Liver Cirrhosis as a Delayed Complication of Stevens-Johnson Syndrome

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Abstract

A 26-year-old woman was referred to our department due to fever and skin rash after having taken medication for a common cold. Physical examination revealed erythematous skin changes on her body associated with mucosal involvement in her eyes and oral cavity. Peripheral blood examination revealed leukopenia and thrombocytopenia. Liver function test showed hyperbilirubinemia. She was managed with high dose intravenous immunoglobulin (IVIG) at 1.0 gm/kg of body weight infused for 5 consecutive days. Although the patient’s skin lesion improved dramatically with IVIG therapy, her hyperbilirubinemia aggravated progressively. Eighteen months after her presentation, liver cirrhosis was diagnosed by ultrasonography, laboratory and liver biopsy findings.

Key words: Stevens-Johnson syndrome, liver cirrhosis, cholestasis, hepatitis

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Introduction

Apart from severe cutaneous manifestations, Stevens-Johnson syndrome (SJS) may be accompanied by fever, myocarditis, myocardial infarction, hepatitis and acute renal failure. In addition, it may compromise the respiratory and gastrointestinal systems (1). Cholestatic liver disease, which may precede skin manifestations of SJS, has been reported to occur in SJS in the medical literature (2). Furthermore, liver cirrhosis as a delayed complication of SJS has not been reported. We report a case of SJS associated with cholestatic hepatitis that eventually progressed to liver cirrhosis.

Case Report

A 26-year-old woman presented to our department with high fever and an erythematous skin lesion that developed 2 days after taking cephradine and acetaminophen for a common cold. Physical examination revealed erythematous skin changes, especially in her anterior chest. Severe mucosal involvement was noted in her eyes and oral cavity. Peripheral blood examination revealed leukopenia (3,000 cells/μL) and thrombocytopenia (83,000 cells/μL) without eosinophilia. Liver function test revealed elevated aspartate aminotransferase 341 IU/L (normal 10-59 IU/L) and alanine aminotransferase 378 IU/L (normal 10-72 IU/L) levels associated with hyperbilirubinemia (serum total bilirubin 2.3 mg/dL). Serologic tests for hepatitis A, B and C viruses, antinuclear factor, RA factor, anti-HIV antibodies, anti-mycoplasma antibodies, IgM anti-EB virus antibodies, anti-Hantaan virus antibodies, p-ANCA and c-ANCA antibodies were all negative. Skin biopsy of her anterior chest lesion showed complete epidermal necrosis and subepithelial spongiosis. She was managed with high dose intravenous immunoglobulin (IVIG) at 1.0 gm/kg of body weight infused for 5 consecutive days. Although the patient’s skin lesion was markedly improved following IVIG therapy, her hyperbilirubinemia became progressively aggravated. Eighteen months after her initial presentation, thrombocytopenia has not recovered (Table 1) and ultrasonographic examination of her liver revealed micronodular cirrhotic changes (Fig. 1). Liver biopsy

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SJS, but to date there are only a few case reports describing
mucosa, tracheal or bronchial erosions, glomerulonephritis,
visceral involvement causing sloughing of gastrointestinal
occur in 92.3% to 100% of patient, and the frequency of
rasions followed by skin detachment as the predominant clini-
sive injury and hepatitis was estimated to occur in
myocardial injury and hepatitis was estimated to occur in

Discussion

SJS may present as a febrile illness associated with mal-
aise, headache, cough, rhinorrhea, and prodromal target le-
sions followed by skin detachment as the predominant clini-
cal findings. Mucous membrane involvement is reported to
occur in 92.3% to 100% of patient, and the frequency of
visceral involvement causing sloughing of gastrointestinal
mucosa, tracheal or bronchial erosions, glomerulonephritis,
myocardial injury and hepatitis was estimated to occur in
8.1% to 61.5% of the patients (3).

Cholestatic liver disease has been reported to occur in
SJS, but to date there are only a few case reports describing
this phenomenon (4, 5). Furthermore, liver cirrhosis as a de-
layed complication of SJS has not been reported. The likely
mechanism by which this association occurs is immune-
mediated destruction and subsequent sloughing of bile duct
epithelial lining causing obstruction (2). Liver disease in the
setting of SJS is a diagnosis of exclusion. We performed a
few serological tests to exclude the possible etiologic factors
associated to the development of hepatitis, such as viral
hepatitis markers and autoantibodies, and excluded the poss-
bility of secondary causes of hepatitis. Corticosteroids have
been used for the treatment of SJS and in one case (4)
may have contributed to the improvement of liver function
tests. There existed a treatment option that might have re-
sulted in accelerated resolution of the hepatitis in this case.
However, we selected to manage our patient with IVIG (6),
and her cutaneous response was dramatic. The patient was
followed up nearly two years and was not given corticoster-
oids. This was due to the patient’s fear of SJS recurrence
cause by corticosteroid, and the physician’s optimism that
her liver function test would recover spontaneously with
conservative treatment.

In this case, the liver biopsy finding showed moderate he-
patic inflammation pattern with septal fibrosis, and this was
compatible with clinical and ultrasonographic findings.

Table 1. Laboratory Values and Clinical Characteristics of the Patient by Days after Admission

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<th>29</th>
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<th>233</th>
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<th>415</th>
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<td>AST/ALT (%)</td>
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Abbreviations: WBC, white blood cell; Seg, segmented neutrophil; PLT, platelet; AST, aspartate aminotransferase; ALT, alanine aminotransferase; TB, total bilirubin; DB, direct bilirubin; Chol, total cholesterol, mg/dL; PT (INR), protrhrombin time (international normalized ratio); aPTT, activated partial thromboplastin time.

*Ultrasonography revealed cirrhotic change of liver and splenomegaly, †Ultrasonography-guided liver biopsy was done.

Figure 1. Microscopic finding of the liver tissue obtained by percutaneous needle aspiration biopsy shows moderate lobular, portoportal activity and septal fibrosis (Hematoxylin and Eosin staining, original magnification ×200).

Figure 2. Ultrasonogram of the liver shows increased echogenicity and micronodular changes with irregular margins, but no occupying lesion.
Thrombocytopenia was noted in her first presentation, but improved after IVIG treatment. However, thrombocytopenia reappeared soon after and persisted despite the improvement of hyperbilirubinemia. We assumed that the liver biopsy findings in this case may reflect the very early stage of liver cirrhosis without typical manifestations. It was better to perform liver biopsy again, but we could not perform it due to the lack of patient’s cooperation.

In conclusion, we report an extremely rare case of liver cirrhosis as a delayed complication of SJS. Further studies are required to evaluate the pathogenetic mechanisms and treatment options in patients with SJS complicated by liver disease.

The authors state that they have no Conflict of Interest (COI).

References