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CONCISE ARTICLE

Pulmonary complications of babesiosis: case report and literature review

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Abstract Reported here is a rare case of babesiosis with pulmonary complications followed by a review of the literature. Babesiosis presents clinically as a malaria-like illness with fever, chills, headache, fatigue with lymphopenia, atypical lymphocytes, mildly or transiently elevated serum transaminases, thrombocytopenia, and increased lactate dehydrogenase (LDH) levels. The diagnosis of babesiosis is based on identification of *Babesia* spp. on a peripheral blood smear. Babesiosis is usually mild in normal hosts, but it may be severe or even fatal in asplenic patients. Pulmonary manifestations are rare in babesiosis, but non-cardiogenic pulmonary edema (NCPE) is the most frequent manifestation. NCPE in babesiosis does not appear to be related to the degree of parasitemia or splenic function and its onset may be early or late. NCPE usually resolves rapidly with supportive treatment; it is rarely fatal. Clinicians should suspect NCPE in patients with babesiosis who acutely develop shortness of breath and have chest radiograph findings compatible with acute pulmonary edema without cardiomegaly or pleural effusions.

Introduction

Babesiosis is a tick-borne illness caused by *B. microti* and other species, e.g., *B. divergens* is transmitted by the *Ixodes* tick. The diagnosis of babesiosis is based on the demonstration of typical red blood cells (RBCs), inclusion bodies, or elevated *B. microti* IgM titers. The first well-documented human case of babesiosis was reported in 1957 and there have been over a dozen subsequent cases [1–8].

The clinical presentation of babesiosis varies from asymptomatic disease to malaria-like symptoms with fever, rigors, myalgias and headache. Babesiosis is characteristically associated with intravascular hemolytic anemia. Hepatomegaly and splenomegaly may be present, and an elevated LDH value should suggest the possibility of babesiosis. Lymphopenia is common in babesiosis and atypical lymphocytes may be present. Other commonly reported laboratory abnormalities include mild or transient elevations of serum transaminases and subnormal high-density lipoprotein levels [9, 10]. Most patients with an intact spleen recover spontaneously. Symptoms are usually more severe in elderly, immunocompromised or splenectomized hosts. The diagnosis of babesiosis is based on epidemiology and clinical findings and on laboratory data including identification of *Babesia* spp. on peripheral blood smear, specific IgM and IgG antibody responses or polymerase chain reaction. Babesiosis is usually treated with a combination of clindamycin and quinine or atovaquone and azithromycin. In severe cases involving asplenia, exchange transfusions have been used [9–18].

Non-cardiogenic pulmonary edema is a recognized complication of *P. falciparum* malaria, but it is rare with babesiosis. A review of the literature revealed few cases of babesiosis with respiratory symptoms [19–23].

Case report

A 63-year-old woman who resided in eastern Long Island, New York, USA, was admitted with fever measuring 38.9–

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39.4°C (102–103°F) and chills of 3 weeks duration. Her medical history was significant for idiopathic thrombocytopenic purpura (ITP) and splenectomy in 1979. Prior to admission, she presented to her primary-care doctor and was started on a week-long course of ciprofloxacin without improvement. She was referred for an infectious disease consultation for a questionable tick bite on her lower back, and oral doxycycline (200 mg q12 h) was begun. Her blood work at the time revealed a leukocyte count of 4.2 k/mm^3, a hemoglobin level of 16 g/dl, a hematocrit value of 50%, and normal serum LDH. Her transaminases were within normal limits and her antinuclear antibodies were positive at 1:160 (speckled pattern). Her IgG titer for Epstein–Barr virus viral capsid antigen was positive, but IgM was negative. Lyme and Ehrlichia IgM and IgG titers were negative.

The following evening she continued to experience fevers and rigors and she went to the emergency room of a local hospital. A peripheral blood smear showed the characteristic intracellular ring forms of *Babesia* (degree of parasitemia, <1%), and she was discharged home on oral atovaquone (750 mg, q12 h) and oral azithromycin (250 mg, q24 h). The next day, the patient reported a rash on her inner thighs and she was readmitted for a possible drug reaction. Atovaquone and azithromycin were discontinued and she was started on intravenous clindamycin (600 mg, q8h) and oral quinine (650 mg, q8h).

