CLINICOPATHOLOGICAL STUDY OF SCLEROTHERAPY
OF ESOPHAGEAL VARICES
I. A REVIEW OF 26 AUTOPSY CASES

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Summary

Twenty six autopsy cases treated by endoscopic injection sclerotherapy (an intravariceal injection method) using ethanolamine oleate were examined for morphological changes in relation to the time intervals following injection. Red thrombi obliterated in the varices were recognized within 20 days of the treatment, and after a month, organization and shrinkage had occurred. Neutrophil infiltration of the esophageal wall was present within four days, and hemorrhage within six days. Edema and necrosis, the degree of which tended to decrease gradually with time, were observed within 20 days. Granulation tissue was first seen 10 days after treatment, followed by increased transformation of fibroblasts into fibrocytes. After two and a half months, an almost cell-free fibrotic-sclerotic stroma was recognized. The results obtained suggest that this treatment creates not only thrombi in vessels which are at risk of bleeding but also fibrosis which prevents rupture of the varices when a sclerosant is leaked or injected into the interstitial tissue. The results might furthermore serve as a basis for a prospective morphological study of patients with varices treated with ethanolamine oleate.

Key Words: Esophageal varices, Ethanolamine oleate, Injection sclerotherapy, Morphology.

Introduction

Although endoscopic injection sclerotherapy (EIS) of varices was first reported by Crafoord and Freckner in 1939, it was little used, as portosystemic shunt surgery or esophageal transection came to be applied for a long time. However, since Johnson and Rogers reported the achievement of a 93 per cent control rate for bleeding in 117 patients with an 8 per cent hospital mortality in 1973, this method has been re-evaluated and accepted as one of the most effective treatments for esophageal varices. In Japan, EIS was initiated in October 1977 by Takase et al., who reported good results with this treatment. Other subsequent papers have left no doubt as to the clinical efficacy of this treatment for bleeding esophageal varices. Nevertheless, to the author's present knowledge, there are few reports in English on the histopathological changes occurring in the esophageal wall treated by the intravariceal injection method, and it appears that in those
reports there was not enough available information on changes in relation to time after injection, since the number of the cases examined histopathologically was small.

This report presents the results of a time-dependent morphological analysis of the esophageal wall treated by the intravariceal injection method, and the results might be used as a basis for comparative predictions, especially the endoscopic findings after treatment.

Materials and Methods

Thirty three cases who had been treated by EIS were autopsied at the Pathology Department of Kurume University Hospital during the period from August 1982 to March 1985. Among the 33 cases, five treated by the paravariceal injection method using 5% phenol-almond oil and two who received injection into gastric varices were excluded. This study consists of 26 cases treated by the intravariceal injection method using 5% ethanolamine oleate (EO) for esophageal varices.

At autopsy the esophagus was opened in continuity with the stomach, the latter along the greater curvature. After formalin fixation five sections were obtained routinely every 2 cm from the esophago-gastric junction, together with further sections to meet the needs of each case. Histologic sections were stained with hematoxylin and eosin (H&E), elastica Van Gieson (EVG) and Mallory-Azan (Azan).

Results

Table 1 shows the main clinicopathological findings. The cases are listed according to the number of days between injection and death. Emergency treatment was performed on 21 cases irrespective of the clinical assessment of liver function as treatment for bleeding esophageal varices, prophylactic treatment being given in five cases. Liver cirrhosis or hepatocellular carcinoma with liver cirrhosis was the principal disease in 25 cases. In 17 cases with blood clot and/or fresh blood in the stomach at autopsy, bleeding was regarded as the main cause of death. However, it was difficult to confirm the hemorrhagic site in 11 of the 17 cases.

The histopathological findings at the lower esophagus where the sclerosant was injected, are separately summarized for superficial tissues comprising the mucosa and submucosa and deeper tissue comprising the muscularis propria, in Table 2. In order to examine the time-dependent morphological changes occurring in the esophagus following EIS in 19 cases who died within 20 days after the first injection, cases 7, 13, 14, 16, and 17 were separately listed because they received several injections, and cases 9, 15, and 17 because of extensive ulceration due to the use of a Sengstaken-Blakemore (S-B) tube. Up to July 1983, a combination EIS of EO and Thrombin® had been performed. Thereafter, EIS using EO alone had been done to avoid the harmful after-effects of Thrombin®, for example anaphylactic shock.

In patient no. 1 who died only three hours after injection, no endothelium was observed in the varices (Fig. 1). Red thrombi comprising red cells and fibrin (Fig. 2), which were obliterated in the vessels, were recognized within 20 days of treatment: Red thrombi in the most early state were seen in patient no. 2 who died nine hours after combination EIS, and in cases 6 and 8 who died two days after treatment involving EO alone. In the patients who survived more than a month after treatment, red thrombi were completely organized and shrunk with recanalization and elastosis in the walls of the vessels (Fig. 3). In most of the organized varices, recanalization was seen, but these veins were microscopic.

Neutrophil infiltration in the esophageal wall was seen by the fourth day. Chronic inflammatory cells (lymphocytes, plasma cells,