Second, we would like to underscore one of the main messages of our article [2], which is that the statistical methods used for estimating the cost impact of an adverse event have a major effect on the results. Costs attributed to adverse events, such as nephrotoxicity, should include only those costs incurred after occurrence of the adverse event. Observing an association between high hospital costs and nephrotoxicity is not a reliable indicator that nephrotoxicity is the direct cause of the higher costs, because many confounding factors probably exist that are common causes of higher cost and nephrotoxicity, including factors that are unmeasured. It is not safe to assume that this confounding is removed simply by building a multivariable regression model, particularly when criteria used for variable inclusion are based solely on statistical significance. The recent study [4] cited by Prendergast and Tong [1] found that nephrotoxicity was one of the factors associated with increased costs in a multivariable regression model, when all costs incurred after study entry, both before and after the adverse event, were grouped together. Another finding from this study worth noting is that the agents that were compared in the clinical trial (amphotericin B lipid complex and liposomal amphotericin B) exhibited similar efficacy but dramatically different incidences of adverse events (e.g., the incidences of nephrotoxicity were 42% and 14%-15%, respectively). However, total poststudy entry costs (excluding the cost of the study drug) across treatment groups were similar, a finding parallel to a study by Cagnoni et al. [5]. Thus, unconfounded, intent-to-treat analyses do not support the contention that nephrotoxicity has a large causal effect on hospital costs.

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Human Granulocytic Ehrlichiosis Presenting as Acute Abdomen in an Adult

Sir—Rickettsial illnesses manifest in many ways, and our knowledge of disease caused by these organisms is still evolving. We read with interest the report by Seydev et al. [1] of human monocytic ehrlichiosis (HME) that caused acute appendicitis in a pregnant woman. Rocky Mountain spotted fever (RMSF) can present with symptoms mimicking appendicitis [2], and another recent article described a child with human granulocytic ehrlichiosis (HGE), acute abdomen, and suspected appendicitis [3]. To date, there have been no reports in the literature of HGE presenting as acute abdomen in an adult. Here, we present such a case.

A 46-year-old white man was hospitalized for diffuse abdominal pain and fever. His only significant medical history was occasional abuse of >1 substance at a time. Five days before admission to the hospital, he noted acute onset of fever and “flu-like symptoms.” He gradually improved and attended a party on the night before admission, where he used cocaine and consumed alcohol. Subsequently, he developed diffuse, severe abdominal pain that was localized in the right lower quadrant (RLQ). He denied a recent history of nausea, vomiting, diarrhea, and dysuria. He was heterosexual and denied having had unprotected sex, used injection drugs, or recently traveled. He wasn’t receiving medication.

In the emergency department, his temperature was 38.8°C, his pulse rate was 102 beats/min, his blood pressure was 130/80 mm Hg, and his respiration rate was 18 breaths/min. He appeared uncomfortable, with rebound tenderness in the RLQ and voluntary guarding; results of stool guaiac-based testing for occult blood were negative.

Abdominal radiographs showed dilated small bowel loops. Abdominal CT revealed terminal ileum wall thickening consistent with ileitis. The patient’s WBC count was 9900 cells/mL (82% neutrophils), and his hemoglobin level was 14.9 g/dL. Results of chemistry testing were normal, except for an albumin level of 3.3 g/dL and an alanine aminotransferase level of 47 U/L. Ciprofloxacin and metronidazole therapy was started, and the surgery department was consulted. Their impression was that the patient had acute terminal ileitis. He was admitted for intravenous hydration therapy and bowel rest and continued to receive antibiotic treatment and to undergo monitoring.

During the 24 h after admission, severe abdominal pain persisted, which required intravenous narcotics. His temperature increased to 40.0°C. Further questioning revealed that, 1 week before the onset of symptoms, he was bitten by a tick in a rural park in upstate New York. He removed and kept the “large” tick. He denied having had any subsequent rash. An eschar at the site of the tick bite was noted.
on his right buttock. Accordingly, doxycycline therapy was initiated, and treatment with metronidazole and ciprofloxacin was continued and discontinued, respectively. Samples were obtained and sent to the laboratory for serological testing for detection of *Borrelia burgdorferi*, *Rickettsia rickettsii*, and HIV, and a blood smear and a buffy coat specimen were analyzed. The patient rapidly defervesced, and his pain decreased. Results of buffy coat analysis, HIV testing, blood smear, and blood cultures were negative. Three days after admission, a small bowel series showed no evidence of pathology. The next day, the patient felt “back to normal,” and he remained afebrile for >48 h and was discharged receiving doxycycline therapy. He was scheduled for a follow-up visit at the clinic the following week.

