Post-Colonoscopic Listeria Septicemia in Ulcerative Colitis during Immunosuppressive Therapy

Masaaki Minami, Tadao Hasegawa, Takafumi Ando, Osamu Maeda, Teruko Ohkura, Michio Ohta and Hidemi Goto

Abstract

A 78-year-old man who had been diagnosed with ulcerative colitis was admitted because of uncontrolled severe, frequent, bloody diarrhea. He was treated with immunosuppressive therapy that included corticosteroid and azathioprine. Colonoscopy was used to assess disease activity. This revealed that the mucosa of his digestive tract from the rectum to the ileum was damaged. He developed a high-grade fever soon after colonoscopy. Blood culture demonstrated Listeria monocytogenes. Treatment was changed to intravenous ampicillin for 20 days. His general body symptoms, including the bloody diarrhea, improved after treatment. We assume that the colonoscopy induced Listeria monocytogenes septicemia through bacterial translocation in this patient.

Key words: Listeria monocytogenes, ulcerative colitis, septicemia

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Introduction

Listeria monocytogenes (L. monocytogenes) is a gram-positive, facultative, anaerobic, short, rod-like bacterium that causes listeriosis (1). Listeriosis is considered a rare infection in adults. It is mainly an opportunistic infection affecting people suffering from malignancy and those receiving immunosuppressive drugs (2).

Ulcerative colitis is a chronic inflammatory disease that affects the colon and rectum (3). It is thought to result from inappropriate and ongoing activation of the mucosal immune system in the presence of a normal luminal flora. The aberrant response to the normal luminal flora is most likely facilitated by defects in both the barrier function of the intestinal epithelium and the mucosal immune system. Corticosteroids are widely known to be effective drugs in ulcerative colitis (4). For steroid-refractory ulcerative colitis, azathioprine is a more powerful immunosuppressive agent than corticosteroids (5). Immunosuppressive drugs, including corticosteroids and azathioprine, may modulate the mucosal immune response.

Colonoscopy is a widely used diagnostic and therapeutic procedure in gastrointestinal tract disease and is only rarely associated with transient septicemia (6). We report a case of septicemia after colonoscopy caused by L. monocytogenes in a patient with ulcerative colitis who was receiving corticosteroids and azathioprine. We also review the pertinent previously reported cases (2, 7, 8).

Case Report

A 78-year-old man who had been diagnosed as having ulcerative colitis from 1997 was admitted to Nagoya University Hospital because of uncontrolled, severe, frequent, bloody diarrhea. The patient suffered from occasional episodes of bloody diarrhea and was treated with corticosteroid and azathioprine. Upon admission, physical examination showed normal vital signs, a soft abdomen, and mild abdominal pain, but no organomegaly. The calculated clinical activity index was 10 (9). Laboratory tests demonstrated mild anemia with hemoglobin of 11.6 g/dl, mild inflammation with CRP of 2.15 mg/dl and a normal white blood cell count. Serum levels of electrolytes, liver enzymes, and cre-
Table 1. Clinical Data on Admission

<table>
<thead>
<tr>
<th>Hematology</th>
<th>Serological test</th>
</tr>
</thead>
<tbody>
<tr>
<td>RBC</td>
<td>CRP 2.15 mg/dl</td>
</tr>
<tr>
<td>Hb</td>
<td>Coagulation tests</td>
</tr>
<tr>
<td>Pt</td>
<td>PT 10.8 s</td>
</tr>
<tr>
<td>WBC</td>
<td>APTT 32.7 s</td>
</tr>
<tr>
<td>Seg</td>
<td>Fibrinogen 351 mg/dl</td>
</tr>
<tr>
<td>Ly</td>
<td></td>
</tr>
<tr>
<td>Mono</td>
<td></td>
</tr>
</tbody>
</table>

Blood chemistry

| AST 17 IU/l | pH 8.5 |
| ALT 16 IU/l | Protein (-) |
| LDH 225 IU/l | Sugar (-) |
| TP 6.3 g/dl | Occult blood (-) |
| Alb 3.3 g/dl | WBC (-) |
| BUN 18 mg/dl  |      |
| Cr 1.0 mg/dl  |      |
| Na 134 mEq/l  |      |
| K 4.7 mEq/l  |      |
| Cl 96 mEq/l  |      |
| BS 121 mg/dl |      |