The patient developed hemolytic anemia with a hemoglobin count of 11 g/dl, hematocrit level of 32%, and a lactate dehydrogenase (LDH) level of 2,647 IU/l. She was transferred to Winthrop-University Hospital for further evaluation. On admission, her temperature was 99.3°F, with a respiratory rate of 16 breaths/min. Her chest and cardiac exams were unremarkable. Her purpura was palpable and painful and thought to represent cold agglutinin (titer 1:256)

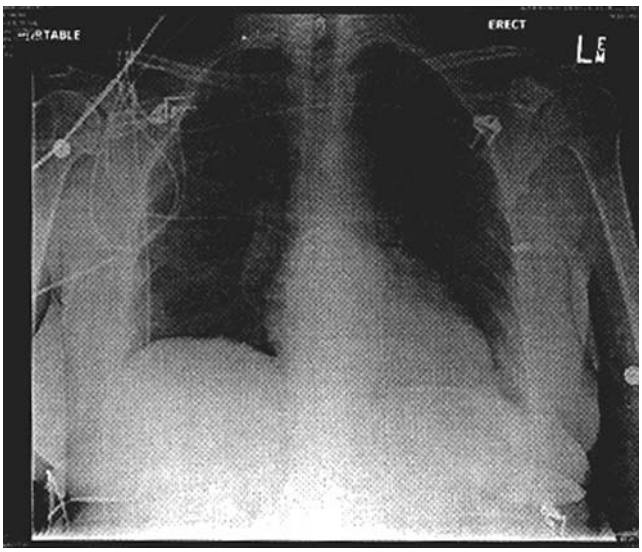

Fig. 1 Normal chest radiograph at admission of a 63-year-old woman with babesiosis

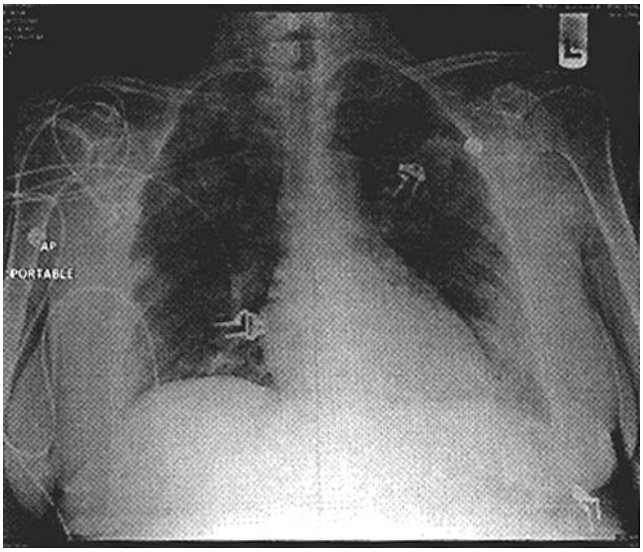

Fig. 2 Chest radiograph performed on day 4 of hospitalization demonstrating a non-cardiogenic pulmonary edema during an acute episode of shortness of breath

vasculitis. Her hemoglobin decreased to 10 g/dl, hematocrit to 28%, and LDH to 1,401 IU/l; her reticulocyte count was 4%, total bilirubin was 7.3 mg/dl, and indirect bilirubin 6.1 mg/dl. The remaining laboratory tests were within normal limits. Her electrocardiogram (EKG) showed normal sinus rhythm. Chest radiograph on admission was clear with no evidence of cardiomegaly, effusion or infiltrates (Fig. 1). The patient underwent an exchange transfusion with 8 U of blood and subsequently received an additional 2 U with no net gain in fluid volume.

On hospital day 4, she developed acute shortness of breath and mild chest discomfort. At that time, she was afebrile, her heart rate was 82 beats/min, and respiratory rate 24 breaths/minute. On examination, she was in respiratory distress, and her breath sounds were decreased in both lower lung fields. She had neither moist rales nor a S_3 gallop rhythm. Chest radiograph showed non-cardiogenic pulmonary edema (Fig. 2).

The patient's shortness of breath improved over the next several days. She did not require further blood transfusions. Repeat chest radiograph showed complete resolution of non-cardiogenic pulmonary edema. The patient was discharged on hospital day 11 and prescribed a 2-week course of oral clindamycin (600 mg, q8h) and quinine (650 mg, q8h).

