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MORPHOLOGICAL EVIDENCE FOR USE OF RADIOOPAQUE EMBOLI BASED ON POLYHYDROXYETHYL METHACRYLATE FOR VASCULAR OCCLUSION

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Endovascular occlusion of blood vessels to arrest bleeding and as a measure reducing blood loss during surgical operations has been extensively used in recent years in surgery. The requirements for embolizing materials are satisfied most closely by the sponge-like hydrogel based on poly-2-hydroxyethyl methacrylate [1]. Emboli of this material do not cause damage or induce an inflammatory reaction of the vascular wall, but by intensifying thrombus formation and with the ability to swell in the lumen of blood vessels, they have a good and immediate obturating effect. Made of biologically inert material, hydrogel emboli are virtually not resorbed, and the obturating effect due to their use is thus stable and long-lasting. In medical practice visual control of the location of the emboli is often essential, and is possible only if the emboli have radioopaque qualities.

The aim of the present investigation was to develop a technology of radioopaque hydrogel emboli, to determine their compatibility with the tissues with which they come into contact, and to test their radioopaque properties.

EXPERIMENTAL METHOD

Hydrogel emboli can be made radioopaque by modifying the chemical composition of the polymer material or by addition of radiooopaque substances to the composition of the material of the emboli, without any chemical bond between the hydrogen and these substances. In the latter case, we are dealing with a dispersed system. We tested two methods of contrasting. The emboli which are being examined in this paper were rendered radioopaque by the addition of iodides, bromides, and polyiodides of silver, and also of α-(3-amino,2,4,6-triiodobenzyl)-butyric acid (Iopagnost) to the hydrogen. Emboli containing silver halides were prepared by successive swelling in aqueous solutions of silver nitrate and potassium iodide. Under these circumstances, silver iodides, insoluble in water and liquid media [2], are deposited in the mass of the hydrogel. When Iopagnost was used it was dissolved in a mixture of monomers from which the embolizing material (hydrogel) was used. During subsequent washing of the emboli

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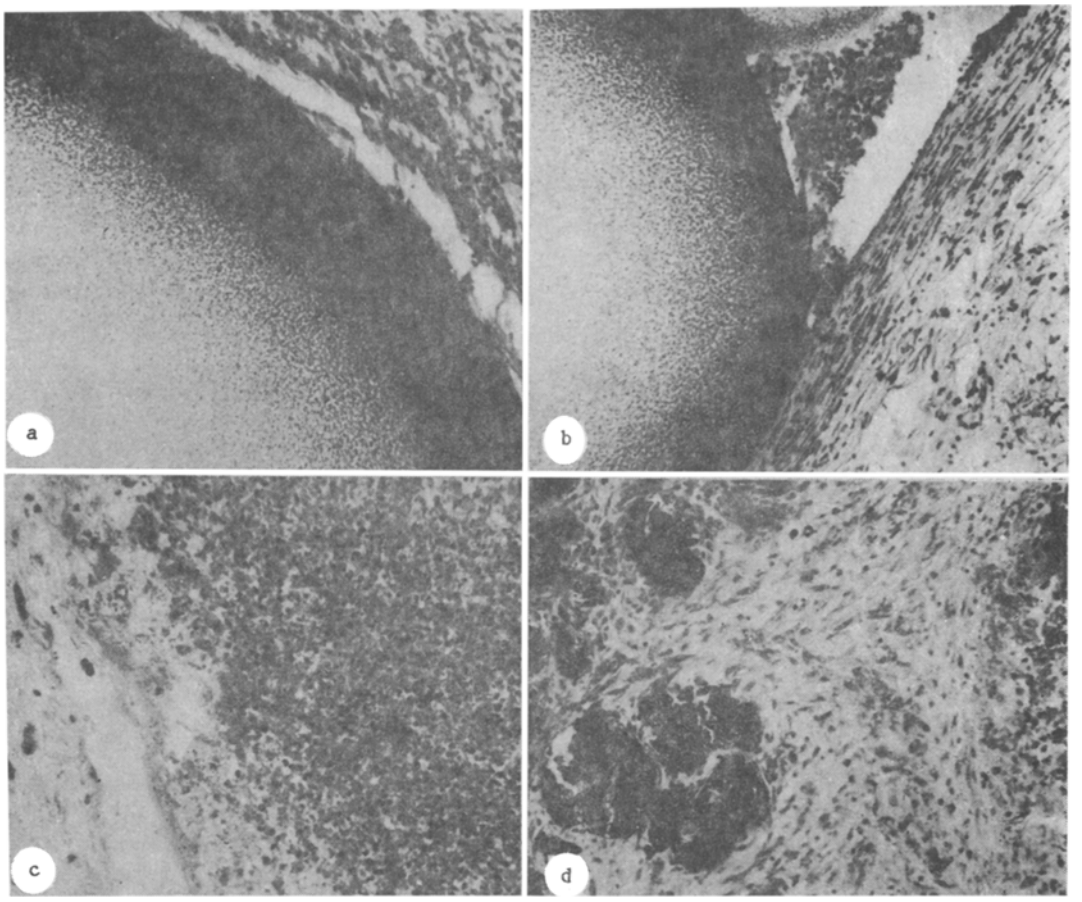

