Adult Onset Schönlein-Henoch Purpura Associated with Helicobacter pylori Infection

Chisho Hoshino

Abstract

Schönlein-Henoch purpura (SHP) is a systemic vasculitis, primarily involving the skin, gastrointestinal (GI) tract, joints, and kidneys. A wide variety of different conditions may be implicated in the pathogenesis of SHP. We report a 33-year-old man who presented with SHP accompanied by gastric Helicobacter pylori (Hp) infection. The GI manifestations and purpuric rashes were dramatically resolved after Hp eradication therapy. To date, very few publications have focused on the possible pathogenetic relationship between Hp infection and SHP.

Key words: Schönlein-Henoch purpura, leukocytoclastic vasculitis, Helicobacter pylori, eradication therapy, chronic gastritis, duodenal ulcer

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Introduction

Schönlein-Henoch purpura (SHP) is known as a leukocytoclastic vasculitis of small vessels, resulting in skin, joint, gastrointestinal (GI) and renal involvement. It is the most common acute vasculitic disorders affecting children, but is relatively uncommon in adults (1). The pathogenesis of SHP remains unclear, but a wide variety of conditions such as bacterial or viral infections, vaccinations, drugs and other environmental exposures may be responsible for the onset (2). Helicobacter pylori (Hp) has been implicated in the pathogenesis of various extradigestive disorders. However, a few previous reports have described an association between gastric Hp infection and SHP (2-5). We report an adult case of SHP accompanied by Hp positive gastritis and duodenal ulcer scar. The patient was successfully treated with Hp eradication therapy.

Case Report

A 33-year-old man was admitted to our hospital because of a 3-week history of intermittent colicky abdominal pain and diarrhea. He had no personal history of allergy, GI diseases, or autoimmune diseases. Four weeks prior to admission, he developed a sore throat and nonproductive cough. He visited a general practitioner and received acetaminophen 1.2 g/day and dextromethorphan 45 mg/day for 4 days without any antibiotics. One week later, he developed intermittent colicky abdominal pain with diarrhea and subsequent purpura on the lower extremities. He took over-the-counter medicine for intestinal distress for a week and ciprofloxacin 200 mg/day and intestinal remedy including bifidobacteria for 4 days prescribed by the same practitioner without benefit. He eventually had difficulty in eating and visited the emergency department of our hospital. On admission, his temperature was 36.9°C. The blood pressure was 110/60 mmHg. The pulse rate was 54 beats per minute. Physical examination revealed diffuse abdominal tenderness with hypoactive bowel sound. There were numerous purpuric rashes on both of lower legs (Fig. 1), while arthritis was not evident. The remainder of the physical examination was unremarkable. Laboratory studies (Table 1) revealed elevated level of C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), elevated level of plasma D-dimer and fibrin degradation products (FDP), and decreased level of coagulation factor XIII activity, while normal results for serum creatinine level, serum IgA level. Neither microscopic hematuria nor proteinuria was present on urinalysis. Occult blood and leukocytes were found in the feces, while bacterial stool
On physical examination, numerous purpuric rashes on both lower legs were present. Complete blood counts and serological tests revealed the following results:

- **WBC:** 8.2×10³/μL
- **Hemoglobin:** 13.8 g/dL
- **Platelet:** 28.4×10⁴/μL
- **ANA:** <1:40
- **Hemoglobin:** 13.8 g/dL
- **MPO-ANCA:** <10 U/mL
- **Platelet:** 28.4×10⁴/μL
- **PR3-ANCA:** <10 U/mL
- **Coagulation tests:**
  - **FDP:** 13.3 μg/mL
  - **D-dimer:** 13.3 μg/mL
  - **ESR:** 40 mm/hr
- **IgG:** 1039 mg/dL
- **IgA:** 222 mg/dL
- **IgM:** 63 mg/dL
- **D-dimer:** 13.3 μg/mL
- **IgG:** 1039 mg/dL
- **IgA:** 222 mg/dL
- **IgM:** 63 mg/dL
- **Factor X:** 61 %

