

ARTERIOGRAPHY DURING EX VIVO RENAL PERFUSION*

A complication

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ABSTRACT—A case of bilateral renal-cell carcinoma unsuccessfully treated with bench surgery is reported. The reason for failure was apparently the toxicity of the contrast media used during the ex vivo arteriographic studies.

In a recent publication we discussed the advantages of a method of renal autotransplantation by which a kidney could be removed, perfused under hypothermia, studied angiographically, and have its structures dissected and repaired before finally revascularized heteropically as an autotransplant.¹ The possibility was discussed of applying the same techniques for special indications, such as malignant disease in a solitary kidney, advanced staghorn calculus disease, renal trauma, or lesions of the ureter, to mention only four examples.^{2,3}

A patient suffering from Lindau-von Hippel disease with carcinoma of both kidneys has since been surgically treated in attempts to partially resect first the right and then the left kidney by autotransplant. Both autografts were lost due to arterial thrombosis probably because of an unsuitable contrast medium used during ex vivo arteriographic studies. The case is reported here, with special emphasis on the choice of contrast medium under conditions of hypothermic ex vivo perfusion.

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Case Report

In December, 1972, a forty-five-year-old man was proved by excretion urography and renal arteriography to have bilateral multicentric renal-cell carcinoma and simple cysts (Figs. 1 and 2). There was a family history of Lindau-von Hippel disease, with one brother currently under treatment for renal-cell carcinoma and 2 other siblings possibly having died of the disease. No metastases were detectable. Kidney function was normal, with a blood urea nitrogen level of 12 mg. and serum creatinine 1.1 mg. per 100 ml.

The patient's right kidney was removed on February 23, 1973, through a flank incision with maximum length of the renal vessels and ureter.^{1,4} The upper pole was expanded by both a large cyst and carcinoma which showed no sign of capsular invasion. The kidney was flushed with a cold, balanced electrolyte solution containing low molecular dextran and heparin (Perfudex) and connected to a Belzer-type kidney perfusion machine† by the two renal arteries (Fig. 3A). The perfusate consisted of cold (7°C.) deflocculated homologous plasma.

†Manufactured by Waters Instruments, Inc., Rochester, Minnesota.

FIGURE 1. Preoperative aortogram showing right kidney vascularized by 2 renal arteries, both supply upper- and lower-pole carcinomas (arrows). Left kidney also contains 2 carcinomas (arrows). Both organs contain multiple small cysts.

