patients with the Zollinger–Ellison syndrome, though it was reported to be effective by itself in a single patient[10] and in combination with fluorouracil in one series of patients.[11]

In 1976 two reports[1,2] were published on the successful use of streptozotocin in the treatment of malignant gastrinoma by direct intra-arterial injection through the celiac axis: prolonged clinical remissions and marked reductions in size and number of metastases occurred. Significant side effects were few and consisted of nausea, vomiting, mild hypoglycemia and a mild transient increase in the levels of serum transaminases. No significant nephrotoxic effects were encountered.

In this paper we have described another case in which remission of metastatic malignant gastrinoma was induced by the intra-arterial use of streptozotocin. A decline in the serum gastrin level to normal was associated with a clinical remission that lasted more than 2 years, and a rise in the gastrin level preceded clinical deterioration by more than 6 months. Therefore, serial determination of this level can be useful in predicting the course of malignant gastrinoma and thus in planning its management.

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Resolution of massive renal artery thromboembolism with conservative therapy

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The clinical diagnosis of renal artery thromboembolism remains difficult in spite of the availability of new radioisotope techniques and improved angiographic procedures. Furthermore, firm therapeutic guidelines for established cases, even when the thromboembolism is massive, are lacking. There is, however, increasing documentation for the efficacy of various forms of nonsurgical treatment, including systemic administration of anticoagulants,[1] direct intra-arterial infusion of heparin,[2] papaverine[2] or fibrinolytic agents,[3] transcatheter thromboembolectomy[4] and supportive care only.[5]

In this report we describe a patient with angiographically proven complete occlusion of the main renal artery in whom systemic anticoagulant therapy was begun 10 days after the vascular accident and in whom the thrombus completely resolved.

Case report

A 63-year-old man was first seen because of bilateral leg pain. He had suffered a myocardial infarction 3 years earlier, followed by recurrent tachyarrhythmias, usually paroxysmal atrial flutter or fibrillation. Angiography showed multiple obstructions in both femoral arteries but patency of the renal arteries (Fig. 1A). His renal function was normal. He underwent bilateral femoral embolectomies and began taking anticoagulants orally.

One year later the patient was transferred to our institution with a 10-day history of epigastric pain, nausea and vomiting. He had been oliguric for several days but was not when transferred.

His temperature was 38.2°C and he had atrial fibrillation, with a ventricular rate of 108 beats/min. His blood pressure was normal, there was no evidence of congestive heart failure, and the peripheral pulses were palpable. The only other abnormality revealed by physical examination was marked tenderness of the right costovertebral angle.

The blood leukocyte count was 13.9×10^9/l, the blood urea nitrogen level 22 mg/dl (urea level 7.9 mmol/l), the serum creatinine level 2.7 mg/dl (239 μmol/l) and the

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creatinine clearance 36 ml/min. The urine contained a trace of protein, and the sediment eight leukocytes and two erythrocytes per high power field; no pathogens were cultured from a specimen. The serum lactic dehydrogenase level was very high, 498 IU/l; the serum levels of alkaline phosphatase and glutamic oxaloacetic transaminase were moderately raised, at 90 and 88 IU/l respectively. The prothrombin time was 12.8 seconds (control time 11.0 seconds). An echocardiogram revealed no abnormalities.

An intravenous pyelogram revealed a nonfunctioning right kidney, and a renal scan showed severe impairment of perfusion of that kidney. A right retrograde pyelogram was normal. Angiography localized the vascular obstruction to the point of origin of the right renal artery from the aorta (Fig. 1B). We tried to catheterize the artery for local infusion of a thrombolytic agent,[3,6,7] but the clot completely occluded the vessel at its point of origin.

After surgical consultation, and considering the long interval before the embolism was diagnosed, we decided to institute intravenous heparin therapy: 4000 IU was administered every 4 hours for 10 days. Thereafter, oral anticoagulant therapy was given again. The patient's clinical condition improved steadily, with abatement of the fever, resolution of the flank pain and disappearance of the gastrointestinal symptoms. An angiogram obtained 3 weeks later demonstrated recanalization of the renal artery (Figs. 1C and 2); by this time the serum lactic dehydrogenase level had returned to normal, the abnormalities of the urinary sediment had cleared and the serum creatinine level had fallen to 2.1 mg/dl (186 μmol/l).

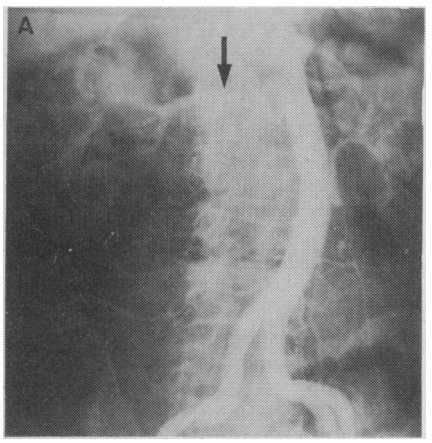

FIG. 1A—Good visualization of right renal artery (arrow) before embolic episode.

