

What is That Bug in My Blood?

Linda A. Smith, PhD, MLS(ASCP)[®]BB[™]
Steven Dallas, PhD, D(ABMM)
Div. Medical Laboratory Sciences
UT Health
San Antonio, TX



Objectives

- List major characteristics used in identification of Babesia sp. in a peripheral blood smear and compare with those of Plasmodium falciparum
- Describe risk factors associated with development of serious complications
- Compare the usefulness of the diagnostic methods for babesiosis



Case - admission

- 59 y.o. female
- Complaint of persistent fever
 - 102°F
- Evaluation of persistent anemia and thrombocytopenia
- Breast cancer treated approx. 18 months ago

Patient history

- Suspected TTP
 - plasmapheresis
- Current treatment for TTP
 - steroids & rituximab
- Received multiple PRBC transfusions in previous 3 months - anemia
- Bone marrow - negative

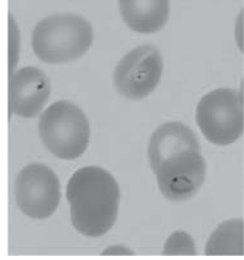
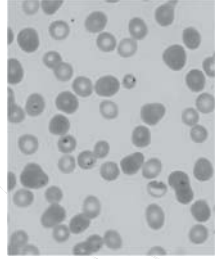
Admission laboratory data

- Elevated liver enzymes
 - ALT 77 (<35 IU/L)
 - AST 58 (<31 IU/L)
 - ALP 213 (45-117 IU/L)
 - LD 688 (92-240 IU/L)

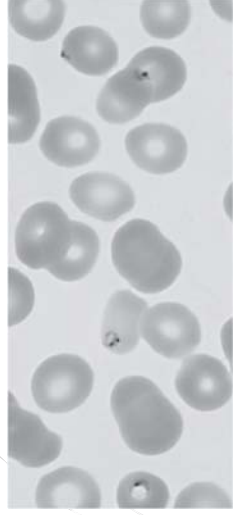
Admission laboratory data

- Hemoglobin 8.4 (11.5-14.9 gm/dl)
- Hematocrit 26% (36-45.5%)
- RBC count 3.1 (4.0-5.0 M/ul)
- Platelet count 76 (140-377 K/ul)
- Evaluation of PBS

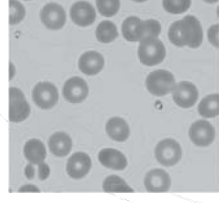
Peripheral blood smear



Peripheral blood smear



Peripheral blood smear



Initial parasitemia 6%

Follow up & treatment

- BinaxNow – negative
- Specimens sent to CDC
 - Serologic testing – P. falciparum and Babesia antibody
- PCR
 - Initially started on anti-malaria treatment
 - Switched to Azithromycin & Atovaquone
 - Blood donors traced

Results

Malaria

- CDC
 - PCR for 5 species of malaria
 - Negative
- Antibody
 - negative

Babesiosis

- PCR for Babesia species
 - Positive
- Antibody titer
 - IgM < 1:20 (<1:20)
 - IgG 1:32 (<1:16)

General information - babesiosis

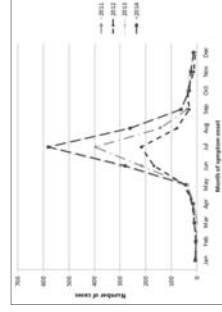
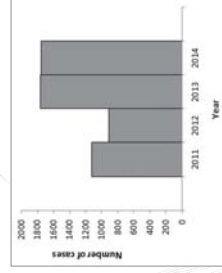
- > 100 species of Babesia
- Majority U.S. infections caused by Babesia microti
 - Endemic in Northeast & upper Midwest
- Other species in U.S.
 - B. duncani & B. duncani-like
 - B. divergens & B. divergens-like



Babesiosis

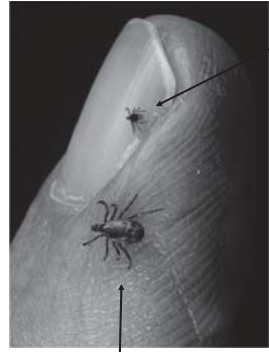
- Since 2011 on CDC's List of Nationally Notifiable Conditions
- Acquired by:
 - Tick bite
 - Vertical transmission from mother to fetus
 - Transfusion
 - Most common cause of transfusion-transmitted disease
 - 1979 – first case
 - By 2009 – 159 cases
 - Now > 200

Number of reported cases of babesiosis



General information

- Vector - deer tick (Ixodes scapularis)
 - Bite of nymphal stage
 - Also transmits
 - Borrelia burgdorferi, Anaplasma phagocytophilum, Powassan virus
 - 10-30% coinfection rate Lyme and babesiosis
- Usual host - white footed mouse



Symptoms

Mild - moderate

- Non-specific
 - Fever
 - Chills
 - Fatigue
 - Headache
 - Myalgia
 - Anemia
 - Thrombocytopenia