**Table 1. Laboratory Results on Admission**

<table>
<thead>
<tr>
<th>Complete blood counts</th>
<th>Serological tests</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WBC</strong> 8.2×10³/μL</td>
<td><strong>ANA</strong> &lt;1:40</td>
</tr>
<tr>
<td><strong>Hemoglobin</strong> 13.8 g/dL</td>
<td><strong>MPO-ANCA</strong> &lt;10 U/mL</td>
</tr>
<tr>
<td><strong>Platelet</strong> 28.4×10⁴/μL</td>
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<td><strong>D-dimer</strong> 13.3 μg/mL</td>
<td><strong>IgM</strong> 63 mg/dL</td>
</tr>
<tr>
<td><strong>ESR</strong> 40 mm/hr</td>
<td><strong>ASO</strong> &lt;30 IU/mL</td>
</tr>
<tr>
<td><strong>Serum chemistry</strong></td>
<td><strong>Mycoplasma Ab</strong> &lt;1:40</td>
</tr>
<tr>
<td><strong>AST</strong> 29 IU/L</td>
<td><strong>HIV-Ab</strong> (-)</td>
</tr>
<tr>
<td><strong>ALT</strong> 13 IU/L</td>
<td><strong>HCV-Ab</strong> (-)</td>
</tr>
<tr>
<td><strong>T.Bil</strong> 0.72 mg/dL</td>
<td><strong>HBs-Ag</strong> (+)</td>
</tr>
<tr>
<td><strong>LDH</strong> 148 IU/L</td>
<td><strong>Factor X</strong> 61 %</td>
</tr>
<tr>
<td><strong>Creatinine</strong> 0.89 mg/dL</td>
<td><strong>Stool examination</strong></td>
</tr>
<tr>
<td><strong>Urea nitrogen</strong> 9.5 mg/dL</td>
<td><strong>Leukocytes</strong> (+)</td>
</tr>
<tr>
<td><strong>CRP</strong> 3.45 mg/dL</td>
<td><strong>Occult blood</strong> (+)</td>
</tr>
<tr>
<td><strong>Urinalysis</strong></td>
<td><strong>Ova and Parasite</strong> (-)</td>
</tr>
<tr>
<td><strong>Protein</strong> (-)</td>
<td><strong>Culture</strong> (-)</td>
</tr>
<tr>
<td><strong>Occult blood</strong> (-)</td>
<td></td>
</tr>
<tr>
<td><strong>Glucose</strong> (-)</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. On physical examination, numerous purpuric rashes on both lower legs were present.
Figure 2. Upper endoscopy of the stomach revealed findings of antrum predominant pangastri-tis, with erythema, friability, flat erosion and intramural bleeding spots mainly in the antrum (Fig. 2A) and rugal hypertrophy in the corpus (Fig. 2B).

Figure 3. Upper endoscopy of the duodenum revealed findings of a ulcer scar in the first portion (Fig. 3A, arrow) and numerous hyperemic and petechial lesions in the first and second portion (Fig. 3B, 3C).

Figure 4. Total colonoscopy showed findings of numerous purpuric lesions mainly in the cecum and ascending colon.

Figure 5. Ascending colonic biopsy demonstrated marked fibrin deposition in a small vessel, a perivascular mixed neutrophilic and lymphocytic infiltrate, extravasation of erythrocytes and leukocytoclasis (Hematoxylin and Eosin staining; x400).

tion or worsening diarrhea. After the treatment, the abdominal manifestations dramatically subsided within 2 weeks and the purpuric skin lesions faded within 5 weeks without further treatment. \(^{13}\)C-urea breath test performed one month after the therapy showed a negative result for urease activity, which suggested successful Hp eradication. At 3 months after the therapy, \(^{13}\)C-urea breath test was re-examined with a positive result when the patient visited our hospital complaining of diarrhea which was presumably caused by viral enterocolitis not recurrent SHP because diarrhea without abdominal pain was transient and purpuric skin lesions were absent. The patient received Hp re-eradication therapy including lansoprazole 60 mg/day, amoxicillin 1,500 mg/day and metronidazole 500 mg/day for 7 days with successful
Discussion

Hp is a spiral gram-negative, microaerophilic, and urease-positive bacterium, which colonizes the gastric mucosa. Hp infection is the major etiologic factor for gastric diseases such as gastritis (7), peptic ulcer (8), gastric cancer, and B-cell lymphoma of gastric mucosa-associated-lymphoid-tissue (MALT lymphoma) (9). Recently, in addition to local tissue damage, a potential role of Hp infection in various extragastric pathologies has been described (10). Autoimmune diseases other than SHP studied for an association with Hp infection include ischemic heart disease, Sjögren’s syndrome, autoimmune thrombocytopenia, extragastric MALT-lymphoma, membranous nephropathy, and acute immune polyneuropathies (11). In 1995, Reinauer et al. first described the case of a 21-year-old woman with SHP and Hp positive gastritis; after Hp eradication therapy, the clinical manifestations were resolved (2). Since then, some similar case reports have been described (3-5). In the present case, antecedent respiratory tract infection other than Hp infection might have been implicated in the onset of SHP. However, serological studies showed no evidence of infections potentially contributing to the pathogenesis of SHP, such as streptococcal and mycoplasma infection.