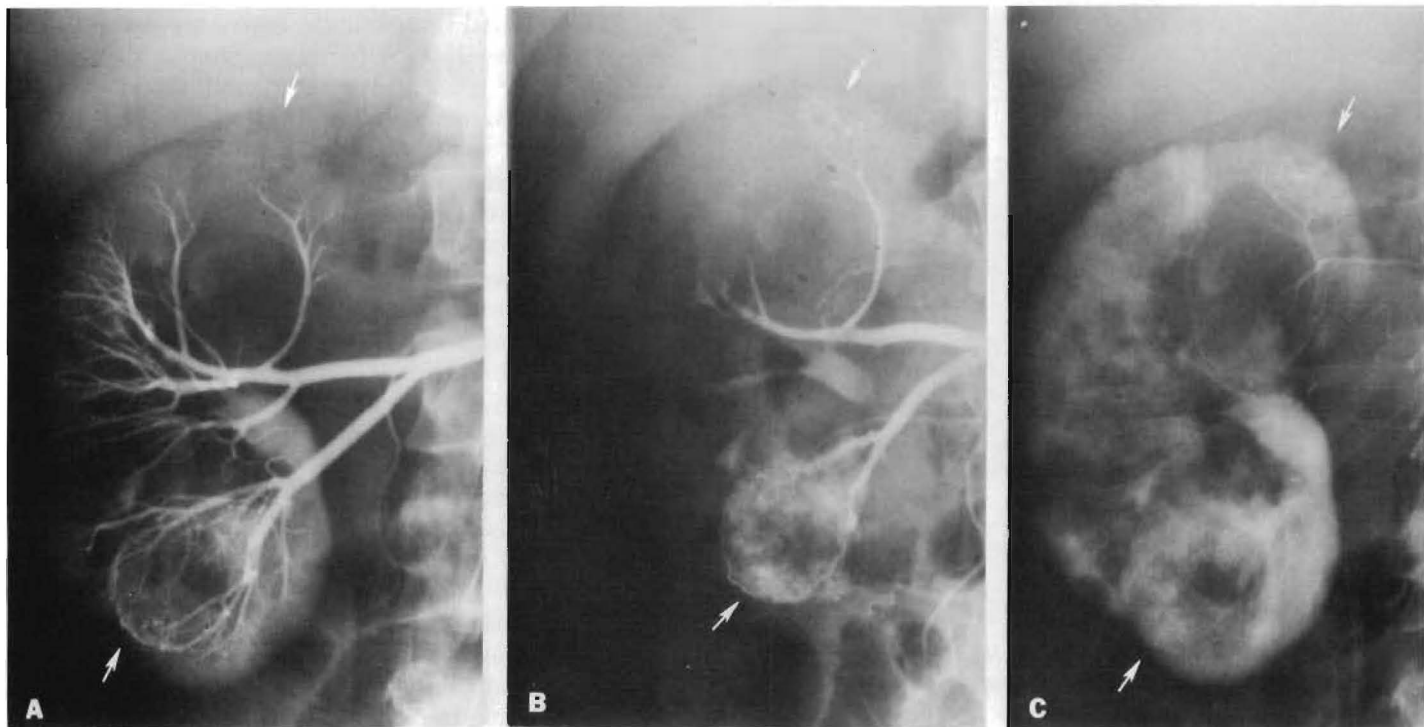


FIGURE 2. Preoperative selective arteriogram with injection of right large lower renal artery: (A) early arterial phase, (B) after epinephrine injection, and (C) nephrogram phase (lesions shown by arrows).

The vascular anatomy of the extracorporeal kidney was then thoroughly studied with arteriograms following the technique which has been described in a previous publication.¹ However, whereas the contrast medium used in the previous reported cases had been 60% meglumine iothalamate (Conray-60), in this case 50% sodium

diatrizoate (Hypaque sodium 50%) was used (total 25 ml.). The kidney was flushed with the perfusate after every arteriogram, and the venous effluent was discarded to avoid recycling of the contrast medium. The carcinoma in the upper pole was supplied by two segmental arteries, one arising from each of the two renal arteries, while

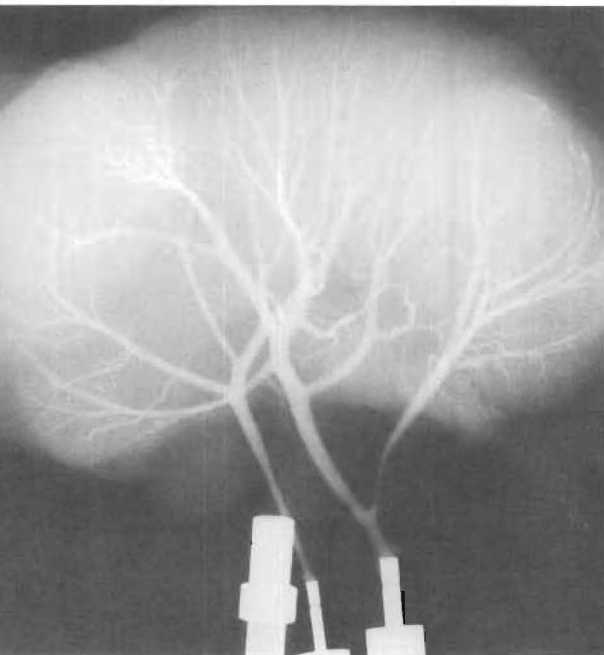
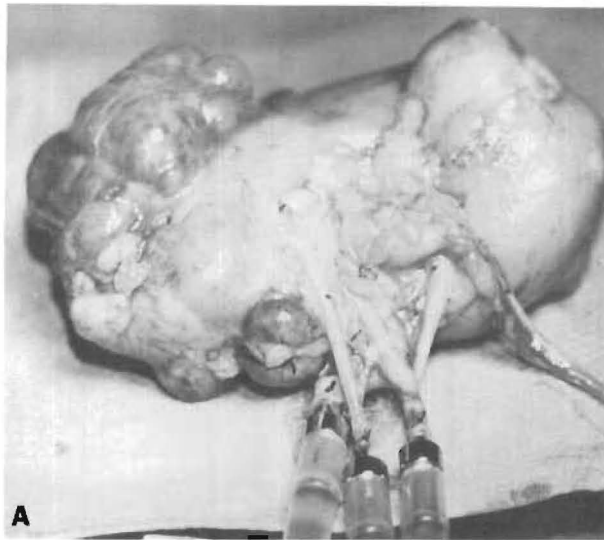


FIGURE 3. Right kidney (A) under hypothermic perfusion, both carcinomas and multiple cysts visible; (B) arteriogram during *ex vivo* perfusion showing double arterial supply and its relationship to tumors.

two segmental arteries, both arising from the lowest of the two renal arteries, supplied the tumor in the lower pole (Fig. 3B).

