Letter to the Editor

NEPHRON

Nephron 1996;74:489

Hemolytic-Uremic Syndrome Associated with Acute *Campylobacter upsaliensis* Gastroenteritis

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Dear Sir,

The majority of the patients with gastroenteritis-associated hemolytic-uremic syndrome (HUS) appear to have been infected with verotoxigenic *Escherichia coli*. Other uncommonly cited infectious etiologic agents have also been associated with the evolution of HUS, and among these reports, campylobacters have been implicated as the cause of preceding gastroenteritis. We detail the first association of *Campylobacter upsaliensis* with HUS and describe our investigations which provide evidence against the possibility of a coinfection with verotoxigenic *E. coli*.

Five days prior to arriving at our hospital, a 14-year-old female suffered from an acute onset of periumbilical crampy abdominal pain. By the next day, she developed profuse watery diarrhea. Because of the severity of the illness, she was investigated and found to have microscopic hematuria, thrombocytopenia (100×10^9/l), and renal dysfunction (creatinine 120 µmol/l, urea 10.2 mmol/l). She was transferred the following day because of progressive thrombocytopenia (45×10^9/l). She was initially managed expectantly, but by the 3rd hospital day, progressive illness was evident: hemoglobin 84 g/l, platelets 92×10^9, creatinine 796 µmol/l, and urea 30.5 mmol/l. A renal ultrasound revealed a moderate amount of peritoneal fluid and increased echogenicity of the renal cortex. A stool specimen yielded a *Campylobacter* species. A peritoneal dialysis catheter was inserted. A renal biopsy specimen demonstrated evidence of thrombotic microangiopathy in early organization, consistent with HUS. The diarrheal episode resolved within 2 days of admission, and, therefore, antibiotics were not specifically prescribed for the campylobacteriosis. Dialysis was continued for 1 week. The clinical course was uneventful, and the patient was discharged after a total of 3 weeks at which time her laboratory investigations included: white blood cell count 5.7×10^9/l, hemoglobin 78 g/l, platelets 181×10^9/l, creatinine 211 µmol/l.

The stool isolate was subsequently identified as *C. upsaliensis*. Blood cultures were specifically subcultured to assess Campylobacter growth, and none was found. Sorbitol-negative *E. coli* were not found. A negative microneutralization assay for free fecal verotoxin was obtained on a stool specimen which had been acquired 5 days into the course of illness when symptomatic diarrhea was still evident. In addition, a random screening of stool coliforms was performed for evidence of verotoxin virulence genes. By the polymerase chain reaction, we attempted to amplify genetic sequences which are components of verotoxin 1 and verotoxin 2 genes [1]; positive bacterial colonies were not identified.

C. upsaliensis is a relatively new member of the Campylobacter family. It appears that cats and dogs may be natural hosts for this bacterium [2]. In addition to gastroenteritis, the bacterium has been identified as a cause of blood-borne infections especially in children and immunocompromised hosts [3]. The epidemiology of *C. upsaliensis* as a cause of gastroenteritis is somewhat uncertain due to the potential of commonly used Campylobacter-selective media to inhibit growth of some strains. The frequency with which *C. upsaliensis* is associated with complications is also not fully understood nor are the mechanisms of pathogenesis, in contrast to *Campylobacter jejuni*. Although renal disease has been associated with Campylobacter gastroenteritis [4], the majority of reports cite *C. jejuni* as the offending pathogen. Most of the latter citations associate *C. jejuni* with HUS rather than with other nephropathies. One other publication proposed that *Campylobacter fetus* might initiate the pathological cascade of HUS. Ours is the first report which establishes a link between nephropathy and *C. upsaliensis*.

In an era when it is clearly understood that most gastroenteritis-associated HUS of childhood is caused by infection with verotoxigenic *E. coli*, the cause-and-effect relationship between renal disease and Campylobacter species may be the subject of controversy. Indeed, previous reports of Campylobacter-associated HUS have not detailed information which excludes concomitant verotoxigenic *E. coli* infection. In our experience, simultaneous isolation of *C. jejuni* and *E. coli* O157:H7 from enteric specimens has been identified on more than one occasion. We propose that there was reasonable evidence from our investigations to rule out an associated verotoxigenic *E. coli* infection.

References

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0028–2766/96/0742–0489$10.00/0

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