

Perspectives and Commentaries

Interventional Radiology in Oncology

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INTRODUCTION

INTERVENTIONAL radiology is a growing field that employs modified diagnostic techniques for therapeutic treatment of specific diseases as an alternative or complement to medical or surgical therapy. Besides special techniques for drainage of fluid collections and stone removal, it includes therapeutic angiography which is basically used to increase regional blood flow, to reduce blood flow or for regional infusion of active drugs. As an example, a catheter used for the diagnosis of a renal lesion can be modified to dilate a stenosed arterial lumen; the same catheter can be the vehicle for occlusion agents or drug infusion.

In cancer treatment, applications of angiography include preoperative vessel occlusion to control blood loss during resection, palliation, control of pain and control of tumor related hemorrhage. Regional chemotherapy has limited application, and its efficacy remains controversial.

Transcatheter occlusion of a vessel is different from a surgical ligation. Embolization is distal and prevents collateral vessels from re-perfusing the lesion, whereas proximal ligation of an artery does not prevent re-perfusion by distal collaterals. Different methods for vessel occlusion are available and should be appropriately selected with respect to the desired effect and regional anatomy. Intravascular electrocoagulation has potential advantages such as precise localization of the occlusion and elimination of the need for foreign material [51]. In our experience, results are inconsistent, and the length of the procedure is prohibitive. All other techniques are based on the use of a diagnostic

catheter as a vector to introduce embolic material into the lesion. When only temporary occlusion is necessary, gelatin sponge (Gelfoam®, Spongel®) is the material of choice. Small pieces of material are soaked and suspended in saline or diluted contrast medium and are injected through the angiographic catheter into the artery to be embolized. One fragment is injected at a time while the blood flow is monitored by small injections of contrast medium. Special care must be taken to avoid reflux of the material and subsequent nontarget embolization. Ivalon-polyvinyl alcohol sponge particles of 250-600 µm can be used to obtain more peripheral and precise arterial occlusion [2, 3]. Since the Ivalon particles are nonabsorbable, the effect of arterial occlusion is more persistent than with Gelfoam. Absolute ethanol has been found to produce extensive coagulative tumor necrosis, and offers the advantage of shortening the embolizing procedure [4]. Material for occlusion of larger vessels includes steel-coil devices and detachable balloons [5]. Plastic polymers like isobutyl-2-cyanoacrylate (IBC-bucrylate) have the advantage of being introduced in the liquid state. They then polymerize when contact with blood occurs in the target organ [1]. The major problem with this material remains its potential carcinogenicity.

RENAL EMBOLIZATION

Preoperative embolization of renal cell carcinoma has become a routine practice and in some selected cases may be used as therapy for an unresectable tumor.

The first renal carcinoma embolization was reported in 1969 by Lalli [6]. Embolization is performed in hypervascular renal carcinoma to decrease the vascularity prior to resection [7]. The

embolization causes edema that increases the normal tissue planes, thereby facilitating nephrectomy, but there is no study determining whether transfusion requirements during surgery are reduced by embolization.

An improvement in survival rate due to an immunological response to necrotic tumoral tissue has been suggested by Wallace *et al.* [8, 9]. They have theorized that the necrotic renal tissue acts as an antigen initiating the development of appropriate antibodies, and they therefore recommend embolizing the renal tumor 4–7 days or more before surgery (the time interval required for the development of an adequate immunological response). This attractive theory has not been proven, and preoperative embolizations are generally performed 24–28 h before or immediately prior to surgery. Infarction resulting from embolization is responsible for the so-called postinfarction syndrome consisting of pain, fever and elevation of the white blood cell count. Nausea, vomiting and sometimes ileus have also been reported. These signs and symptoms which may be associated with the presence of gas in the embolized renal carcinoma as demonstrated on a CT scan are normal and should not be diagnosed as a renal abscess.

We prefer to perform an embolization immediately before surgery to avoid these problems. The choice of embolizing agent depends on the vascularization of the tumor. The use of alcohol is very effective in producing tumor necrosis [4, 10]. We generally use particulate Gelfoam or polyvinyl alcohol sponge (Ivalon) in conjunction with coils [11, 12]. These coils must be placed distally to avoid their displacement into the aorta during clamping of the renal artery. In very rare and selected cases embolization is performed as the primary form of therapy. It may also be very successfully employed for palliative management of hematuria secondary to nonresectable tumors.

HEPATIC TUMORS

Embolization has been used for the management of liver tumors of varied histology, and is generally used for treating unresectable hepatic neoplasms. Patients with primary or metastatic lesions have recently undergone embolization with added chemotherapy with very good results [13–17].

Although the treatment of choice of hepatoma remains hepatectomy, in unresectable tumors, hepatic artery embolization appears to be one of the most effective treatments [13, 14, 18–21].

Since a hepatic tumor is supplied with blood exclusively from arteries, arterial embolization would seem to be an effective treatment for such tumors. Devascularization of hepatic neoplasms is generally achieved using both Gelfoam particles or Ivalon and coils. Embolization achieved a

reduction in tumor bulk in 70–80% of hepatomas and alleviated local symptoms in 80% [18]. The reported cumulative 1-year survival rate is 45% [20].

