DOI: 10.7860/JCDR/2017/26117.9848

Case Series

Internal Medicine Section

Respiratory Symptoms as Prominent Manifestation of Brucellosis: A Case Series

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ABSTRACT

Brucellosis is a zoonotic infection primarily affecting the reticuoendothelial system: spleen, liver and bone marrow. Despite the fact that multisystem infection in brucellosis is usually reported, pulmonary involvement is considered to be very rare. We report four cases (three male and one female, farm workers) of pulmonary brucellosis who presented with signs and symptoms of lower respiratory infection. All of them underwent thorough clinical examination and laboratory tests before the diagnosis of pulmonary brucellosis was confirmed. All patients were hospitalized for at least eight days and given appropriate antibiotic therapy. Follow up after 12-24 months showed no lasting effects from the infection and laboratory tests were found within the normal limits.

Keywords: Brucella, Pneumonia, Pulmonary brucellosis, Zoonotic infection

INTRODUCTION

Brucellosis is a zoonotic bacterial infection caused by the genus *Brucella*. These small aerobic intracellular coccobacilli, which are Gram-negative and non spore forming, shed in the urine, milk, placenta and other fluids of animals, mainly domestic. Humans are accidental hosts [1]. Transmission is generally achieved either through direct contact with contaminated animals, or through ingestion of unpasteurized dairy products and inhalation of infectious aerosol particles, suggesting that *Brucellae* enter the human body through skin or mucous discontinuities [2]. Symptoms include fatigue, malaise, anorexia and body aches. Fever is the most common sign [3]. Pulmonary involvement rarely occurs as a result of inhalation of infected aerosol or hematogenous spread and pulmonary manifestations including pleural effusions and pneumonias, can be found in up to 16% of complicated cases [4].

CASE SERIES

Case 1

A 55-year-old shepherd was admitted to the Emergency Department (ED) by a general practitioner due to persistent fever, along with productive cough and fatigue that started eight days ago and did not respond to empiric antibiotic therapy with cefuroxime axetil. Physical examination was unremarkable and laboratory exams revealed mild leukopenia, elevated C-Reactive Protein (CRP) and slightly high Erythrocyte Sedimentation Rate (ESR) [Table/Fig-1]. Chest x-ray was negative for lobar pneumonia but ground glass opacity was found in high resolution Computerized Tomography (CT) scan. The diagnosis was confirmed by positive Wright agglutination and detection of IgM antibodies by ELISA. Initiation of anti-brucella treatment with doxycycline 100 mg P.O, twice daily and rifampicin 600 mg/day P.O, resulted in significant clinical improvement on day three. The patient remained asymptomatic and on day 10 and he was discharged. Follow-up at three months and 12 months was unremarkable.

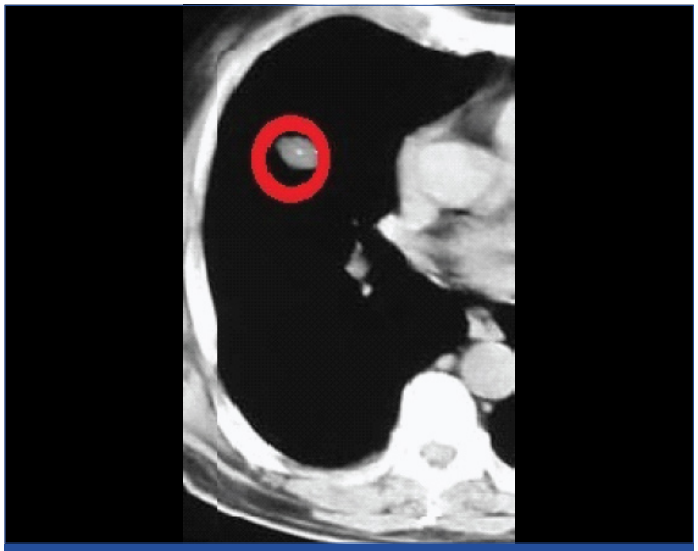
Case 2

A 49-year-old, never-smoker farmer presented to the ED with low grade fever and fatigue for more than 15 days. He had been treated for brucellosis with bone involvement 12 months before the onset of the new symptoms. He complained of pain in joints and non productive cough as well. The auscultation revealed true bronchospasm wheezes in the left hemithorax. Inflammatory markers were high [CRP: 15.7 mg/l (0-1mg/l), ESR: 50 mm/hr (<25 mm/hr)], the liver biochemistry was abnormal [Serum Glutamil Oxaloacetic Transaminase (SGOT): 68 U/L (10-30 U/l), Serum Glutamic Pyruvic Transaminase (SGPT): 70 (10-30 U/l)] [Table/Fig-1] and pulmonary

