A Case of Methicillin-Resistant Staphylococcal Enterocolitis with Subsequent Development of Lymphocytic Colitis

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Staphylococcus aureus (S. aureus) is occasionally a normal inhabitant of the gastrointestinal tract, and rarely considered a cause of enterocolitis. Methicillin-resistant Staphylococcal enterocolitis may cause persistent diarrhea leading to severe complications and even death, without appropriate treatment. Lymphocytic colitis (LC), a subtype of microscopic colitis, is a relatively common cause of chronic watery diarrhea. We report the case of a 73-year-old woman with profuse watery diarrhea caused by methicillin-resistant S. aureus. Soon after treatment of her enterocolitis with vancomycin the patient’s general condition and symptoms improved, although the diarrhea persisted. Through colonoscopic biopsy and immunohistochemical staining, overt LC was diagnosed, and prompt therapy with budesonide was initiated.

Key Words: Methicillin-Resistant; Staphylococcus aureus; Enterocolitis; Lymphocytic Colitis

INTRODUCTION

Prevalence of in-hospital methicillin-resistant Staphylococcus aureus (MRSA) infection is ever increasing due to increased administration of histamine H2-blockers, antibiotics, and antacids.1 Lymphocytic colitis (LC), a subtype of a relatively well-established form of microscopic colitis, is a disease entity of growing concern due to its increasing prevalence.2 Of the many causes, infection is a known predisposing factor for LC.2 Reports of MRSA enterocolitis are not common, and there has been no previous report of MRSA enterocolitis as a cause or aggravating factor of LC. We present a unique case of LC, which subsequently developed following MRSA enterocolitis.

CASE REPORT

A 73-year-old woman was referred to our hospital due to persistent diarrhea. Approximately one month prior, she began having frequent, painless, watery diarrhea as many as 20 times a day. The patient had been taking regular NSAIDs for five years as the result of a compression fracture of the lumbar spine after a fall. Other than that, she had no prior history of underlying illness including diabetes mellitus, tuberculosis, thyroi-
diabetes, asthma, or rheumatoid arthritis. She was previously admitted to a local hospital because of persistent diarrhea, and had been prescribed fluoroquinolone, ranitidine, and loperamide. Initial peripheral blood tests revealed a white blood count of 2,400/mm³ with a hemoglobin level of 11.3 g/dL, and platelets 189,000/mm³. Erythrocyte sedimentation rate and C-reactive protein were 8 mm/hr and 0.31 mg/dL, respectively. The levels of AST/ALT/alkaline phosphatase were within the normal range at 39/28/40 IU/L as were serum BUN and creatinine levels at 10 and 0.7 mg/dL, respectively. However, Na/K/HCO₃ levels were 141/2.1/33 mEq/L, indicating severe hypokalemia. An initial thyroid function test was normal with TSH at 1.99 μIU/mL and free T4 at 1.34 ng/dL. Stool osmolar gap was 36 mEq/L, and initial Clostridium difficile toxin assay and PCR results were negative. She was placed on a nil-per-os (nothing by mouth) diet with intravenous fluids and electrolyte supplements. The diarrhea persisted despite management attempts. An initial colonoscopy revealed severe mucosal edema (Fig. 1) and a biopsy specimen from the transverse colon showed infiltration with inflammatory cells in the lamina propria (Fig. 2). On the tenth hospital day, MRSA was isolated from the culture specimen obtained from the initial colonoscopic biopsy. Oral vancomycin therapy (1 g/day) was initiated, and thereafter the frequency and amount of diarrhea started to decrease. Vancomycin was administered for a total of 18 days, and was stopped when the patient was switched back to a regular diet. The patient was discharged as her general condition and laboratory findings gradually improved. However, despite improvements, the patient still suffered from frequent watery stools, and follow-up colonoscopy was performed a month after discharge. Hypervascular mucosal changes were observed throughout most of the colonic mucosa, with occasional spontaneous bleeding (Fig. 3). Multiple biopsies were taken from all parts of the colon, revealing clusters of intra-epithelial lymphocytes (IEL) (Fig. 4A) compatible with a finding of LC. Immunohistochemical staining with CD3 (Fig. 4B) and CD8 (Fig. 4C) revealed strong

Fig. 1. Colonoscopy showing severe colonic edema with nearly no visualization of the vessels.

Fig. 2. Microscopic finding. Biopsy specimen showing inflammatory infiltrates in the lamina propria (H&E stain, x400).