Liver metastases of colorectal carcinoma were also treated by embolization in selected cases. The indications were unresectable tumors, no other possible effective treatment and failure of arterial or intravenous chemotherapy and radiation therapy [17, 21]. Patients with certain metastatic endocrine tumors are among those who clearly benefit from therapeutic embolization. Hepatic embolization is the treatment of choice for symptoms of the carcinoid syndrome resistant to medical treatment [22, 23].

A post-infarction syndrome develops almost invariably after embolization and is associated with pain, fever, nausea and vomiting. These effects usually persist for 3–7 days and must be treated symptomatically. Sequential segmental arterial occlusions minimize the symptoms. Cirrhosis, portal vein and biliary tract obstruction, and extensive metastatic disease are only relative contraindications to hepatic artery embolization. Abscess formation following hepatic embolization is very rare, and the hepatorenal complications can be minimized by careful monitoring of fluids and electrolytes.

BONE TUMORS

Embolization has been used as a method of decreasing intraoperative blood loss as well as for palliation of unresectable malignant bone tumors [24–26]. Clinical applications include palliation of pain resulting from metastases of renal cell carcinoma or from tumors of the pelvic bones [27–32].

Most of the observations described were carried out on metastases of renal cell carcinoma. The survival rate after embolization varies, depending on the series, from 8 to 10 months [24–26]. Some bone tumors of other origin have also been embolized: sarcoma, and metastases of thyroid, uterine, colorectal and prostatic origin.

In all cases, a spectacular reduction of pain has been reported as well as an improvement of the general status. Cases of reduction of tumor volume and bone recalcification have been described [31]. The antalgic effect results from the reduction of the vascularization and of the size of the lesion, thereby decreasing the distention of the periosteum.

Our own experience includes preoperative embolization of various pathological fractures, which we performed by injecting Gelfoam particles a few hours before surgery. This procedure significantly reduced blood loss during surgery allowing orthopedic treatment of some very extensive and hypervascularized lesions.

MISCELLANEOUS APPLICATIONS

Embolization has been used for treatment of malignancies of pelvic genitourinary organs [33–35]. Pelvic embolization is an effective method of controlling persistent hematuria in advanced malignancies of the bladder.

Transcatheter occlusion has also been employed for gynecological tumors [36, 37], central nervous system tumors [38, 39], retroperitoneal tumors, hemoptysis in lung cancer, etc.

INTRA-ARTERIAL CHEMOTHERAPY

Arterial infusion is not a new procedure in cancer chemotherapy, as it was first reported in 1950 by Klopp *et al.* and Bierman *et al.* [40, 41].

This technique has been utilized in a wide variety of malignancies. The advantages of intra-arterial chemotherapy can be attributed to a higher concentration of drug delivery in the target organ combined with higher local peak concentration. The total dose may thus be reduced, which results in lower systemic toxicity. A catheter is generally left in the vessel supplying the tumor and sequential infusion chemotherapy is performed.

Various groups using numerous protocols and drugs have treated patients with unresectable liver tumors or after surgery. The combination of intra-arterial chemotherapy with embolization has also been described [13–16]. At present, infusion therapy is generally performed through an implantable pump with arterial or portal vein infusion.

The liver is one of the organs most frequently involved by metastases, and hepatic intra-arterial chemotherapy has also been used as a palliative method of treating inoperable metastases [15–17]. Here again the major problem of infusion chemotherapy remains the long-term patency of the catheter, its stability and the risk of thrombosis of the infused arteries [42]. Displacement of the catheter can lead to infusion in nontarget organs such as the gastric artery, with subsequent toxic gastritis [43, 49].

In addition to embolization some authors have advocated the use of intra-arterial chemoembolization. Administration of the capsules intra-arterially into the vascular bed of tumors causes trapping within the tumor vasculature and subsequent sustained release of the drug [17, 45].

The bladder derives its blood supply from the

internal iliac arteries, which are relatively easy, except in atherosclerotic patients, to catheterize. Generally, infusion chemotherapy was used as an adjuvant therapy and was performed prior to or after surgery [46, 47]. We have treated 20 patients with previously untreated invasive transitional cell carcinoma by bilateral injection of Adriamycin® in the internal iliac arteries. A total of 160 mg of Adriamycin® was injected, with the procedure repeated one month later. Only 10 patients received two full courses of chemotherapy. We were unable to give chemotherapy to four elderly atherosclerotic patients, and six patients received partial treatment because it was impossible to catheterize their arteries on both sides or because a second infusion was not possible. Among the 10 evaluable patients who received complete treatment, there were four complete responses and one partial response. All responders remained free of disease after a follow-up period of 14–27 months. The patients who experienced only partial response still had carcinoma *in situ* at the first follow-up cystoscopy plus biopsy, and no further spread of tumor.

Various reports of regional chemotherapy as treatment for head and neck tumors, pelvic neoplasms and gastric carcinoma have appeared [48–50].

Many controversies concerning indications and results of intra-arterial chemotherapy remain and much research is needed to determine the best chemotherapeutic agents or combinations to be used, to determine the optimal number of courses, to improve patient selection and to overcome various technical problems.

CONCLUSION

Although transcatheter management of tumors offers several theoretical advantages its clinical usefulness has not been convincingly demonstrated. Embolization of unresectable or metastatic neoplasms must be considered as an adjunct therapy that might improve quality of life. For some complications of neoplasms like hemorrhage embolization remains the best treatment. Regional infusion chemotherapy is currently limited to selected cases of hepatic and pelvic tumors, and its efficacy still remains controversial.

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