RBC: red blood cell, Hb: hemoglobin, Pt: platelet, WBC: white blood cell
AST: aspartate aminotransferase, ALT: alanine aminotransferase,
LDH: lactate dehydrogenase, TP: total protein, Alb: albumin, BUN: blood urea nitrogen,
Cr: creatinine, Na: sodium, K: potassium, Cl: chloride, BS: blood sugar, CRP: C-reactive protein, PT: prothrombin time, APTT: activated partial thromboplastin time

Figure 1. Colonoscopy findings, showing the geographic ulcer. Colon biopsy finding in the inset, showing only granulation tissue.

atininewerewithinnormalranges(Table1).Theresultsofstoolcultureshowedanormalflora.Colonoscopywasused
toassesdiseaseactivity.Itrevealedthatthemucosaofthe
patient’sdigestivetractfromthectumtotheileumwas
extensivelydamaged,withanappearanceresemblingageo-
graphic ulcer (Fig. 1). Matts endoscopic score was 4 (10).
Colon biopsy findings showed only granulation tissue, and
intestinal mucosal tissue was not seen in biopsy specimen
(Fig. 1). Following colonoscopy, the patient developed a fe-
ver of 39.2°C. Although the patient showed marked signs of
fatigue and malaise, physical examination was unremark-
able. He was not in a state of shock. The white blood cell
count showed a total of 5,500 cells/μl with 20.8% lympho-
cytes, 74.8% neutrophils, 0.6% eosinophils, and 4% mono-
cytes. Although, cytomegalovirus (CMV) infectious colitis
was first suspected, CMV antigenemia was negative. We
considered enteric bacteremia because of intestinal ulcera-
tion among the endoscopic findings, and intravenous ce-
fotiam was given as empiric therapy. A gram-positive rod
bacterium was isolated from blood cultures from samples
collected 3 days later (Fig. 2). Because a strongly immuno-
suppressed status was likely to worsen the infection,
azathioprine treatment was stopped. However, corticosteroids
were continued because of deterioration of the ulcerative co-
litis. Five days after the treatment, the bacterium was con-
formed as L. monocytogenes. The patient’s treatment was
changed to intravenous ampicillin and this treatment was
continued for 20 days. His general symptoms, including the
bloody diarrhea, improved. Repeated colonoscopy did not
exacerbate his clinical symptoms, including the septicemia.
After we confirmed the eradication of listeriosis by blood
culture, performed twice, the patient was discharged
Figure 2. *Listeria* monocytogenes from blood, showing rod bacteria and red blood cells.

Figure 3. Clinical course of the patient after hospitalization.

Discussion

*L. monocytogenes* was first implicated as a cause of human disease by Nyfeldt in 1929 (11). It is ubiquitous in foodstuffs, the environment, and animals (12). Listeriosis affects pregnant women, newborns, persons with immune system dysfunction due to drugs or illness, and the elderly. The diagnosis is made by identification of the organism from blood or cerebrospinal fluid. The mortality rate is high (13–34%) (12, 13); among the nonimmunosuppressed patients, 80% had a CNS infection, and 52% of immunosuppressed patients had septicemia (14). Clinically, a wide variety of symptoms may be observed, including septicemia, fever, endocarditis, meningitis, polyserositis, cutaneous infections, and sepsis (14). In the present case, our systematic investigation of the origin of patient’s infection revealed only septicemia, which did not cause meningitis.

*Listeria* is generally susceptible to ampicillin and aminoglycosides, and these drugs have been recommended (7). For *L. monocytogenes*, resistance to antibiotics of the penicillin family such as ampicillin has not yet been found under natural conditions (15). The effectiveness of the penicillin family is due to their high affinity for penicillin-binding protein 3 (PBP3), which is the essential transpeptidase participating in the construction of peptidoglycan, the main constituent of the bacterial cell wall (16). Cephalosporins are inactive against *Listeria* because they have only weak affinity for PBP3. *Listeria meningitis* has developed during therapy with cephalosporins (17). In immunocompromised patients, therapy should be prolonged since treatment for listeriosis for less than 2 weeks leads to a high incidence of relapse (15, 18). In the present case, intravenous amoxicillin for 20 days was given in place of cefotiam and the treatment was successful.

