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ORIGINAL ARTICLE

Necrotizing fasciitis in liver cirrhosis

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Summary *Background:* Necrotizing fasciitis (NF) is associated with a high mortality rate. Hepatitis is endemic in Taiwan, and liver cirrhosis is associated with the development of NF. The characteristics of these patients, however, have not been well documented or the predictors of mortality clearly identified. The purpose of this study is to identify predictors of mortality in patients with liver cirrhosis and necrotizing fasciitis.
Methods: This study was conducted at the Chi-Mei Medical Center in southern Taiwan. Demographic data, clinical characteristics, and the microorganisms responsible for NF in patients with liver cirrhosis were recorded. To identify independent predictors associated with mortality, univariate analysis followed by multivariate logistic regression modeling was performed.
Results: During the period 2003–2011, a total of 55 patients with liver cirrhosis and NF were treated at the Chi-Mei Medical Center. Most patients had infections by monomicrobial Gram-negative bacilli. Univariate analysis revealed that severity of liver cirrhosis, shock, band polymorphonuclear neutrophil (>10%), international normalized ratio (>1.5), serum creatinine (>2.0 mg/dL), serum albumin (<2.5 g/dL), and activated partial thromboplastin time (>60 seconds) were significantly associated with mortality. However, multivariate logistic regression analysis revealed that serum albumin of <2.5 g/dL was the only independent predictor of mortality in patients with liver cirrhosis and NF.
Conclusion: NF in the vast majority of cirrhotic patients was caused by Gram-negative bacilli. Hypoalbuminemia (serum albumin <2.5 g/dL) was associated with mortality in patients with

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liver cirrhosis and NF. Further studies are needed to assess whether resuscitation with albumin-containing solutions lowers the mortality rate in such patients.

1. Introduction

Necrotizing fasciitis (NF), first reported by Wilson in 1952,[1] is a soft tissue infection with fascial necrosis. It has an estimated incidence of 1000 cases/year in the USA. The predisposing conditions are mainly diabetes mellitus, alcoholism, end-stage renal disease, malignancy, liver cirrhosis (LC), malnutrition, gout, corticosteroid use, and trauma.[2] The most common initial sign is tender erythema in the infected area. Other common symptoms originating from the skin are edema of the limbs, induration of the skin, purulence, fluctuance, and local heat. NF is a severe disease of sudden onset requiring the administration of high doses of intravenous antibiotics as well as aggressive surgical debridement. Despite improved medical care and better understanding of this disease today, the mortality rate remains high (24–34%).[3] LC predisposes patients to serious bacterial infections. In fact, the incidence of infection is 5–7 times higher in these patients than in other hospitalized patients.[4] Infection in cirrhotic patients involves organisms that gain access to the gastrointestinal tract by escaping phagocytosis in the hepatic reticuloendothelial system.[5] Hepatitis is endemic in Taiwan and LC has been shown to be associated with NF.[6,7] However, the characteristics of this specific group of patients have not been well documented and the risk factors of mortality have not been clearly identified. The purpose of this study is to present our clinical experience in treating NF in patients with LC and identify risk factors of mortality.

2. Methods

This study was conducted at the Chi-Mei Medical Center in southern Taiwan. The medical records of patients with liver cirrhosis who were diagnosed to have NF from 2003 to 2011 were reviewed. This study was approved by the ethics committee of our hospital. The diagnosis of NF was established according to the International Classification of Diseases, 9th revision (NF, 728.86; in combination with LC, 571.2 or 571.5). The final diagnosis of LC was based on hepatosplenic ultrasonography findings and the definitive diagnosis of NF on operative findings of necrosis of the fascia.

The characteristics of the patients were obtained from the medical records. Etiology of the disease, patient data, the cause and severity of LC, affected sites, clinical symptoms, laboratory examination results, and results of microbiologic testing comprised the primary variables. Hepatotropic viruses were identified using common serological techniques. The modified Child–Pugh classification system was used to grade the severity of LC at admission for each patient.[8] The modified Child–Pugh classification of the severity of liver disease was determined according to the degree of ascites, the plasma concentrations of bilirubin and albumin, the prothrombin time, and the degree of encephalopathy. A total score of 5–6 was considered Grade A, 7–9 was Grade B, and 10–15 was Grade C. Laboratory results were obtained in the emergency room or within 24 hours after admission to the hospital. The white blood cell (WBC), band polymorphonuclear neutrophil (PMN), and platelet counts, activated partial thromboplastin time (aPTT), international normalized ratio (INR), and levels of hemoglobin, C-reactive protein, serum creatinine, glucose, and albumin were dichotomized, with a cutoff point based on clinical experience and previous reports. Shock was defined as a systolic blood pressure of $<$90 mmHg. Wound cultures were obtained in the emergency room or during the initial surgery. Microbiologic results were recorded for patients with positive cultures for organisms. The primary study outcome was 30-day mortality.

To identify risk factors associated with mortality, we first performed a series of Chi-square or Fisher's exact tests. Variables with a $p < 0.05$ were considered potential risk factors and were therefore included in a stepwise multivariate logistic regression model to determine the most important independent predictors of 30-day mortality. Statistical significance was defined as a $p < 0.05$, unless specified otherwise. Data analyses were performed on a personal computer using the statistical software package SPSS for Windows (Version 17.0; SPSS Inc., Chicago, IL, USA).

3. Results

3.1. Etiology, patient characteristics, and affected sites

From January 2003 to December 2011, a total of 55 patients with liver cirrhosis and NF were treated at the Chi-Mei Medical Center. The overall mortality rate was 51% ($n = 28$) and all deaths occurred within 30 days of hospitalization. The patients comprised 42 men and 13 women with a mean age of 59.0 $\pm$ 12.4 years. The cause of NF was either unknown ($n = 27$, 49%) or trauma ($n = 10$, 18%), when added together, in more than half of the patients. Six of the patients (11%) had a history of exposure to dirty water or fish-fin injury and two patients (4%) had a history of seafood intake before the episodes (Table 1). All the six patients with a history of exposure to dirty water or fish-fin injury were infected by *Vibrio* species. One patient with a history of seafood intake was infected by *Vibrio* species and others by *Aeromonas* species. No association was noted between mortality and age $>$60 years. In addition, there were no differences in comorbidities including diabetes mellitus, cancer (by history), heart disease, and end-stage renal