Fig. 3. Follow-up colonoscopy one month post-discharge showing neoangiogenesis with mucosal friability.
positive staining of lymphocytes. The patient’s symptoms showed marked improvement following six weeks of budesonide treatment (9 mg/day).

**DISCUSSION**

This case represents a patient with a series of both severe acute and chronic diarrhea, due to a confirmed case of MRSA colitis that subsequently developed into LC. MRSA is one of the most notoriously known causes of hospital-acquired infection. It may cause persistent diarrhea, which is usually odorless, watery, and very substantial. The lack of response to therapy may lead to severe dehydration and shock, multiple organ failure, disseminated intravascular coagulation, and even death.3 A diagnosis of MRSA enterocolitis can be suspected when there is a large amount of diarrhea with no other organism cultured in the stool sample except MRSA.4

As for the present case, we may have been fortunate to culture MRSA in the stool on the tenth day of admission. In most cases, prior administration of drugs such as broad spectrum antibiotics, aminophylline, histamine H2-blockers, and magnesium-containing antacids, along with high osmolar intravascular injections and total parenteral nutrition are commonly documented. Since the patient had already been treated with fluoroquinolone and a H2-receptor blocker prior to admission, these factors may have contributed to the pathogenesis of MRSA enterocolitis which causes rapid clinical deterioration and is thought to be the result of toxic shock syndrome. Toxic shock syndrome toxin-1 (TSST-1) stimulates mast cells, causing the secretion of various cytokines including IL-1, TNF-α, and IL-2, which consequently induce diverse clinical manifestations.5

If treatment with large volume of fluid replenishment along with oral vancomycin administration is not ini-
tiated in the early phase of the disease, the clinical course may be drastic and the prognosis poor. Even if adequate treatment has been initiated with early administration of oral vancomycin, the mortality rate may reach over 10%.5

LC is a fairly common cause of chronic non-bloody diarrhea, although it has been underestimated clinically due to relatively normal colonoscopic findings or misdiagnosed as irritable bowel syndrome even in the face of continuing diarrhea.6 The pathogenesis of this disease entity is yet to be precisely determined, but is assumed to be multifactorial. Immunologic reactions due to luminal factors, drugs such as NSAIDs and ranitidine, or food such as gluten are thought to be involved.7 In addition, thyroiditis, celiac disease, diabetes mellitus, asthma, and rheumatoid arthritis have been reported to be related7 as well as infection, and organ transplantation.8-10 Microscopic assessment of colonic mucosal biopsies is currently the only means of verifying a diagnosis of LC. In the present case, both CD3 and CD8 immunohistochemical staining was performed, and a diagnosis of LC was established with more than 20 IEL present per 100 epithelial cells.11 Various different hypotheses have been raised regarding the pathophysiology of LC, of which infection has been suggested as one of the causes.11,12 In the present case, the authors suspected the etiology or at least an aggravating factor of LC to be the previous case of MRSA enterocolitis, since the persistent diarrhea began and continued despite treatment of the causal organism, and microscopic evidence of LC confirmed the diagnosis. It should be noted that the initial biopsy specimen of the colon obtained from the first colonoscopy already showed the evidence of inflammatory cell infiltration in the lamina propria, with several IEL. At that time, the severity was not noticeable, which may have led us to overlook the disease. Medical therapy is generally successful, and budesonide is the best-documented treatment for LC.13,14 It is the drug of choice for patients unresponsive to antidiarrheal drugs and other medical regimens.13,14 In this case, the diagnosis of LC was made at a later stage, and budesonide was prescribed by the out-patient department.

We presume two possibilities concerning the evolution of the disease: first, both disease entities could have occurred simultaneously, or there was a subsequent manifestation of MRSA enterocolitis following the overuse of antibiotics, with initially quiescent underlying LC. In the present case, based on the findings of a number of IEL within the lamina propria on the initial colon biopsy specimen together with the clinical manifestation, the authors tend to lean towards the possibility of underlying LC with subsequently superimposed MRSA enterocolitis.

In conclusion, it should be noted that LC can occur or worsen after various infectious conditions, of which MRSA enterocolitis should be considered as one possible cause. MRSA enterocolitis is a rare condition, especially when not related to a post-surgery manifestation in an immunocompetent patient. Once MRSA enterocolitis is suspected, a decision to administer oral vancomycin together with vigorous fluid resuscitation must be made promptly, since the disease course is very rapid. If no response is seen within a few days of treatment, a differential diagnosis should be considered. LC should always be considered in cases of chronic diarrhea, and if clinically suspected, a meticulous review of each biopsy specimen taken from all regions of the colon is warranted.

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