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Application of Fibrin Adhesive in the Urinary Bladder

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Summary. The investigations on rats and pigs showed that the transuretheral haemostasis of the urinary bladder damaged by radiotherapy is possible by means of fibrin adhesion. The spraying procedure has to be carried out by means of a special balloon-catheter in a bladder filled with CO_2. During spraying the bladder must be kept constantly free of pressure.

Key words: Fibrin adhesive, Hemorrhage of the bladder, Transurethral hemostasis Radiotherpay-damaged urinary bladder.

Introduction

Changes in bladder mucosa following radiotherapy can lead to life-threatening heamorrhage either immediately or chronically [1, 6]. Present methods of haemostasis in these cases are unsatisfactory. As fibrin adhesion is, in principle, useful in capillary bleeding [3, 4, 7, 10, 13, 14], it might also be applied to bladder mucosa damaged by radiotherapy. The exposed urinary rat bladder was examined to determine whether fibrin adhesive stemmed such capillary bleeding of the mucosa promoted the healing a haemorrhagic cystitis. A practicable technique for the endoscopic application of the adhesive to the bladder wall is presently under development.

Material and Methods

The hemostatic properties of the fibrin adhesive were examined on the opened rat bladder (Table 1). 18 Wistarrats (in Brevimytal anaesthesia) served as a model for these control investigations. Mucosal bladder haemorrhage was induced mechanically. Both components of the fibrin adhesive were injected simultaneously using the fast glueing method [11] with a commercial double-piston syringe or spray catheter. Subsequently the urinary bladder was closed again. The necropsy of the animals performed one to eight days later consisted of macroscopic and histologic examination of the urinary bladder and a urinalysis.

Application Procedure

The possible means of application of the fibrin adhesive in the urinary bladder were as follows:

- Endoscopic application by visual means through a cystoscope
- Blind application through the rotation of a special catheter in the bladder.

Fibrin adhesion was carried out by means of commercial spraying sets. First the method was carried out on the bladder model, then on a pig's bladder filled with CO_2. During spraying with CO_2 gas the bladder must be kept constantly free of pressure in order to avoid distension with the attendant danger of bladder injury. A pneumatic overflow vessel was used to compensate for high intravesical pressure. For example, using this vessel the pressure on the isolated pig bladder was held constant at a 3.5 cm water column (Fig. 1).

To spray on area of 220 cm^2, corresponding to a bladder of approx. 300 ml capacity, at least 4 ml of adhesive was necessary. A further 0.5 ml was necessary to fill the approx. 65 cm long spray catheter. For such a spraying procedure approximately six to eight litres of CO_2 were used. This had to be released from the bladder by decompression.

Results

The fibrin adhesive adhered well to the exposed damaged bladder mucosa. With heavier bleeding, however, it can lead to clotting and rejection of the adhesive. Application with the spraying head has the advantage over the double piston syringe that the mucosa is simulatenously drained by the flow of gas.

After opening the urinary bladder one to eight days following the application of the adhesive, residual fibrin adhesive was not evident macroscopically. Following careful histologic examination of the urinary bladders a certain number of the animals showed microscopic fibrin adhesive

Table 1. Number (*n*) of the test animals (rats) and type of treatment as well as the effect-time of the fibrin adhesive

Treatment of the test animals	Experimental phase (days)						Total
	1	2	3	4	6	8	[*n*]
Mechanical lesion with fibrin-adhesion (*n*)	1	3	3	2	2	1	12
Mechanical lesion without fibrin-adhesion (*n*)			2	1		1	4
Fibrin-adhesion alone (*n*)	1	1					2

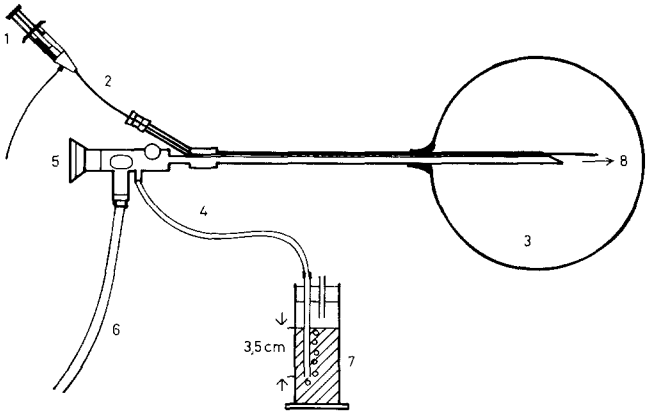

Fig. 1. Test model of endoscopic application of the fibrin adhesive (*1*, double piston syringe; *2*, spray catheter; *3*, pig's bladder; *4*, connection to the vessel serving as pressure release; *5*, cystoscope; *6*, light cable; *7*, vessel for pressure decompression; *8*, spraying direction)