A total of three *Listeria septicemia* cases with ulcerative colitis have been described previously. These reported cases and the present cases are reviewed in Table 2 (2, 7, 8). As no patient suffered from meningitis, one possible explanation of the low frequency of *Listeria meningitis* in ulcerative colitis is that *Listeria organisms* are not transferred to the central nervous system by phagocytosis and are killed extracellularly by adequate antibiotic therapy (19). Of these four cases, three cases were associated with endoscopic proce-
dure. Although colonoscopy is a widely used procedure, septicemia following colonoscopy is generally rare (6). Although contamination at endoscopy carries a risk of infection, all of our endoscopes are always carefully disinfected and the bacterium was not found in other patients undergoing endoscopy on the same day. L. monocytogenes is present in the human intestine, and it has been suggested that this might be the portal of entry to the systemic circulation (20). In the present patient, the Listeria bacterium was probably already present in the colon, and a colon with an ulcerative lesion may offer a route by which Listeria may invade in light of our endoscopic findings. We did not find L. monocytogenes from stool culture because it might be difficult to detect L. monocytogenes from stool as a conventional clinical examination (13). The interval between colonoscopy and the onset of Listeria septicemia in our patient would seem to implicatethe procedure as the precipitating factor in the development of his septicemia. As the issues of the prevalence of septicemia following colonoscopy in immunosuppressed ulcerative colitis patients and protocols for the prevention of possible bacteremic complications have not been previously addressed, further studies investigating this problem are recommended.

This is first case report of Listeria septicemia in a patient with ulcerative colitis who was receiving corticosteroids and azathioprine in Japan. Recently, powerful immunosuppressive therapy that includes steroids and azathioprine has been performed in patients with ulcerative colitis. These agents are effective in the treatment of exacerbation of ulcerative colitis, but severe infectious disease may occur because of the patient’s immunosuppressed status. Although colonoscopy is safe in immunocompetent patients, it may induce severe infectious disease in immunosuppressed patients. Based on this case report, we propose that physicians pay attention to infectious complications in patients undergoing immunomodulation therapy through.

In conclusion, although the organism is not frequently recovered from human clinical specimens, L. monocytogenes is one of the most important risk factors associated with colonoscopy in immunosuppressed patients with ulcerative colitis.

Acknowledgement

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References


Table 2. Documented Cases of Listeria Septicemia in Patients with Ulcerative Colitis

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Age (years)</th>
<th>Sex</th>
<th>Country</th>
<th>UC status</th>
<th>Drug</th>
<th>Meningeal signs</th>
<th>Therapy drug</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (ref. 2)</td>
<td>45</td>
<td>Female</td>
<td>Israel</td>
<td>Unknown</td>
<td>Steroid</td>
<td>No</td>
<td>Unknown</td>
<td>Died</td>
</tr>
<tr>
<td>2 (ref. 7)</td>
<td>56</td>
<td>Female</td>
<td>Israel</td>
<td>Pancolitis</td>
<td>ACTH</td>
<td>No</td>
<td>ABPC, GM</td>
<td>Recovered</td>
</tr>
<tr>
<td>3 (ref. 8)</td>
<td>49</td>
<td>Female</td>
<td>Netherlands</td>
<td>Pancolitis</td>
<td>Steroid</td>
<td>No</td>
<td>AMPC</td>
<td>Recovered</td>
</tr>
<tr>
<td>4 (present case)</td>
<td>78</td>
<td>Male</td>
<td>Japan</td>
<td>Pancolitis</td>
<td>Steroid, AZA</td>
<td>No</td>
<td>ABPC</td>
<td>Recovered</td>
</tr>
</tbody>
</table>

UC, ulcerative colitis; ACTH, adrenocorticotropic hormone; ABPC, ampicillin; AMPC, amoxicillin; GM, gentamicin; AZA, azathioprine