CHEMOTHERAPY OF BRAIN TUMORS BY INTRA-ARTERIAL INFUSION

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Several recent reports have dealt with the treatment of malignant tumors of the brain by the isolation-perfusion method.\(^3\,7\,13\,14\) In a small number of patients with primary or metastatic malignancies of the brain, the administration of short-acting chemotherapeutic agents under normal or slightly increased body temperature has been shown to produce palliation for varying periods of time. The main advantage of the isolation-perfusion method is its ability to deliver a relatively large concentration of a drug to the brain without producing much systemic reaction. However, the equipment and preparation necessary for this type of therapy are elaborate, and the system requires the attention and supervision of a team of physicians.\(^10\,11\)

A method of chemotherapy which can be administered by individual physicians without elaborate equipment or a team of auxiliary help, but which provides equal or better therapeutic results than the isolation-perfusion method, forms the basis for this preliminary report.

TECHNIC

The technic, somewhat similar to that suggested by others,\(^12\) was developed by trial and error, and is now carried out as follows:

A No. 16 gauge Tuohy needle is introduced into the common carotid artery under local anesthesia and a carotid arteriogram is performed, using 8 cc. of a 50 per cent solution of sodium diatrizoate (Hypaque). This establishes a baseline from which the results of chemotherapy can be evaluated objectively by means of subsequent visualizations. A polyethylene (or Teflon) catheter about 12 in. long, passing through the lumen of the 16 gauge needle, is introduced into the artery and advanced to a point 1 in. above the bifurcation. The position of the tip of the plastic tube is determined by injecting 1 cc. of sodium diatrizoate through a blunt-tipped No. 20 needle fitted to the end of the catheter. To prevent clotting, the tube is flushed with a solution of heparin in saline every 2 min.

After satisfactory position of the tip of the plastic tube has been established, the outer No. 16 Tuohy needle is withdrawn. The inner tube is held steady to prevent its dislocation. Slight pressure is applied to the opening in the skin for a few minutes after removal of the needle to control the oozing of blood. Reflux of the blood in the plastic tube is prevented by injection of a heparin solution (1 mg. to 1 cc.) into the tube, with the aid of a three-way stopcock connected to the No. 20 needle threaded to the end of the plastic tube.

Frequent irrigations are not necessary, but it is advisable to flush the tube every 8 hrs. to maintain its patency. The plastic tube is anchored to the skin around the puncture hole with adhesive tape to prevent its dislodgement (Fig. 1). Sometimes it may be desirable to keep the patient under some degree of restraint to prevent him from pulling the tube out.

For the vertebral artery, a No. 17 Tuohy needle is inserted, and a proportionally smaller plastic tube is used. Occasionally, it may be necessary to introduce the catheter into the vertebral artery by surgical exploration rather than by the percutaneous approach. We have found it safer to delay chemotherapy for at least 12 hours after the arteriogram.

METHOD

In the cases to be described, an indwelling catheter was placed in the cerebral vessel to be infused. Previously reported attempts to infuse the cerebral vessels were made by injecting the chemotherapeutic agent through a needle.\(^4\,9\) The advantages of the
indwelling-catheter technic are obvious, because this intra-arterial catheter permits the use of fast-acting alkylating agents as well as slow-acting antimetabolites. In this series, the catheter in the cerebral vessel was left in place for as long as 6 weeks without any harmful effect.

The catheter is connected to a rubber tube which runs between the discs of a pump regulating the flow of the fluid coming from the intravenous bottle containing the chemotherapeutic agent. The pump (Fig. 2) costs less than $100, and requires only occasional attention during a 24-hour period. It runs continuously for weeks at a time. Since the discs of the pump are in contact only with the outer wall of the rubber tubing during its “milking” action, the sterility of the entire system is maintained. The rate of infusion can be varied from 1 cc. per min. to 1 cc. per hr. The type of chemotherapeutic agent and the condition of the patient should be considered in choosing the speed of the infusion.

MATERIAL

Intra-arterial-infusion therapy was administered to 12 patients with primary malignant brain tumors who had not responded to conventional methods of therapy.

Nitrogen mustard was chosen in preference to other short-acting alkylating agents because of the availability of an antidote. Six patients received nitrogen mustard at a rate of 5 to 10 mg. administered over a period of 30 min. Simultaneously with the intra-arterial infusion of nitrogen mustard, 100 mg. of sodium thiosulfate were given intravenously for each mg. of nitrogen-mustard solution, to protect the patient from the systemic toxicity of the nitrogen mustard. Sodium thiosulfate was prepared in 10 per cent solution from 1 gm. ampoules produced by the Eli Lilly Company. It was possible to prevent depression of the hematopoietic system by the use of sodium thiosulfate in patients receiving nitrogen mustard daily for 6 days. The administration of nitrogen mustard in doses larger than 5 mg. a day was accompanied by edema of the eyelids, protrusion of the eyeball, discoloration of the skin of the forehead, and edema of the brain, as was demonstrated in 1 case on postmortem examination.

Six other patients with glioma of the brain were given Methotrexate. This anti-metabolite, in daily doses of 12 to 14 mg. dissolved in 1200 to 1400 cc. of saline, was administered at a rate of 1 cc./min. The use of citrovorum factor as an antidote was delayed until mild symptoms of toxicity of the drug appeared. This usually occurred after 80 mg. of Methotrexate had been administered within a period of a week. The