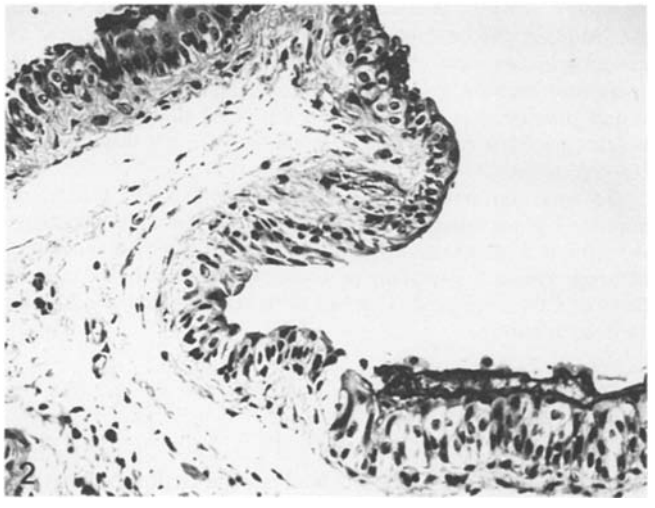

Fig. 2. Mucosa of the urinary bladder with intact, unpathologic urothelium and thin fibrin adhesive layer at the surface. No morphological signs of inflammatory reaction either at the urothelium or in the lamina propria (HE, x189)

residues, which within the preserved mucosal bladder area were found to be completely free of inflammation over the intact epithelium. Even in the lamina propria no inflammatory reactions were to be observed (Fig. 2).

When the injury took place one to two days previously, a loose exudate was generally found consisting mainly of granulocytes but also of a few lymphocytes and plasmacytes over which some of the fibrin adhesive material could still be found (Fig. 3). After a maximum of one week an early fibrous tissue reaction was found with the formation of numerous capillaries, proliferation of fibroblasts with significant fibrous tissue formation and a scanty infiltrate consisting of lymphocytes, plasma cells and granulocytes. Occasionally, fibrin adhesive residues were observed on the surface of a healing mucosal defect. (Fig. 4).

In two cases the fibrin adhesive was introduced into the intact urinary bladder in such large amounts that the whole bladder was almost filled with it. On the following day the adhesive was still present macroscopically, after one further day no fibrin adhesive was to be found macroscopically. Histologically these two urinary bladders showed no significant changes.

The urine from the bladders which were treated with adhesives after injury was always macroscopically clear. With the control animals it was still discoloured with old blood three days after the mechanical lesions, and only 4 to 8 days later was without pathologic findings.

Discussion

The results gained confirm the satisfactory hemostatic effect on capillary mucosal bleeding of fibrin adhesive application as shown in the visual urine controls. Histologic examination confirmed that healing of the wound is accelerated after fibrin adhesive application [5]. The rapid fibrin elimination either after application to the damaged mucosa or even after instillation in the undamaged urinary bladder cannot only be explained by the high fibrinolytic tissue activity of the rat [5, 8, 12]. The urine itself has a fibrinolytic effect and may therefore have an irrigating effect in the bladder lumen.