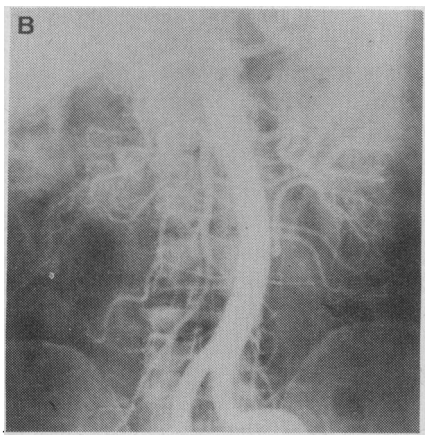

FIG. 1B—Complete occlusion of same vessel at its aortic origin shortly after thromboembolism.

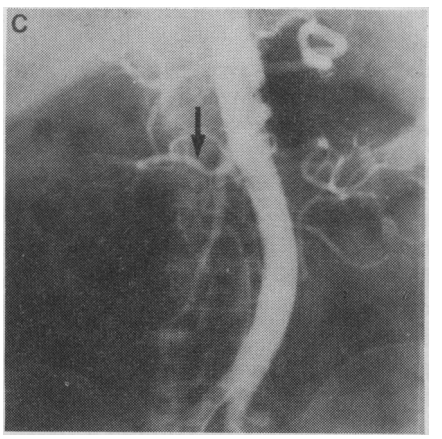

FIG. 1C—Recanalization of same artery (arrow) 3 weeks later, following systemic anticoagulant therapy.

Discussion

Numerous reports have indicated that conservative — that is, noninvasive — treatment of renal thromboembolism results in satisfactory recanalization of the obstructed vessel.[1,2,8-10] In one study that attempted to compare surgical and medical treatment of renal thromboembolism through an analysis of the literature, medical treatment was found to be associated with a lower patient mortality (13%) and a higher rate of kidney salvage (77%).[11] In a more recent review of 16 cases of renal artery embolism managed conservatively (embolectomy was performed in an additional case) it was noted that 12 patients had received systemic anticoagulant therapy; 2 died of other problems, but the 10 who survived, including the 3 survivors with bilateral emboli, either maintained or regained adequate renal function, although 3 (2 with bilateral emboli and 1 with a unilateral embolus) required dialysis for a short time.[12]

Although some of the surgical literature has stressed early and aggressive surgical approaches to renal artery embolism,[13] other papers have pointed to the often disappointing outcome of surgery and the fact that a return to normal renal function is rare, even after early surgical intervention.[14] There have been several reports of cases in which surgery has reversed anuria and azotemia secondary to massive renal arterial obstruction as late as 6 weeks after the event;[15] however, in at least an equal number of cases renal function has returned to normal after supportive care only.[16]

The reasons for the favourable outcome of conservative management are not completely clear, but the presence of collateral blood vessels and the activation of fibrinolytic systems may be contributing factors.

After renal artery embolism, blood usually continues to flow to

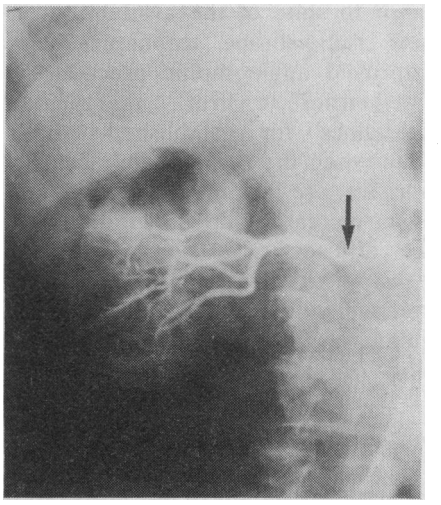

FIG. 2—Selective right renal arteriogram, obtained after abdominal aortogram depicted in Fig. 1C, showing mild segmental stenosis in proximal third of vessel (arrow).

the renal parenchyma for two reasons: (a) there may be flow around the embolus, as is often demonstrated by angiography; and (b) in response to the occlusion, capsular, peripelvic and periureteric collateral vessels immediately begin to perfuse the kidney.[17]

In vivo fibrinolysis is controlled by an enzymatic process that involves the conversion of an enzyme precursor (plasminogen) into a proteolytic enzyme (plasmin), a reaction mediated by activators found in blood vessels, other body tissues and, in small quantities, the circulating blood.[18,19] Upon release from arterial endothelial cells, such factors may locally activate plasminogen, which is known to be in contact with the fibrils of fibrin within the clot.[20] The activation of these fibrinolytic systems is well illustrated by the recent use of selective renal artery embolization of autologous clot to control renal hemorrhage. Such clots have spontaneously resolved, sometimes within hours after their introduction into the arterial tree.[21,22] Experiments in animals have confirmed the return of renal perfusion,[23,24] even after the injection of a massive clot.[25]

Our case demonstrates that there is a place for conservative management, even in massive renal artery thromboembolism, particularly when underlying medical problems increase the risks of surgery. The most appropriate form of medical therapy, however, remains to be defined. It may well be that spontaneous physiologic revascularization of the arterial tree is the most important factor underlying the success of conservative treatment, with heparin merely preventing further clot formation. The role of systemic or local use of fibrinolytic agents in the treatment of renal artery thromboembolism has not been well studied, but the use of these agents may prove to expedite the normal mechanisms for clot resorption.

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