The branches supplying the upper-pole carcinoma were ligated and injected distally with methylene-blue dye. The upper pole was resected. The same procedure was followed in the lower pole (Fig. 4A). During this time the perfusion of the organ was intermittently interrupted to avoid excessive perfusate leakage through the cut parenchyma. The perfusate leaks were controlled, and two major calices were

ligated. A final arteriogram with the same contrast medium confirmed the good vascularization and the absence of tumor in the remnant of the kidney (Fig. 4B). Gross examination of the resected poles showed that both carcinomas were well circumscribed, and that the resection had been carried out at a reasonable distance from them. The resected kidney tissue weighed 70 Gm. Histologic examination confirmed the diagnosis of multicentric renal-cell carcinoma.

The patient's flank incision was closed. He was placed in a supine position, and an anterior lower abdominal incision was made on the left as is done in a kidney homotransplantation.⁴ The renal vein anastomosis was performed end-to-side to the external iliac vein. The main trunk of the hypogastric artery was anastomosed end-to-end to the large lower renal artery, and the smaller superior renal artery was anastomosed to a segmental branch of the lower renal artery. The kidney remnant was revascularized after a cold ischemic time of five hours and seven minutes. The autograft turned pink, but after a few minutes became slightly bluish and soft. No explanation was found for this abnormality. The procedure was completed by a classical ureteroneocystostomy.

Postoperatively, Mercury-197 renal scan performed on the second postoperative day showed decreased isotope accumulation in the autograft. On the eighth day, there was no uptake at all. The kidney was removed and was found to be completely infarcted. The main arteries had a few organized thrombi, and the vein was completely thrombosed with extension to the iliac as well as the femoral vein. No obvious surgical mistakes were discovered, but it was assumed that one had been committed. No residual carcinoma was identified.

One month later, the same procedure was performed on the left kidney. At the end of the *ex vivo* dissection of the organ and removal of both poles, about 50 per cent of the original kidney was left without residual renal-cell carcinoma. This was vascularized by a single renal artery. As with the other kidney, *ex vivo* arteriograms were performed with 50% sodium diatrizoate but in addition, also with 66% meglumine and 10% sodium diatrizoate (Renografin 76) totaling 25 cc. The autograft was placed in the right iliac fossa, anastomosing the renal artery end-to-end to the hypogastric artery and renal vein end-to-side to the external iliac vein after six and one-half hours of cold ischemia. The phenomenon previously described occurred—the graft turned pink for a few minutes and then became bluish and soft.

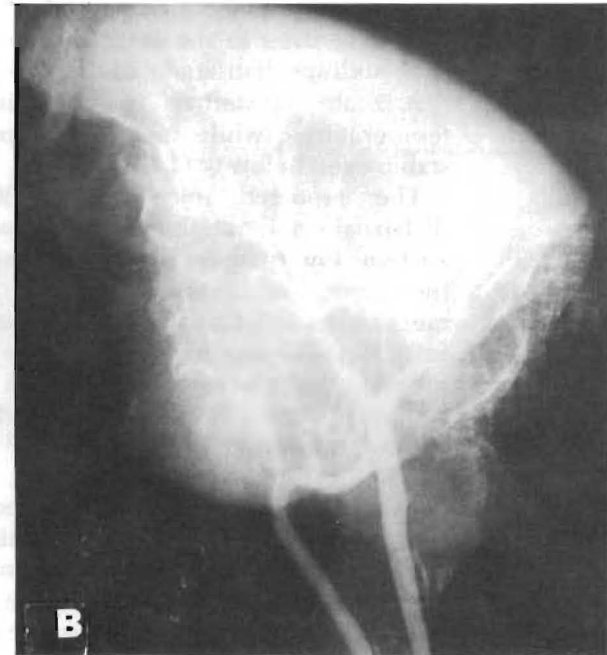
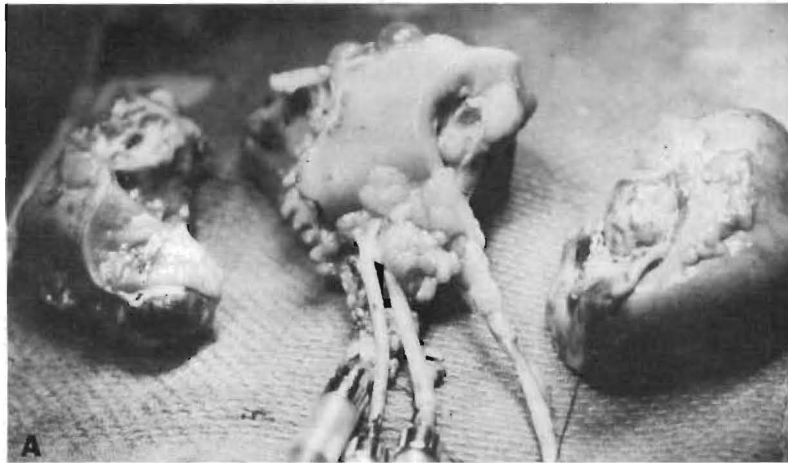


FIGURE 4. (A) Resected carcinomas after definition of vascularization by injection of methylene blue dye; remnant of one third of right kidney ready for autotransplantation. (B) Final arteriogram during *ex vivo* perfusion after resection of tumors.

