Oesophageal varices treated by sclerotherapy: a histopathological study

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SUMMARY Of 31 cases of haemorrhage from oesophageal varices treated by sclerotherapy eight came to necropsy. The oesophagus and proximal stomach were studied by means of a serial block technique and the histopathological findings in each case were recorded on two full-scale maps: one representing superficial tissues including the submucosa and the other the deeper tissues. The patterns of thrombosis, ulceration, necrosis, and fibrosis were studied in relation to the time interval since injection. Thrombosis and tissue necrosis were present within 24 hours of sclerotherapy, ulceration after seven days, and fibrosis after a month. Fibrosis was sometimes associated with stricture formation, which readily responded to dilatation. Patients with fibrosis had a reduced incidence of rebleeding.

Haemorrhage from oesophageal varices is a frightening and often lethal complication of cirrhosis of the liver. A portocaval shunt does not appear to prolong survival and may be followed by encephalopathy and neuropsychiatric syndromes, even in those patients with good liver function.¹ This procedure has therefore been abandoned at our hospital in favour of oesophageal sclerotherapy. In order to study the effects of this treatment we examined the oesophagus of patients coming to necropsy by means of the serial block technique used by Mochizuki in his work on gastric cancer in Japan.² Our findings are described in this paper.

Methods

Each varix at the lower end of the oesophagus was injected with 3 ml of sclerosant through an end-viewing fibre-endoscope using a fine injection needle (Olympus NM3). Apart from case 2 where ethanolamine oleate injection BPC was used, the sclerosant was STD (sodium tetra-decyl sulphate 3% w/v). Up to four varices were injected at a time, the treatment being repeated at weekly intervals until the risk of bleeding was small, and thereafter at monthly intervals in surviving patients until all varices had disappeared.

Of 31 cases of bleeding oesophageal varices

treated by sclerotherapy eight came to necropsy. The oesophagus was opened in continuity with the stomach, the latter along the greater curvature, both being removed as one specimen and laid out flat on a tray during fixation in formol saline. The specimen was photographed as soon as practicable. After fixation, the outline of the specimen was traced onto paper with an underlying carbon copy to provide a stain-free map. The oesophagus and proximal stomach were sliced transversely to provide 50-75 adjacent blocks whose position and identity number were marked on the map (Fig. 1). Their large size necessitated hand processing of the blocks. Paraffin sections were stained by haematoxylin and eosin and by MSB trichrome. During histological examination, the position of thrombosed (in one case dilated non-thrombosed) blood vessels and the extent of necrosis and ulceration were marked on the coverslip using felt-tipped pens according to a colour code. The slide markings were transferred to the corresponding site of the relevant block on the map. For clarity, two maps were prepared for each specimen, one of superficial tissues comprising mucosa and sub-mucosa and the other of deeper tissues comprising muscularis propria and outer connective tissue.

Results

The necropsy findings in the oesophagus from patient no. 1, who survived only one day after

Fig. 1 Case 1. Oesophagus. Left: gross appearance. Centre: histological map of superficial tissues. Right: map of deeper tissues.

injection of varices with STD, are illustrated in Fig. 1. The gross appearance of the viscus is shown on the left and the maps of the histological findings in the superficial and deeper tissues are shown in the centre and on the right respectively. Thrombosed vessels were numerous and the maps represent the distribution of zones in which thrombosed vessels were present, except in the case of very large vessels, several of which are shown individually. The latter represent the actual varices into which injection was made. It can be seen that the extent of the thrombosed vessels was greater in the submucosa than in the muscularis propria and outer connective tissue. The other major histological finding was tissue necrosis, which was extensive in the superficial tissues but less in the deeper tissues.

The extent of tissue necrosis was greatest in the oesophagus of patient no. 2, the only one in our series to be injected with ethanolamine oleate (Fig. 2). This viscous material was still demonstrable at the sites of injection two days later.

In order to study the natural history of the lesions after injection of the varices each oesophagus was examined in a similar manner. The findings were then listed according to the number of days between injection and death (Table). When several injections had been given, the cases were arranged

in the order of the median time interval.

As a rule, thrombosis of blood vessels was considerably more extensive in the superficial than in the deeper tissues. The one exception was case 6 where the extent of deep thrombosis was more comparable with the superficial thrombosis (Fig. 3); ulceration was present in addition to necrosis. This patient did not have cirrhosis but portal hypertension and non-cirrhotic portal fibrosis secondary to exposure to vinyl chloride monomer, death following development of an angiosarcoma.

Thrombosed vessels were found in all but case 7 where bleeding had been controlled completely after four sclerosant injections: there were numerous dilated vessels but no thrombosis was found in the entire specimen. There was, however, considerable fibrosis involving both superficial and deeper tissues. It is of note that fibrosis of significant degree was only demonstrated in cases 5, 7, and 8 in whom there had been a lapse of at least one month from the time of injection to death.

In three of the first four cases, who received one or two treatments, death resulted from variceal haemorrhage within one week of the last injection. Examination of sections revealed only partial thrombosis in a number of vessels with evidence of haemorrhage from some of them. None of the

Fig. 2 Case 2. Oesophagus. Left: histological map of part of oesophagus showing large extent of necrosis (superficial and deep tissues) with related thrombosed vessels. Right: diagram of histological section to show depth of necrosis with related thrombosed vessels. The mucosal surface is uppermost.

