ANAPLASMOSIS

Disease Overview

Anaplasmosis is caused by the rickettsial bacterium (*Anaplasma phagocytophilum*) that survives and reproduces predominantly within white blood cells (neutrophils) of infected hosts. Anaplasmosis was formerly known as human granulocytic ehrlichiosis; and *A. phagocytophilum* was previously referred to as *Ehrlichia phagocytophilum*.

Historically, anaplasmosis has been a rare condition in Canada. However, there have been an increasing number of areas where *Ixodes scapularis* ticks are established and breeding in southern Canada, including New Brunswick and an increase in the number of cases.

Symptoms

Although cases of tick-borne illness can occur during any month of the year, most cases occur when ticks are most active, in the spring, summer, and fall. Most people will have mild or moderate illness, though severe illness is possible. Symptoms typically resolve within 30 days, even without treatment.

Anaplasmosis is characterized by an acute and usually self-limited non-specific flu-like illness (e.g. fever, chills, headache, myalgia, arthralgia, malaise, fatigue). Less commonly noted manifestations include gastrointestinal manifestations, respiratory symptoms, and neurological issues. Skin rash may be present (<10% of patients) but could also indicate co-infection with *Borrelia* spp. or other tick-borne diseases.

Laboratory abnormalities are common in the early phase and can include leukopenia, thrombocytopenia, elevated aminotransferase levels, and nonhemolytic anemia. Severe illness can include renal failure, respiratory distress, hemorrhage, meningitis, encephalitis, and sepsis.

Reservoir

Ixodes ticks (*I. scapularis* in eastern North America, *I. pacificus* in western North America, and *I. ricinus* in Europe) are vectors capable of transmitting the pathogen to people during tick feeding. Blacklegged ticks (*I. scapularis* and *I. pacificus)* can transmit other tick-borne diseases; coinfection of Anaplasma with *Borrelia burgdorferi* (Lyme disease) has been described.

Reservoir hosts support the circulation and maintenance of the pathogen. Vertebrate reservoirs are natural hosts for ticks and once infected, remain infected life long and continue to transmit the pathogen to feeding ticks. In North America reservoir hosts for anaplasmosis are small rodents (i.e. white-footed mice, deer mice) and white-tailed deer.

Mode of Transmission

Primarily vector-borne transmission via bites from infected blacklegged ticks. The typical time required for transmission between ticks and humans is 24 to 48 hours; however, a small number of infected nymphs were found to transmit the bacteria in less than 24 hours (i.e. 12 hours).

Transmission has been documented less commonly through blood transfusion and organ transplant, and rarely through direct handling of infected reservoirs (i.e. white-tailed deer).

Incubation period

5 – 21 days

Most symptomatic patients who can recall a tick bite report this bite to have occurred between 7 to 14 days prior to symptom onset.

Period of Communicability

No evidence of natural transmission from person to person.

Individuals may have subclinical infection and remain infective without symptoms prior to transmission via blood transfusion or solid organ transplantation. The period of infectivity is not yet established but case reports have reported ranges of days to weeks between primary infection and subsequent transmission.

Risk Factors

Increased risk for acquiring illness:

- Exposure to blacklegged ticks

Increased risk for acquiring/severe illness:

- Coinfections with other tick-borne diseases (e.g. *Borrelia burgdorferi*), delayed treatment, advanced age, weakened immune system (due to cancer, AIDS, transplantation, or certain medications).

Surveillance Case Definition

Confirmed Case

Confirmatory laboratory evidence of infection, including transfusion transmission, AND

- Clinical evidence of infection (includes fever and at least one of the following: headache, malaise/asthenia, arthralgia/myalgia, mild anemia, thrombocytopenia, leukopenia, elevated hepatic transaminase concentrations, or elevated numbers of immature neutrophils)

OR

- Without clinical evidence of infection.

Confirmatory laboratory evidence of infection

- Detection of *Anaplasma phagocytophilum* DNA in an appropriate clinical specimen by amplification of a specific target by Nucleic Acid Amplification Test (NAAT)

OR

- Serological evidence of a four-fold change in IgG-specific antibody titre to *A. phagocytophilum* antigen by indirect immunofluorescence assay (IFA) in paired serum samples. The first sample taken in the acute phase (in first week of illness) and the second taken in the convalescent phase (2-4 weeks after the first sample)

OR

- Demonstration of *A. phagocytophilum* antigen in a biopsy/autopsy sample by immunohistochemical (IHC) methods

OR

- Isolation of *A. phagocytophilum* from a clinical specimen in cell culture with confirmation by specific PCR.