The true role of Hp infection in these extragastric diseases remains unclear. However, various potential causative mechanisms have been proposed: The presence of more toxic Hp strains induces a strong inflammatory response, directly or indirectly, with the release of bacterial and host-dependent cytotoxic substances (12); genetic predisposition of the individual (12); antibodies against Hp cross-react with some extragastric tissues (13).

SHP is the most common acute vasculitic disorders affecting children, but is less common in adults (1). In most cases, SHP is a self-limited condition. However, one-third of patients have been reported to have recurrent symptoms (14). In adulthood, SHP represents a more severe clinical syndrome with a higher frequency of renal involvement and requires more aggressive therapy (1). In a retrospective review of 250 adult SHP patients, 32% of patients showed renal insufficiency (creatinine clearance <50 mL/min) and 11% of patients reached end-stage renal failure (15). Thus, in the management of SHP, it is important to prevent renal involvement or recurrence.

In general, patients with SHP are treated supportively or symptomatically because of the self-limited nature, whereas in patients with severe GI manifestations or renal complications, corticosteroid therapy is considered. Recently, a randomized controlled study confirmed that corticosteroid therapy is effective in reducing the intensity of abdominal pain and joint pain and in shortening the duration of mild nephritis (16). However, there is no evidence that it is effective in preventing recurrence or the development of nephritis.

The association of Hp infection with SHP may be underestimated because endoscopic examination is not systematically performed in patients with SHP. In children, the Hp positive rate of SHP patients with GI manifestations and that of relapsed patients with GI manifestations were up to 58.3% and 81.3%, respectively, which were significantly higher than that of SHP patients without GI manifestations (28.1%) or healthy children (6.7%) (17). Thus, if gastric Hp infection plays an important role for the onset of SHP, Hp eradication would be a definitive therapy to improve the prognosis by protecting against recurrence or renal complication. In the future, further studies of more large series of cases are needed in order to verify whether the association of Hp infection with SHP is causal or occasional and to evaluate the usefulness of Hp eradication therapy in SHP.

GI involvement in SHP is seen predominantly in the small bowel including the duodenum and also it affects the stomach in a high percentage of cases (18). In the present case, despite the lack of histological examination, endo-
scopically, numerous hyperemic and petechial lesions in the duodenum were thought likely due to leukocytoclastic vasculitis as with purpuric lesions of the colon, while Hp infection as well as SHP was considered to be significantly responsible for the pathogenesis of this gastritis because endoscopic findings such as erythema, friability, flat erosion and rugal hypertrophy have been reportedly closely associated with Hp infection (19).

The present case refused to undergo follow-up endoscopic examination after the first eradication therapy. Thus, the effect of Hp eradication was evaluated by a non-invasive 13C-urea breath test. The reasons for the conversion to a positive result on the second urea breath test is considered to be two-fold: First, a new strain other than previous one colonized (reinfection). Second, the first eradication therapy decreased the bacterial load, which resulted in negative result on the first urea breath test, but the same strain re-colonized or re-grew (recrudescence). The latter mechanism was presumably implicated in the recurrence of Hp infection because in developed countries, recrudescence is considered to be responsible for most of the recurrent cases within the first year after successful eradication (20).

When the second urea breath test showed a positive result, no manifestations of recurrent SHP were present. The reason for that remains unclear, but patients with underlying Hp infection may require some additional factors to develop SHP or it may take a certain amount of the time from Hp infection to develop SHP like the onset of Hp-related gastric diseases.

In conclusion, upper endoscopy and Hp examination should be considered to confirm the presence of upper GI involvement or gastric Hp infection in SHP patients, especially with serious GI manifestations. If gastric Hp infection is evident, Hp eradication could be a therapeutic option because it has potential to prevent progression and induce complete remission with short-term medication, low medical costs and less significant adverse effects.

References


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