Severe

- Acute respiratory distress
- DIC
- Organ failure
 - renal
 - hepatic
- Altered mental state
- Death

Characteristic laboratory values

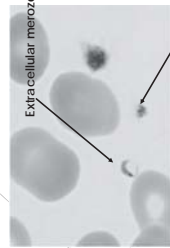
- ↓ hemoglobin / hematocrit
- ↓ Platelets
- Neutropenia -variable
- ↑ LD
- ↑ Liver enzymes
- ↑ Creatinine (severe)

Clinical diagnosis

- Travel history
- Insect bite history
- Medical history
 - Certain conditions predispose to more severe clinical course

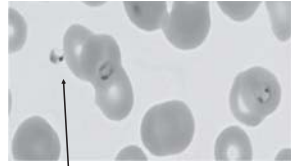
- Peripheral blood smear
 - Small, delicate ring forms
 - Single or double
 - Round, oval, pear-shaped
 - Maltese cross (tetrad)
 - Lack pigment

Extracellular

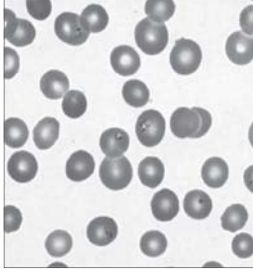


Extracellular merozoite

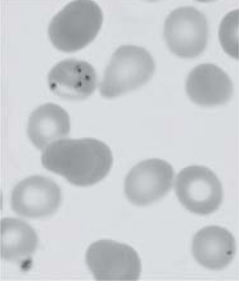
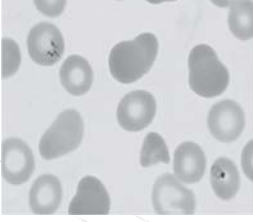
Platelet



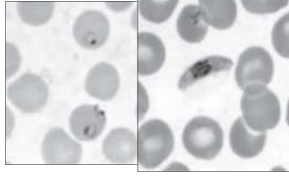
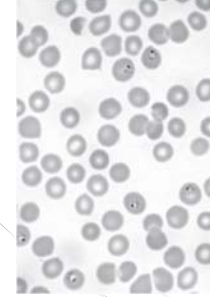
Ring form Babesia



Tetrads / 'Maltese Cross'



Plasmodium falciparum



Other diagnostic methods

- Serologic
 - Negative in early infection
 - Species specific
 - Cannot distinguish current vs. past infection
- Molecular
 - Not sensitive enough for detection low level infection
 - Immunocompromised
 - Also detects 'dead' RNA

Detection

Antibody

- IgM - > 1:64 acute
- IgG > 1:1024 acute
 - > 1:64 12 months after infection
- Sensitivity 88-96%
- Specificity 90-100%

Molecular

- Amplification 18S rRNA
- Sensitivity 95-100%
- Specificity 100%

Treatment

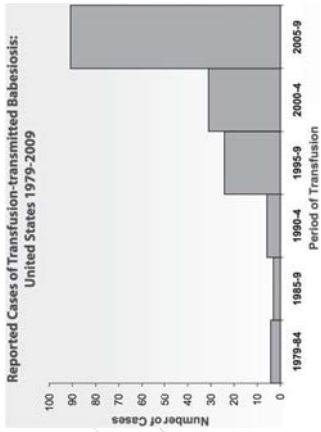
- Asymptomatic
 - 7-days Atovaquone & Azithromycin
- Mild → moderate
 - 7-10 days Atovaquone & Azithromycin
- Severe / Immunocompromised / refractory
 - May require both Clindamycin & Quinine AND Atovaquone & Azithromycin
 - Repeated treatments of one or both combinations

Additional treatment - exchange transfusion

- Used in severe cases
- Removes
 - Infected RBCs
 - Cytokines & free hemoglobin
 - extracellular merozoites

Indications

- Parasitemia > 10%
 - ↓ parasitemia 50-90%
- Hgb < 10g/dl
- Renal, hepatic, pulmonary impairment
- Elderly (> 50 y.o.) or very young (< 1 y.o.)
- Pregnant



Transfusion transmitted babesiosis

- Incubation longer
- 1-9 weeks
- Symptoms vary
 - More severe in those with co-morbidities or asplenic
- Mortality ~ 10 – 20 %
- Occurs any time of year

Transfusion-transmitted Babesiosis by state - 2013



Issues in prevention of TTB

- Current donor questions
 - Not effective
 - Donor asymptomatic
 - Low level and/or protracted parasitemia
 - NO routine serologic test
 - Regional antibody prevalence varies
 - No re-entry algorithm
- Proposed serological screening of donors
- NAT testing of donors
- Pathogen reduction
 - Currently approved for plasma & platelets
 - Not for RBCs
 - Concern with damage to RBC
 - Animal research indicates could be effective

Transfusion-transmitted babesiosis (TTB)

- Babesia -- #1 transfusion-transmitted pathogen in US
- Documented components
 - Red blood cells
 - Responsible for majority of infections
 - Refrigerated
 - Frozen
- Whole-blood derived platelets
 - Residual RBCs in unit