Campylobacter Jejuni and Cytopenias

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ABSTRACT

BACKGROUND: Leukopenia and thrombocytopenia in a febrile patient are not uncommon and may be a diagnostic clue in patients without an alternative explanation for cytopenias. This has not been reported in *Campylobacter jejuni* infections.

METHODS: A healthy patient with fever, rigors, and an acute diarrheal illness was noted to have a white blood cell count of 2.65×10^9/L and platelet level of 125×10^9/L. Retrospective chart review of all adult *C. jejuni* stool-positive cases admitted over 1 year revealed leukopenia in 6 of 20 (30%), thrombocytopenia in 5 of 20 (25%), and both in 1 of 20 (5%).

RESULTS: Cytopenias were mild, transient, and not associated with prolonged hospital stay or complications.

CONCLUSIONS: Acute *C. jejuni* infections should be added to the differential diagnosis of acute febrile illnesses that may be associated with leukopenia or thrombocytopenia. Cytopenias can be an important diagnostic clue in febrile illnesses, and their differential is presented.

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KEYWORDS: *Campylobacter jejuni*; Leukopenia; Thrombocytopenia

An acute febrile illness associated with leukopenia and thrombocytopenia in a patient without a prior condition causing cytopenia (eg, chemotherapy or chronic liver disease) has a broad differential diagnosis that ranges from benign to immediately life-threatening conditions (**Table 1**).

A self-limited intercurrent viral infection is the most common cause,[1] but an erroneous designation on presentation of septicemia or toxic shock syndrome as a viral infection may be dangerous. Thus, a timely accurate diagnosis of this not unusual

CLINICAL SIGNIFICANCE

- Acute *Campylobacter jejuni* gastroenteritis can cause leukopenia or thrombocytopenia. This has not been reported and may be frequently encountered.

- The finding of cytopenia associated with an acute febrile diarrheal illness can serve as a diagnostic clue and prompt testing for *Campylobacter* and appropriate treatment.

- Noniatrogenic leukopenia and thrombocytopenia in an acutely ill febrile adult patient have a unique differential diagnosis that needs to be better recognized.

presentation and recognition of its many causes are mandatory.

A healthy (except for hypertension) 80-year-old man was admitted with a 5-day history of fever, rigors, and painless watery diarrhea associated with fecal incontinence and marked lassitude. Examination was noncontributory. Hemoglobin was 12 mmol/L, white blood cell count was 2.65×10^9/L (neutrophils 1.8, lymphocytes 0.4), and platelet count was 125×10^9/L, associated with pre-renal azotemia, C-reactive protein 127 mg/L, and serum albumin 2.7 g/L. Urinalysis and blood cultures were negative. *Campylobacter jejuni* was identified in the stools, and the patient fully recovered with intravenous fluids and fluoroquinolones. His blood count on discharge was normal.

C. jejuni infection is a prominent cause of acute diarrheal illness in the general population and in travelers worldwide.[2] However, the literature focuses on its clinical manifestations or its more "exotic" late-onset complications: reactive arthritis, Guillain-Barré syndrome, and thrombotic

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Table 1   Differential Diagnosis of Acutely Ill Febrile Adult Patient with Noniatrogenic Leukopenia and Thrombocytopenia*

Viral infections
    Herpes viruses: EBV, CMV, HHV6, VZV, HSV
    Measles, rubella
    Hepatitis viruses A and B
    HIV infection and AIDS
    Parvovirus B19
    Dengue virus infection†
    Severe acute respiratory syndrome coronavirus†
    Influenza viruses
    Nonspecific viral infections/postinfectious
    Post-viral vaccines
Bacterial infections
    Overwhelming sepsis, any organism (especially Gram-negative)
    Toxic shock syndrome (staphylococcal, streptococcal)
    Typhoid fever (*Salmonella typhi* and *paratyphi*)
    Shigella enteritis
    Campylobacter infections
    Rickettsial infections† (spotted fevers, typhus)
    Human ehrlichiosis and anaplasmosis†
    Coxiella burnetii infections† (Q fever)
    Bartonella infections† (cat scratch disease)
    Brucellosis†
    Leptospirosis†
    Tularemia†
    Lyme disease† (*Borrelia burgdorferi*)
    Relapsing fever† (Borrelia sp.)
    Tuberculosis (*Mycobacterium tuberculosis*)
    Mycoplasma pneumoniae infection
Parasitic infections
    Toxoplasmosis†
    Malaria
    Visceral leishmaniasis†
Varied conditions
    Sarcoidosis
    Systemic lupus erythematosus
    Lymphoma or leukemia (eg, LGL syndrome)
    Felty's syndrome
    Hemophagocytic syndrome

AIDS = acquired immunodeficiency syndrome; CMV = cytomegalovirus; EBV = Epstein-Barr virus; HHV6 = human herpesvirus 6; HIV = human immunodeficiency virus; HSV = herpes simplex virus; LGL = large granular lymphocyte; VZV = varicella zoster virus.

*Excluding patients with prior cytopenias due to cancer/cancer treatment, portal hypertension, autoimmune disease, or ethnic leukopenia. White blood cell count occasionally may be normal despite high fever ("relative" leukopenia).

†Zoonosis.

</table>

thrombocytopenic purpura.[2,3] Data on patients' blood counts in uncomplicated cases (the majority) were hard to find. One publication noted a left shift (>10% band forms) in 55% of patients with stool cultures positive for *Campylobacter*, and 27.4% had a white blood cell count $<10 \times 10^9$/L associated with a left shift.[4]

To examine the prevalence of leukopenia or thrombocytopenia in *C. jejuni* infection, we performed a retrospective chart review of all stool-positive cases in adults (mean age, 54.2 years; range, 20-87 years) admitted over the last year to the department of general medicine in a single academic hospital.

Stool cultures were done by plating on *Campylobacter* agar (containing several antibiotics to inhibit normal stool flora) and incubating at 42°C in a microaerophilic environment for 48 to 72 hours.

Twenty *Campylobacter*-positive patients were found. Four additional patients had preexisting cytopenias secondary to underlying diseases or chemotherapy and were excluded. Six (30%) of 20 patients with *C. jejuni* gastroenteritis had leukopenia ($<4.0 \times 10^9$/L), 5 patients (25%) had thrombocytopenia ($<130 \times 10^9$/L), and 1 patient (reported) had both (5%). The cytopenias were mild (mean white blood cell count 3.15×10^9/L, mean thrombocyte count 123×10^9/L), rapidly transient in all cases (1-2 days), and not associated with prolonged hospital stay or complications. None of the patients developed late-onset complications.

C. jejuni infections should be added to the differential diagnosis of acute febrile illnesses that may be associated with leukopenia (or "relative" leukopenia) and thrombocytopenia (**Table 1**). This clinical presentation is not uncommon. It can be an important clue in diagnosis, and its differential should be better known.

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