Inclusion Bodies in Tick-Borne Diseases Diagnosed in Patients from Northern Wisconsin

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Clinical Vignette

Case 1

A 65-year-old man from northern Wisconsin, presented to the clinic with complaints of fever, chills, myalgias and severe fatigue. He lived on a farm and frequently visited the woods for hiking. On examination he was found to be febrile without hepatosplenomegaly or lymphadenopathy. His hemoglobin was 8 g/dL, white count was 2.8 with 1100 neutrophils, and the platelet count was 55,000/mm³. A peripheral smear was ordered.

Examination of the Wright-stained peripheral smear (figure 1) shows a neutrophil with an intracytoplasmic inclusion body termed a morulae (Latin for mulberry). The presence of such intra-cytoplasmic inclusions in neutrophils is classically associated with human granulocytic anaplasmosis. The patient was successfully treated with doxycycline 100 mg orally twice a day for 10 days. On a follow up visit he was found to be asymptomatic with complete normalization of his blood counts.

Figure 1. Wright-stained peripheral smear showing a neutrophil with an intracytoplasmic inclusion body, or morulae (arrow), classically associated with human granulocytic anaplasmosis.

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The Aperture, like the opening in the lens of a microscope that allows light to pass through, is a forum for art, humor, and images that provides a portal for new or different views of medicine and research.

Figure 2. Peripheral smear showing red blood cells with parasitic inclusions forming a piroplasmic tetrad, or maltese cross (arrow), pathognomonic for babesiosis.

Case 2

A 35-year-old man from northern Wisconsin, presented to the clinic with complaints of fever, chills and severe fatigue. He lived on a farm and frequently visited the woods for hiking. On examination he was found to be febrile with presence of a mild splenomegaly. His hemoglobin was 8 g/dL and the platelet count was 35,000/mm³. A peripheral smear was ordered.

Red blood cells with parasitic inclusions were seen in the patient's peripheral smear (figure 2). The parasites are 1 to 5 µm in diameter with spherical, oval or tear drop shapes. The pathognomonic feature is the presence of the parasitic piroplasmic tetrad in the red cells, forming the Maltese cross. This smear is diagnostic for infection with *Babesia microti* in humans. The patient was successfully treated with clindamycin and quinine.

Discussion

The term "Human Ehrlichiosis" describes a spectrum of related tick borne infections in human beings. The three most commonly seen infections are human granulocytic anaplasmosis (HGA) caused by *Anaplasma phagocytophilum*, human monocytic ehrlichiosis (HME) caused by *Ehrlichia chaffeensis*, and human ewingii ehrlichiosis caused by *Ehrlichia ewingii*.¹ The commonly associated vectors include *Ixodes scapularis* in the eastern United States, and *Ixodes pacificus* in the western United States, with small mammals such as white-footed mice being likely reservoirs.²

Blood smear evaluation is useful in the diagnosis of HGA. In the U.S., between 25% to 75% of cases reported demonstrate morulae in the peripheral blood examination, with the maximal sensitivity of this modality being during the first week of infection.³ Although no clinical trials have been conducted,

current data suggest that all forms of ehrlichiosis respond well to tetracyclines. The currently recommended treatment regimens for HGA and HME include doxycycline 100 mg orally or intravenously every 12 hours for 5 to 14 days, or rifampin 300 mg orally every 12 hours for 7 to 10 days.^{4,5}

The Maltese cross formation, pathognomonic for the diagnosis of babesiosis, is often described in infections with *Babesia microti*, *Babesia equi* and *Theileria parva*. In mice infected with *Babesia microti*, Maltese cross formations have been thought to represent a protective response against the host immune system, creating an environment favorable for the progression of the parasitemia.⁶ This phenomenon, however, has not yet been described in human beings, and remains a theoretical concept yet to be confirmed.^{7,8}

The combination of quinine and clindamycin has long been considered standard therapy for the treatment of babesiosis.⁵ However, this combination has been associated with a relatively high incidence of adverse drug reactions such as nausea, vomiting, tinnitus, diarrhea and cardiac dysrhythmia.⁵ In a prospective, non-blinded, randomized trial, a combination of azithromycin (500 mg on day one, followed by 250 mg for 6 days) and atovaquone (750 mg every 12 hours for 7 days) was found to be as effective as standard therapy with quinine and clindamycin, for the treatment of non-life threatening babesiosis, and more importantly, was associated with fewer adverse effects.⁹

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