Table Details of eight cases that came to necropsy

Case no.	Injections (no.)	Days after		Thrombosis		Ulceration	Necrosis		Fibrosis	Cause of death
		First injection	Last injection	Superficial	Deep		Superficial	Deep		
1	1	1	1	+++	+	—	++	++	—	Carcinomatosis
2	1	2	2	+++	+	—	+++	+++	—	Bleeding varices
3	1	7	7	++	+	—	++	+	—	Bleeding varices.
										Carcinoma of bronchus
4	2	18	7	+++	+	+++	++	—	—	Bleeding varices
5	4	60	4	+	+	+	+	+	++	Hepatic failure.
										Primary biliary cirrhosis
6	4	84	2	+++	+++	+	++	+	—	Angiosarcoma
7	4	83	33	—	—	+++	—	—	+	Hepatic failure.
										Biliary cirrhosis
8	7	167	51	++	+	++	—	—	+	Hepatoma.
										Alcoholic cirrhosis

remaining five cases died from variceal haemorrhage, multiple injections having obliterated or greatly reduced the size of the varices.

Discussion

Variceal sclerotherapy controls acute haemorrhage,³ prolongs survival,⁴ and does not predispose to encephalopathy. It is not without hazards, however, and these are underlined by our findings in the present study.

Unlike the treatment of varicose veins in the leg, where the sclerosant injection is confined within the vein, some penetration into the interstitial tissue may occur when injecting oesophageal varices through a gastroscope. A degree of tissue necrosis therefore seems likely. Indeed deliberate injection into the perivenous tissues has been used by European workers to produce variceal obliteration, despite the occurrence of a small number of cases of oesophageal wall necrosis.⁵ Preliminary studies in this hospital, however, suggest that intravenous injection of STD is more effective than perivenous injection (unpublished data). It is possible that the use of a flexible oesophageal sheath⁶ to trap sclerosant in the varices may lead to less tissue necrosis, but we believe that the requirement of a general anaesthetic outweighs the possible advantages of the sheath. We have chosen STD as our sclerosant, not only because it is less viscous, but also because animal studies have shown that it produces no more tissue necrosis than ethanolamine oleate if placed subcutaneously and is a better thrombotic agent when injected intravenously.⁷

HAEMORRHAGE

During the first week after injection the greatest

hazard was a further haemorrhage, probably due to inadequate thrombosis, as additional injections led to a diminution in variceal size and a reduction in the risk of bleeding. It was possible to obliterate the varices completely in patients who survived with an average of six treatments. Cases 6 and 7 required four treatment sessions and case 8 needed seven sessions, the varices eventually being obliterated.

ULCERATION

Ulceration was present in all cases that survived the first week. It was associated with initial heartburn which disappeared before the ulceration healed by re-epithelialisation of the surface. This was an endoscopic observation mainly on those cases which survived. At least some residual ulceration was present in cases 4–8, although in some instances pain on swallowing had not been evident for several weeks.

NECROSIS

Necrosis, particularly that involving the muscularis propria, gave cause for concern because of the possibility of perforation. This complication did not arise in the present series but has been described by other authors.^{3,5} Nevertheless, from examination of the oesophagus at laparotomy in one of the surviving cases requiring transection to control severe bleeding, it was clear that perforation was a possibility as areas of necrosis involving the whole oesophageal wall were found three days after the injection of sclerosant. Similar changes were described in the dog⁸ with coagulation necrosis and acute inflammation resulting from perivenous injection of sclerosant. Superficial ulcers occurred if the volume of injected sclerosant was 2 ml or more; no ulcer developed when 1 ml or less was injected.

Fig. 3. Case 6. Oesophagus. Top: gross appearance of gastro-oesophageal region. Bottom left: histological map of superficial tissues. Bottom right: map of deeper tissues.

FIBROSIS

Fibrosis was mainly beneficial in its effects. In all cases in which it occurred to a significant degree, the varices disappeared or became very small. In a few cases the fibrosis was sufficient to produce oesophageal stenosis and dysphagia. This responded readily to oesophageal dilatation. With this proviso, fibrosis appeared to be the most desirable effect. An agent which could induce thrombosis and fibrosis without ulceration or necrosis would clearly be an advance on the present sclerosing agents such as ethanolamine oleate and STD, with which relatively large zones of tissue necrosis appear to be unavoidable unless seepage of the sclerosant into the interstitial tissues can be prevented.

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References

- 1 Conn HO. Therapeutic portocaval anastomosis: to shunt or not to shunt. *Gastroenterology* 1974; **67**: 1065–71.
- 2 Mochizuki T. Method for examination of early gastric cancer. In: Murakami T, ed. *Early gastric cancer*. Tokyo: University of Tokyo Press, 1972: 57–65.
- 3 Johnston GW, Rodgers HW. A review of 15 years experience in the use of sclerotherapy for control of acute gastric haemorrhage from oesophageal varices. *Br J Surg* 1973; **60**: 797–800.
- 4 Macdougall BRD, Westaby D, Williams R. Controlled trial of injection sclerotherapy in patients with cirrhosis and variceal haemorrhage. (Abstract). *Gut* 1981; **22**: A886.
- 5 Paquet KJ, Oberhammer E. Sclerotherapy of bleeding oesophageal varices by means of endoscopy. *Endoscopy* 1978; **10**: 7–12.
- 6 Williams KGD, Dawson JL. Fibreoptic injection of oesophageal varices. *Br Med J* 1979; **2**: 766–7.
- 7 Blenkinsopp WK. Comparison of tetradecyl sulphate of sodium with other sclerosants in rats. *Br J Exp Pathol* 1968; **49**: 197–201.
- 8 Sugawa C, Okumura Y, Lucas CE, Walt AJ. Endoscopic sclerosis of experimental oesophageal varices in dogs. *Gastrointest Endosc* 1978; **24**: 114–6.