Fig. 1. Histological changes in soft tissues and arterial wall in zone of their contact with embolizing material. a) Fragment of embolus (transverse section) composed of hydrogel, rendered opaque with silver salts, and implanted into lumen of fermoral artery (8th day after implantation) of a rabbit. Highest concentration of silver granules in peripheral parts of embolus. Vessel wall represented by intact muscular layer. Van Gieson's stain. 160 ×; b) hydrogen embolus rendered opaque with silver salts, in lumen of hepatic artery (3rd day after implantation of embolus), necrosis of intima present, muscular layer of vessel wall intact. Hematoxylin and eosin. 160 ×; c) hydrogen embolus rendered opaque with Iopagnost, implanted subcutaneously into a rabbit (8th day after implantation). Nuclear debris from disintegrated polymorphis present in pores of embolus. Embolus surrounded by capsule of young connective tissue. Hematoxylin and eosin. 260 ×; d) Necrosis of fatty areolar tissue and of skeletal muscles in neighborhood of hydrogel embolus, rendered opaque with silver bromide. Necrotic muscle fibers, permeated by lime salts, are dark in color (8th day after implantation). Van Gieson's stain. 160 ×.

with water, the water-insoluble Iopagnost was deposited in the mass of the polymer. To study the effect of radioopaque emboli with the body tissues in contact with them, in experiments on 22 rabbits they were implanted subcutaneously and in the lumen of the femoral artery. Experiments were carried out with implantation of emboli with different concentrations of radioopatue substances in order to choose the optimal version. This is the composition with the property of adequate x-ray contrast, with minimal traumatic effect on the tissues. A comparative morphological investigation was carried out 7 days after implantation.

EXPERIMENTAL RESULTS

In emboli contrasted with silver salts, microscopic examination revealed black granules, most numerous in their peripheral parts. With a higher concentration of iodide granules in the peripheral zones of the embolus, they had the appearance of black conglomerates (Fig. 1a, b).

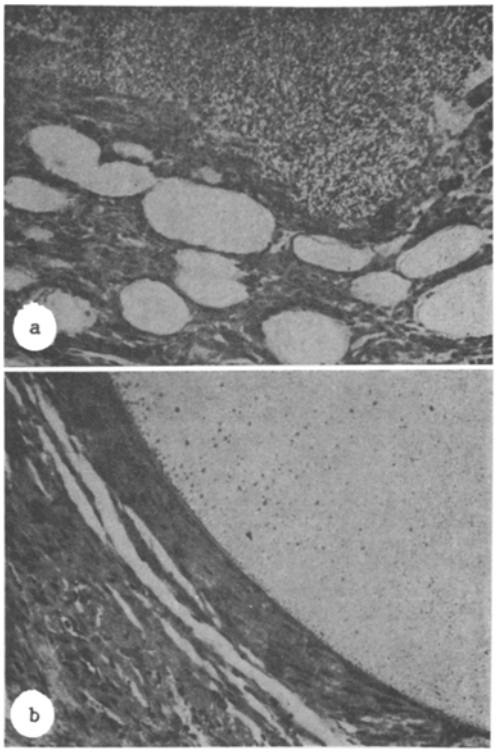

Fig. 2. Reaction of tissue structures to hydrogen rendered opaque with silver iodide. Hematoxylin and eosin. 160 ×. a) Hydrogel embolus rendered opaque with silver iodide, implanted subcutaneously into a rabbit. Connective-tissue capsule around embolus (8th day after implantation); b) hydrogen embolus rendered opaque with silver iodide, in lumen of hepatic artery 30 days after endovascular occlusion (clinical material obtained at operation). Reduction in number of silver iodide granules compared with early periods of observation. Integrity of muscular coat of artery, in which destructive changes are absent.