Discussion

Babesiosis is a tick-borne zoonosis that presents as a malaria-like illness. Like malaria, babesiosis presents as an acute infectious disease characterized by acute hemolytic intravascular anemia. In areas where babesiosis is endemic, patients presenting with an acute ill-defined febrile illness, character-

Table 1 Review of babesiosis cases complicated by non-cardiogenic pulmonary edema

Reference	Year	No. of cases	Age (years)	Sex	Parasitemia (%)	Splenectomy	Associated disorders	Time from onset of symptoms to NCPE (days)	Days intubated	Time from onset of symptoms to NCPE resolution (days)	Fatal outcome
Gordon et al. [19][a]	1984	1	79	F	10	–	Abdominal abscess	13	+/(6)	–	+[b]
Rowin et al. [16]	1984	1	25	F	6	+	–	NK	–	NK	–
Golightly et al. [17]	1984	1	37	F	2	+	–	14	–	11	–
Iacopino and Earnhart [22]	1990	1	63	F	30	–	–	30+	+/(NK)	NK	–
Boustani et al. [20]	1994	3	65	F	15	–	–	9	+/(5)	5	–
			40	M	1	–	–	30+	+/(2)	2	–
			74	M	0.1	–	–	NK	–	6	–
Horowitz et al. [21]	1994	1	70	M	2	–	–	7	+/(10)	NK	–
Hatcher et al. [23]	2001	7	35	M	2	+	Alcoholism	NK	NK	NK	–
			43	F	10	–	Diabetes	NK	NK	NK	–
			74	M	4.5	–	Diabetes, CAD	NK	NK	NK	–
			62	M	30	+	Alcoholism	NK	NK	–	+[c]
			55	M	22%	–	Alcoholism	NK	NK	NK	–
			73	M	8	–	CAD, COPD, G6PD deficiency	NK	NK	–	+[c]
			73	M	5.6	–	–	NK	NK	NK	–
PR	2006	1	63	F	<1	+	–	30+	–	7	–

NK: not known, *NCPE*: non-cardiogenic pulmonary edema, *CAD*: coronary artery disease, *COPD*: chronic obstructive pulmonary disease, *PR*: present report

[a] All infections were tick-borne except for one acquired via transfusion

[b] Cause of death not related to *Babesia* or respiratory complications

[c] Cause of death due to *Babesia*/respiratory complications

ized by fever, headache and chills, should have babesiosis included in the differential diagnosis. An elevated LDH level in such patients is an early and sensitive indicator of intravascular hemolysis and it favors the diagnosis of babesiosis versus Lyme disease or ehrlichiosis [6–8]. The diagnosis of babesiosis is confirmed by evidence of intra-erythrocytic ring forms and/or the presence of characteristic tetrads in peripheral blood smears [1–8].

In splenectomized patients, babesiosis may be severe or life-threatening. In patients with intact splenic function, babesiosis is usually mild; with treatment, it resolves without complications. Pulmonary complications are rare and may be related to fluid overload from exchange transfusions or non-cardiogenic pulmonary edema. To the best of our knowledge, the case presented here is the most recent of only 16 reported in the literature to date. Our patient was an elderly splenectomized woman whose course was complicated by non-cardiogenic pulmonary edema during her hospitalization. In spite of her asplenic status and the case being complicated by a non-cardiogenic pulmonary edema, she made a successful recovery. She had a prolonged course of infection, as evidenced by the slow decline in her LDH level, as well as her hemoglobin and hematocrit levels over time; this was ascribed to her lack of splenic function [8, 16–18].

In reviewing the literature on the pulmonary complications of babesiosis, we found 15 cases not related to fluid overload. It appears that non-cardiogenic pulmonary edema in babesiosis is unrelated to the degree of parasitemia or to the presence or absence of a spleen. In the reported cases of babesiosis, the onset of non-cardiogenic pulmonary edema was found to occur early or late and sometimes followed the initiation of anti-*Babesia* chemotherapy. The mechanism of non-cardiogenic pulmonary edema in babesiosis is not well understood, nor is the mechanism of NCPE in malaria known (Table 1).

Clinicians treating babesiosis should be aware that non-cardiogenic pulmonary edema is the most frequent, albeit rare, pulmonary manifestation or complication of babesiosis. Non-cardiogenic pulmonary edema in babesiosis should be considered in patients with babesiosis who acutely develop shortness of breath and have a chest radiograph showing increased interstitial markings in the absence of cardiomegaly or pleural effusions. Ventilator support may be required in severe cases of babesiosis complicated by non-cardiogenic pulmonary edema or, less commonly, acute respiratory distress syndrome (ARDS). Non-cardiogenic pulmonary edema associated with babesiosis usually resolves rapidly with supportive treatment, unless it is complicated by ARDS. Babesiosis complicated by non-cardiogenic pulmonary edema resolves in up to a week and is rarely fatal [19–23].

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