Probable Case

Supportive laboratory evidence of infection AND

- Clinical evidence of infection (includes fever and at least one of the following: headache, malaise/asthenia, arthralgia/myalgia, mild anemia, thrombocytopenia, leukopenia, elevated hepatic transaminase concentrations, or elevated numbers of immature neutrophils)

OR

- Blood or solid organ transplant recipient with an epidemiological link to a confirmed or probable anaplasmosis case. For the purposes of surveillance, epidemiologic linkage between a transfusion recipient and a blood donor is demonstrated if all the following four criteria are met:
    1. Laboratory evidence of *A. phagocytophilum* infection in the recipient and donor; AND
    2. Transfusion recipient received one or more red blood cell (RBC) or platelet unit(s) within one year before the collection date of the recipient's positive specimen; AND
    3. Transfused unit(s) was/were plausibly infectious based on assessment of donor infectivity at time of donation of implicated unit(s); AND
    4. Transfusion-associated infection in the recipient is considered at least as plausible as tick-borne transmission.

Supportive laboratory evidence of infection:

- Serological evidence of elevated IgG antibody to *A. phagocytophilum* in a single specimen by IFA where the endpoint titre is four-fold greater than the screening dilution of the assay,

OR

- Identification of typical morulae (microcolonies of A. phagocytophilum) in the cytoplasm of granulocytes by microscopic examination.

Diagnosis and Laboratory Guidelines

The diagnosis is based on an assessment of exposure risk, clinical signs and symptoms, in addition to laboratory testing.

Serology (antibody) testing. Serology testing is via a commercial Indirect Immunofluorescence Assay (IFA) kit; This is a semi-quantitative test for the detection of IgG antibodies to *A. phagocytophilum*. An acute (collected early after the onset of symptoms) and a convalescent (collected 2-3 weeks later) can demonstrate a four-fold change in IgG-specific antibody titre in paired serum samples. A cut-off threshold antibody titre ≥ 1:64 by IFA is used to defined elevated titres against A. phagocytophilum at the National Microbiology Laboratory.

- Single IgG serum endpoint titres ≥ 1:64 are suggestive of infection at an undetermined time and may be indicative of either past infection or early response to a recent infection. Antibody titres remain elevated for years following clearance of infection; therefore, a single elevated IgG antibody titre result is usually insufficient to confirm acute/active infection.
- IgG endpoint titres less than 1:64 suggests that the patient does not have a current infection.
- A four-fold or greater increase in IgG titre between two serum samples drawn at least 2 weeks apart and tested in parallel is considered presumptive evidence of a recent or current infection with *A. phagocytophilum*.

Molecular detection (PCR). Detection of *Anaplasma* DNA by PCR of whole blood. Extracted DNA is tested by PCR assays specific for A. phagocytophilum, sequencing for confirmation and strain determination can be done. This method is most sensitive during the first week of illness.

Immunohistochemical (IHC) staining of organism from skin, tissue, or bone marrow biopsies. Microscopy strongly supports diagnosis of anaplasmosis when typical morulae are present, however identification requires morphological expertise and may not distinguish between A. phagocytophilum and other organisms.

Requests for Anaplasma serology and PCR testing are forwarded to the NML in Winnipeg for testing. Turnaround time is up to 30 business days.

Reporting

Per Policy 2.2 Disease and Event notification to OCMOHE and Disease and Event Reporting section

- Enhanced surveillance. For all confirmed and probable cases, an enhanced surveillance form should be completed and sent to OCMOHE within 5 days of completing the interview.
- Routine surveillance (RDSS) for all confirmed cases.

For probable or confirmed cases who have history of donation or transfusion (blood/blood products) within one year of the infection, a Disclosure of Information to Canadian Blood Services Transfusion Transmissible Infections (TTI) must be completed and sent to Canadian Blood Services.

Case Management

Education

Case or relevant caregiver should be informed about:

- Nature of infection, length of communicable period, mode of transmission and disease ecology
- Tick bite prevention

Investigation

Obtain travel history, outdoor activity, and tick exposure to determine if source of infection occurred within a recognized endemic area or not.

Obtain history on receiving blood transfusion or solid organ transplant within one year before collection date of positive specimen for case.

Obtain history on blood donation for previous twelve weeks.

Exclusion/Social Distancing

Not applicable.

Treatment

Doxycycline is first-line treatment for suspected anaplasmosis in patients of all ages.

Immunization

Not applicable.

Contact Management

Education

Not applicable

Investigation

Contacts of cases are not at risk as there is no person-to-person transmission (except for blood transfusion or organ transplantation).

Exclusion/Social Distancing

Not applicable.

Prophylaxis

Not applicable.

Outbreak Management

Activate the local outbreak plan when an outbreak is declared.