It was removed after a one-half-hour observation period during which intra-arterial injections of papaverin and procaine were attempted without success. The anastomoses were perfect, but there were widely distributed fresh clots in the secondary and tertiary arterial branches.

Histologic examination of the specimen confirmed the presence in the large arteries of aggregated fibrin, platelets, and erythrocytes with extensive thrombosis in the smaller arteries. There was no residual renal-cell carcinoma. The patient is now on chronic hemodialysis awaiting kidney transplantation.

Comment

In this case, there were no preoperative signs of extrarenal malignant disease. Para-aortic lymph nodes and perinephric fat removed during the surgical procedure were carefully examined and found to be free of tumor. Finally, no residual cancer was identified in both removed autografts. Consequently, the patient should have been a good candidate for the proposed partial kidney resection(s).

After the first unsuccessful kidney autotransplantation in this patient, the loss of the organ was assumed to be due to some unrecognized technical mistake. However, the failure of the second autograft for similarly inexplicable reasons prompted special inquiries of both a prospective and retrospective nature. Slight hypocoagulability of intraoperative blood samples was found. No cold agglutinins were

detected in the serum. Results of skin tests with the three contrast media previously used were negative.

The perfusate used was homologous deflocculated plasma processed in exactly the same way as in the past.⁵ The blood type of the plasma donor and the patient were the same. The perfusion had been carried out at 7° to 10°C. as is done routinely in kidney preservation for transplantation purposes. The ischemia time was shorter than in most of our preserved cadaveric kidney transplants

It was suspected that the contrast medium could have been responsible. In this case, instead of using 60% meglumine iothalamate,¹ 50% sodium diatrizoate, and 66% meglumine and 10% sodium diatrizoate were administered.

All of these contrast media are used regularly for various forms of arteriography *in vivo*. They are all triiodinated derivatives of benzoic acid, prepared in hyperosmolar solution. This hyperosmolarity is responsible for much of the toxicity of these drugs.⁶ *In vivo* and *in vitro*, at high concentrations, they produce crenation of red cells, hemolysis, and red-cell agglutination.⁷⁻⁹ Coagulation factors are disturbed by an increase in thrombin time, interference with polymerization of the fibrin monomers, and decrease in factor V.^{8,9} They are known to damage the vascular endothelium^{10,12} and, if crenation of red cells occurs, the vascular resistance may increase.¹³ Many of these toxic effects seem to be less prominent with the preparations which contain the meglumine cation instead of sodium.⁶ In the

present context, the most important difference is that, according to the manufacturer's literature, 50% sodium diatrizoate and meglumine sodium diatrizoate crystallize or precipitate at low temperatures, while meglumine iothalamate is stable even below 0°C.

The repeated injections of 50% sodium diatrizoate and meglumine and sodium diatrizoate at low temperatures were suspected to be the cause of autograft losses. Since 60% meglumine iothalamate had been used successfully in past cases under otherwise similar conditions, the gravest doubts were only about sodium diatrizoate and were entertained about meglumine and sodium diatrizoate.¹

To test the toxicity hypothesis, 12 mongrel dogs' kidneys were autotransplanted after being cooled to 4°C. by the infusion of chilled lactated Ringer's solution. Then 50% sodium diatrizoate, meglumine and sodium diatrizoate, and meglumine iothalamate were injected intra-arterially in doses of 20 to 30 ml.

With all 3 contrast media, the kidneys turned bluish and remained soft after revascularization if they were not washed after the injection. This finding was less striking for the organs treated with 60% meglumine iothalamate. None of the dogs receiving kidneys so treated were able to survive.

On the other hand, if the kidneys were carefully washed with lactate Ringer's solution immediately after injection of the contrast medium, as suggested by Alfidi and Magnusson,¹⁴ the organs were temporarily cyanotic after autotransplantation, but they were able to sustain the animal's life after revascularization. Again, the best results were obtained with 60% meglumine iothalamate in that the transient cyanosis was both less intense and of shorter duration.

From these studies, it was concluded that the choice of contrast medium for ex vivo renal

arteriography under conditions of hypothermia is critical, and that the best agent under these circumstances is meglumine iothalamate. Whatever the contrast medium, it should be thoroughly and immediately washed out with electrolyte solution.

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