No	Sex	Age	Possible Exposure	Prominent Symptoms and Signs	Other Symptoms	Lung CT Scan	WBC (10^3/mm^3)	PLT (10^3/mm^3)	CRP (mg/l)	ESR (mm/h)	Other Lab finding	Cultures		WRIGHT test	ELISA IgM
												blood	sputum		
1	M	55	Shepherd	Fever, productive cough	Fatigue	Ground glass opacity	4.0	172	9.4	32	None	–	–	+ 1/1280	3,8 (+)
2	M	49	Farmer	Low-grade-fever, non productive cough, bronchospasm	Pain in joints, anorexia	Pulmonary nodules	6.8	220	15.7	50	SGOT=68 SGPT=70 (U/L) Sacroiliitis	+	–	+1/640	4.2 (+)
3	F	68	Shepherd	Fever, paroxysmal cough	Fatigue, pain in joints	Basal right side pneumonia, thoracic lemphadenopathy	4.1	102	8.3	38	None	–	–	+1/320	3 (+)
4	M	72	Farmer	Fever, dyspnoea, hypoxemia	Anorexia	tree-in-bud sign	9.9	198	11.2	49	None	–	–	+1/320	3.2 (+)

[Table/Fig-1]: The characteristics, clinical and laboratory findings of each patient.
WBC: White Blood Cells, PLT: Platelets, CRP: C-reactive protein, ESR: Erythrocyte Sedimentation Rate, SGOT: Serum Glutamil Oxaloacetic Transaminase, SGPT: Serum Glutamic Pyruvic Transaminase, (+): positive, (-): negative, M: Male, F: Female

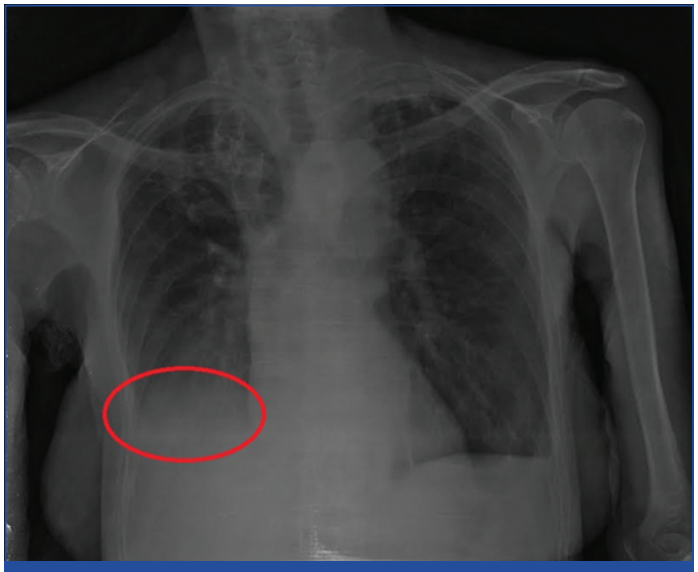
nodules were observed in the CT scan [Table/Fig-2]. Two out of three blood cultures BACTEC Plus Aerobic/F and Anaerobic/F [Becton Dickinson, Allschwil, Switzerland], incubated for 10 days were positive for Brucella species. The Wright agglutination test and the ELISA IgM antibodies set the diagnosis. The patient was treated for brucellosis relapse with six week doxycycline (200 mg/day, orally) plus rifampicin (900 mg/day, orally) combined with gentamicin (5 mg/kg, intramuscularly) for the initial two weeks. The patient was lost to follow up.



[Table/Fig-2]: Pulmonary nodule in the chest CT scan of a patient (hemithorax) with pulmonary brucellosis was a non specific finding.