When Iopagnost was used for contrasting, no granules of radioopaque material could be seen, but polymorphis and nuclear debris from disintegrating leukocytes were contained in the pores of the hydrogel at the times of investigation (Fig. 1c).

Emboli containing silver bromides in concentrations of 26-30% damaged the tissues the most. Tissue damage was expressed as coagulation necrosis of skeletal, muscular, adipose, and connective tissues in the zone of their immediate contact with the embolus in the case of subcutaneous injection of the emboli, and of the intima and, to some extent, of the media when implanted by the intravascular route. Necrosis was accompanied by a polymorphonuclear reaction. Necrotic areas of muscle were often permeated with lime salts (Fig. 1d).

When the emboli were contrasted with Iopagnost, two concentrations of this substance in the mass of the polymer were tested (10 and 17%). With the higher concentration of Iopagnost the degree of injury to soft tissues and the vascular wall in contact with the emboli was rather less than when silver bromide was used (Fig. 1c). With a concentration of 10% of Iopagnost in the hydrogen, necrosis was not observed in the zone of body tissues in contact with the emboli. On subcutaneous implantation of the emboli, a capsule consisting at this time of young connective tissue formed around them. Swollen fibroblasts, capillaries, and a few collagen fibers could be identified in it (Fig. 1c).

In the case of emboli rendered opaque with silver iodide, adequate opacity was given by a concentration of 30% in the polymer. At this concentation, a small band of coagulation necrosis could be seen in the soft tissues surrounding the implanted hydrogel embolus, but incomparably shallower than when silver bromide was used. Beyond the band of necrosis was a capsule composed of young connective tissue and consisting of swollen fibroblasts, capillaries, and a few collagen fibers. Moderate infiltration of the capsule by polymorphis was pres-

ent (Fig. 2a). When an embolus of this composition was implanted in the lumen of the femoral artery, histological examination of sections revealed necrosis of the intima to a varied depth, accompanied by complete integrity of the muscular coat of the vessel wall. Variations in the depth of damage to the intima were attributable to the uneven distribution of the silver iodide grains in the surface layer of the emboli.

Thus according to the results of morphological investigations, least damage to the tissues accompanied by adequate radioopacity was provided by emboli containing 10% Iopagnost and 30% silver idoide. The depth of aseptic coagulation necrosis in the zone of contact of the embolus with soft tissues and the vessel wall was between 80 and 200 μ. Complete preservation of the muscular coat and partial preservation of the intima of the thin femoral artery of the rabbit suggest that emboli rendered opaque with 10% Iopagnost and 30% silver idoide are perfectly safe for clinical use. Since Iopagnost preserves its radioopaque properties for not more than 2 weeks, whereas emboli with silver iodide possess more prolonged radioopacity, preference must be awarded to emboli with silver iodide.

After the necessary toxicologic studies, hydrogen emboli rendered opaque with 30% silver iodide were used in clinical practice for endovascular occlusion of the renal artery and for preoperative preparation for liver operations. Investigations were conducted on three patients under observation for 1 to 30 days after endovascular occlusion. Their results were similar to those of the experimental study. Superficial necrosis of the intima with a mild leukocytic reaction, accompanied by complete preservation of the muscular coat and adventitia of the artery, were observed 1-3 days after endovascular occlusion (Fig. 2a). The tissues surrounding the artery at the site of the radioopaque emboli were intact. The same layers of the vascular wall still remained intact 1 month after endovascular occlusion (Fig. 2b), but some degree of atrophy was present. No leukocytic infiltration could be seen. The emboli contained silver iodide granules, but fewer than at the earlier times. Radioopacity was preserved.

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