Initial results of ELISA revealed elevated antibody titers to *B. burgdorferi*, and results of serological tests for detection of *R. rickettsii* were negative; thus, doxycycline therapy was continued for 21 days. He brought in the tick, which was identified as an *Ixodes* species. Western blotting for *B. burgdorferi* was negative. A second round of samples was obtained from the patient and sent to the laboratory for serological testing, the results of which revealed a 1:20 titer of HGE IgM antibodies (normal titer, <1:2). Results of serological tests for detection of *R. rickettsii* and *B. burgdorferi* were negative.

HGE has a nonspecific clinical presentation, and the full spectrum of manifestations remains to be characterized. Most infections result in mild illness, with a lower incidence of rash and severe disease than that associated with HME [4]. This patient presented with acute abdomen and terminal ileitis. High fever and distress led to some consideration for surgical intervention. Doxycycline therapy was administered only after he recalled having been bitten by a tick, and his symptoms rapidly improved. HGE was diagnosed on the basis of this rapid clinical improvement during receipt of doxycycline therapy, the resolution of the terminal ileum inflammation, and the positive HGE IgM antibody titers.

RMSF is well known to mimic appendicitis and has resulted in inappropriate surgery [2]. HME was recently reported to cause acute appendicitis in a pregnant woman [1] and is associated with many abdominal symptoms, including severe pain, diarrhea, nausea, vomiting, and weight loss [4]. HGE was previously not thought to present in this fashion. This is the first report of HGE manifesting as acute abdomen in an adult. In another recent case report, HGE presented as severe right lower quadrant pain in a 5-year-old girl who ultimately underwent an appendectomy, although results of pathological analysis revealed only mild, nonspecific serositis [3].

This case illustrates that HGE can cause severe gastrointestinal manifestations in adults. Therefore, it is important to include HGE and other rickettsial diseases in the differential diagnosis for acute abdomen, to obtain a thorough history of possible tick exposures in regions where these illnesses are prevalent, and to initiate doxycycline therapy when appropriate.

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**References**


**Obstructive Sleep Apnea Due to HIV-Associated Lipodystrophy**

Sir—Fatigue and excessive daytime sleepiness are frequent clinical features in HIV-positive patients [1]. Numerous factors might contribute to HIV-related fatigue, such as anemia, wasting, infection, or psychological stress. We report a case of obstructive sleep apnea (OSA) observed in a patient with HIV-associated lipodystrophy.

A 52-year-old HIV-positive man was referred to the sleep laboratory (Justus-Liebig-University; Gießen, Germany) with clinical suspicion of OSA. He took a combination of zidovudine, lamivudine, and didanosine (at daily doses of 600, 300 and 400 mg, respectively). The clinical course of HIV infection had been stable, and surrogate markers revealed a good response to antiretroviral therapy (CD4 cell count, 500 cells/μL; virus load, <50 copies/mL). The patient had a normal weight (body mass index, 26.1). Physical examination revealed marked lipodystrophy, with deposition of adipose tissue around the neck (neck circumference, 53 cm). Otorhinolaryngological evaluation revealed a narrow pharyngeal lumen but no anatomical abnormalities, such as adenotonsillar hypertrophy. CT demonstrated extensive accumulation of subcutaneous fat around the neck (figure 1). Polysomnography revealed the presence of OSA (apnea-hypopnea index, 30 events/h; mean oxygen saturation [SaO2], 96.2%; lowest SaO2, 84%; sleep efficiency, 85%; nonrapid eye movement sleep 1 + 2 (i.e., light sleep), 66% of total sleep time; nonrapid eye movement sleep 3 + 4 (i.e., deep sleep), 18% of total sleep time; rapid eye movement, 16% of total sleep time; arousal index, 27 arousals/h).

The patient was offered continuous positive airway pressure therapy; however, he refused to start this form of treatment. Thus, he was finally treated with a mandibular advancement splint. Because there