may result in focal forms of infection. Endocarditis, glomerulonephritis, uveitis, splenic abscess, hepatic abscess, and prosthetic device infection all represent hematogenous spread of the infection [4-12].

Brucella infection of prosthetic devices includes breast implants, prosthetic joints, prosthetic heart valves, and one report of an infected pacemaker [13].

The prevalence of human brucellosis is related to milk and milk products, occupational exposure, and cultural and socio-economic conditions producing close contact with domestic animals and their environment. Common routes of infection include inoculation through cuts and abrasions in the skin or via the conjunctival sac, inhalation, or ingestion via the gastrointestinal tract. Human-to-human transmission is rare. There have been case reports of transmission via blood transfusion and bone marrow transplantation from infected donors. Sexual intercourse is a possible means of transmission. Neonatal infection can be acquired transplacentally or during delivery.

Mastitis and udder abscesses are common in animals due to *Brucella*; however, recently they have been documented in humans. In three of the reported cases [7,14,15] the infection probably represented hematogenous spread as it involved both breasts simultaneously.

Figure 3. Breast brucellosis showing necrotic debris and numerous neutrophils admixed with histiocytes, giant cells and poorly formed granulomas (PAP, 200 X).

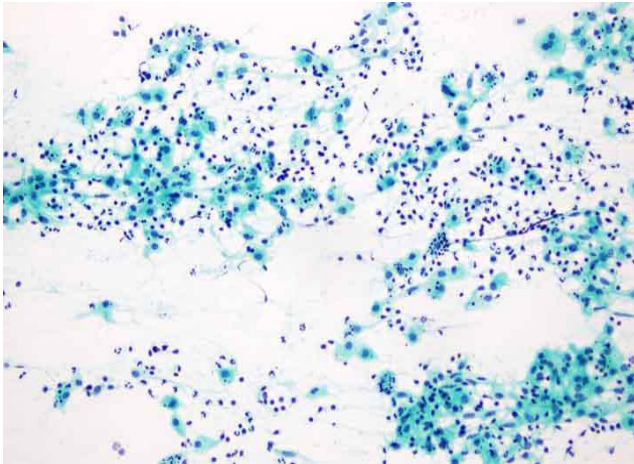
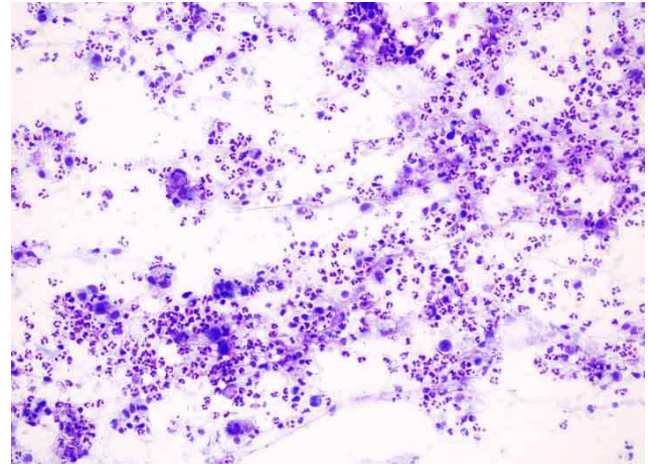


Figure 4. Numerous neutrophils in an abscess-like fashion mixed with histiocytes (DO, 100 X).



Cokca *et al.* [15] have described bilateral multiple breast abscesses with axillary lymphadenopathy caused by *B. melitensis* in a pregnant female. Two patients in our series also presented with breast abscess. The treatment of breast abscess was needle aspiration in two previous cases described by Cokca *et al.* [15] and Tsironi *et al.* [16].

Guerleyik *et al.* [17] and Erdem *et al.* [18] described needle aspiration adequate management for preliminary diagnosis and proper local treatment. A single case of granulomatous mastitis due to brucella has been described in the literature by Gilbert *et al.* [19]. Four cases in our series showed granulomatous inflammation on FNAC.

The cytomorphic features are not well characterized in the literature because patients are usually diagnosed through a combination of clinical findings and serological tests, and sometimes patients are not subjected to biopsy or fine needle aspiration cytology. The smears in our series were very cellular with poorly formed epithelioid granulomas in two cases; numerous dissociated giant cells were also identified while few of them were associated with the granulomas. Neutrophilic background was a common feature in all cases. The granulomatous reaction was in intimate relation with the benign ductal epithelial cells. The presence of giant cells dissociate from granulomas was a helpful feature. No Caseation necrosis was identified. Caseous necrosis is usually not seen in

brucellosis except for *B. suis*, which is uncommon in our country.

Brucellosis should be kept in mind in the differential diagnosis of breast abscess/mass in areas where ingestion of unpasteurized milk and milk products is common. *Brucella* is a slow-growing organism in the culture, and there is a possibility of misdiagnosing cases with unusual presentation. Diagnostic difficulties may also occur particularly if the patient lives in a brucellosis-free country. Needle aspiration of the lesion may help in establishing a preliminary diagnosis and has the advantage of material submission for microbiologic cultures and helps in focal treatment along with long-term combined antibacterial treatment for the control of systemic infection.

Brucella is susceptible to tetracycline, rifampicin and ampicillin. Treatment should be combined and prolonged for complete resolution.

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