As the succesful fibrin application in the prostate cavity [2] indicates, similar treatment to the bladder could be indicated in the following cases:

- Capillary bleeding of the mucosa,
- diffuse large bleeding sources,

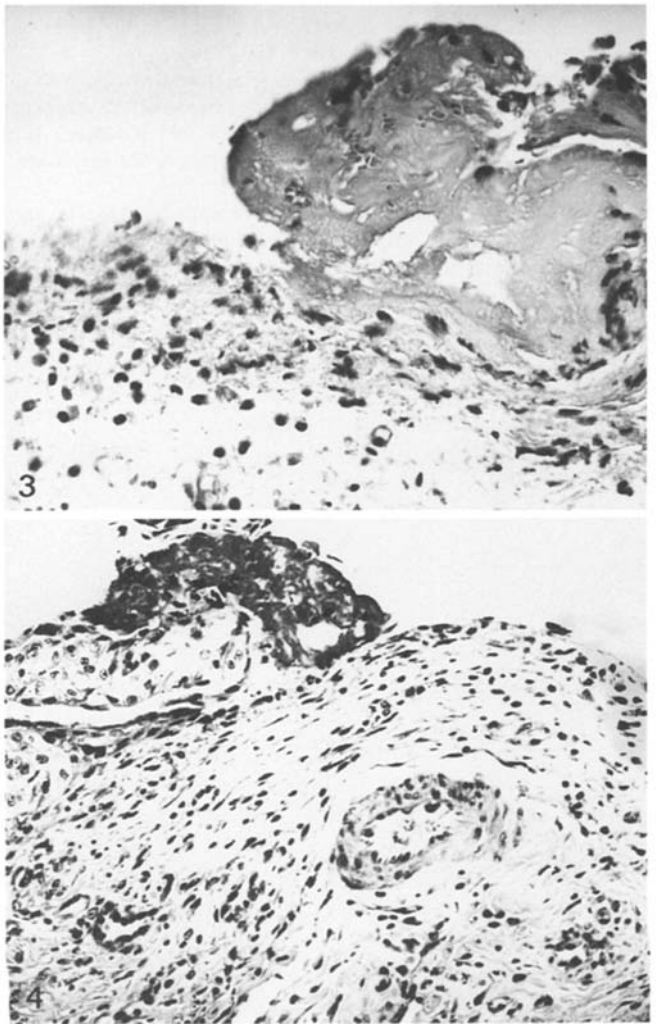

Fig. 3. Inflammatory exudate consisting of fibrin and granulocytes at the surface of a new wound approx. 1 day after application of the fibrin (HE, x492)

Fig. 4. Early fibrous tissue organisation of on older mucosa defect with formation of granular tissue and numerous capillaries, proliferation of fibroblasts with already significant formation of fibers and a loose inflammatory infiltrate consisting of lymphocytes. Additionally, in the marginal area of the defect still recognisable fibrin adhesive residues (HE, x189)

- failure of conventional haemostatic procedures such as laser and electrocoagulation. The instillation of Formalin, which was also used, has proved to be unsafe and is encumbered with considerable side-effects.

However, an essential precondition for fibrin adhesion to the bladder mucosa is the transurethral application technique.

The investigations on the bladder model and on the isolated pig bladder showed that the spray adhesion under direct cystoscopic vision and four-way spray-catheter (6 fr.) is only applicable with localised bleeding of a circumscribed wall area (e.g. the side or posterior wall of the bladder). The large-area adhesion must be carried out without visual aid by rotating the spray-catheter; only by such means is an adequately rapid application possible. With bleeding which cannot be drained shortly before the spraying procedure, there is the danger that the fibrin adhesive will separate immediately in clots. Effective haemostasis can only be achieved in such cases if, in addition, the adhesive is held snug against the bladder wall by mechanical means, e.g. by a balloon. The balloon catheter must be placed in the bladder together with the spray catheter, in order to fill up the balloon immediately after the spraying procedure to a volume corresponding to the bladder capacity. After a certain time the balloon can be deflated and the catheter removed with the sprayset.

During the spraying procedure decompression of the bladder is especially important; under physiological conditions, acceptable bladder pressure lies below 70 cm H_2O. As the whole drainage and spraying procedure takes, in total, only approx. 15 s, in which time six to eight liters of CO_2, corresponding to 20 to 25 times the bladder volume, may be infused simultaneous suction, possibly through a suprapubic punctur [9], is required.

The experimental prerequisites and application techniques for the transurethral fibrin adhesion of capillary bleedings in the bladder are therby fulfilled.

Conclusions

Transurethral haemostasis of the urinary bladder damaged by radiotherapy, was possible by means of fibrin adhesion as illustrated by experiments on rats and isolated pig bladders.

Application was effected by filling the bladder with CO_2 via a spray catheter. Pressure compensation must be assured during the spray procedure and, possibly, when applying the adhesive layer by means of a balloon.

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