Case 3

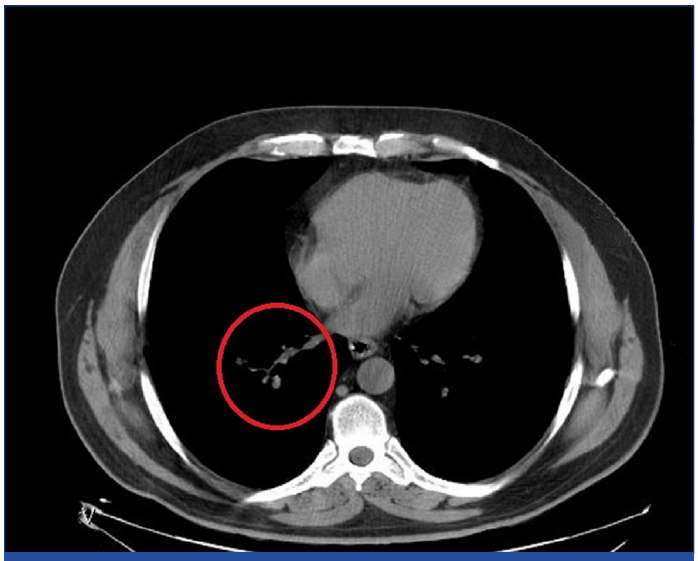
A 68-year-old hypertensive female who lived in a rural area and had received anti *Brucella* treatment 17 years ago was hospitalized for fever, paroxysmal cough and joint pain without signs of arthritis. CRP was elevated but ESR was within the normal range. Leukocytes and platelets were slightly low [Table/Fig-1]. Chest x-ray was consistent with lobar, basal right side pneumonia and showed ground glass opacities [Table/Fig-3]. The CT scan revealed thoracic lymphadenopathy as well. Having positive Wright agglutination test and ELISA IgM antibodies, the patient was treated for brucella reinfection with doxycycline 200 mg/day P.O. and rifampicin 600 mg/day P.O. for six weeks. Semiannual clinical and paraclinical follow up revealed total resolution of the infection.



[Table/Fig-3]: Basal pneumonia in the chest x-ray of a woman with pulmonary Brucellosis.

Case 4

A 72-year-old male farmer presented to the ED complaining about gradually established with dyspnoea, fever and productive cough. He had past medical history of chronic ischemic heart disease. He was hypoxemic and, therefore, he underwent a lung CT scan which revealed a tree-in-bud sign [Table/Fig-4]. The patient had been treated for Brucellosis 21 years ago. Sputum and blood cultures were negative but Wright agglutination test as well as Elisa IgM antibodies set the diagnosis for Brucella reinfection with pulmonary involvement [Table/Fig-1]; the patient received triple antibiotic therapy with intravenous gentamicin 5 mg/kg for seven days and then with doxycycline 100 mg P.O. twice daily and rifampicin 600 mg/day P.O. for 45 days. The patient was followed up for two years and no sign of relapse was detected.



[Table/Fig-4]: Chest CT scan of a patient with pulmonary Brucellosis [Case 4]. Note the tree-in-bud sign.

DISCUSSION

The most common and virulent species of *Brucella* that infect human are *Brucella melitensis* (typically associated with sheep and goats) and *Brucella abortus* (associated with cattle) [5]. Human brucellosis generally occurs through direct exposure to the pathogen. All of our patients had direct contact with domestic animals or their raw products before the onset of the symptoms. Any organ may be affected. One of our patients had additional liver involvement while another one had previously been treated for osteoarticular brucellosis. Pulmonary involvement in brucellosis may occur through inhalation and therefore, the immune system associated with the lungs play an important role in mediating the initial recognition of infection [6]. Nonetheless, *Brucella* species are intracellular pathogens and, therefore, they manage to avoid the cellular immune response and establish infections for prolonged periods [7]. The onset of symptoms may be acute or insidious and almost always they are non specific [8]. The general symptoms of our patients were non specific as well. The initiation of symptoms for one of our patients was considered to be acute and, therefore, we assumed that he suffered an acute, first ever pulmonary brucellosis. As far as laboratory tests are concerned, thrombocytopenia and leukopenia are thought to be strongly associated with brucellosis [9], yet only two of our patients had an abnormal total blood count. There are few reports of respiratory involvements and a wide spectrum of lung disease has been reported [10]; empyema [11], pleural effusion [12], solitary nodules [13], interstitial pneumonia [14] and even pneumothorax [15] and pulmonary embolism [16] have all been reported and they can even be the sole symptom of brucellosis. The clinical manifestations of our four patients were consistent with lower respiratory infection. Due to prolonged and

non specific symptoms, tuberculosis, granulomatous diseases and tumors should not be neglected in the differential diagnosis of pulmonary Brucellosis [8]. Isolation of *Brucella* spp. from any clinical specimen or detection of agglutinating antibodies combined with detection of non agglutinating antibodies or PCR confirm the diagnosis [5].

CONCLUSION

Brucellosis is a systemic infection, signs and symptoms of which are non specific. Keeping in mind that brucellosis is a good mimic, clinicians should always consider it in any patient with personal history of exposure to a possible source of infection.

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FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Dec 18, 2016**
Date of Peer Review: **Feb 11, 2017**
Date of Acceptance: **Mar 09, 2017**
Date of Publishing: **May 01, 2017**