AJH 2001; 14:831–834

Case Report

Treatment of Atheroembolization With Corticosteroids

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Aortic atheroembolization is a feared complication of invasive procedures such as arteriography, often leading to devastating complications including renal insufficiency. To date, even in cases with evolving renal failure, there is no recommended treatment. This case report describes the successful treatment with corticosteroids of a patient with deteriorating renal function after renal arteriography and angioplasty, resulting in rapid and sustained improvement in renal function. The implications of this observation are discussed. Am J Hypertens 2001;14:831–834 © 2001 American Journal of Hypertension, Ltd.

Key Words: Atheroemboli, renal artery stenosis, atherosclerosis, renal failure, renal angioplasty.

Although iodinated contrast nephropathy is a widely recognized complication of arteriography, a less frequently considered but much more feared and damaging complication is cholesterol embolization, also called atheroembolization. Although it may occur spontaneously, it is seen more frequently after manipulation in the aorta during arteriographic and interventional procedures, and is associated with complications including renal insufficiency, ischemia of the intestinal tract, and peripheral vascular insufficiency with claudication, digital pain, or gangrene.

The process is self-limited in some, but progressive in other patients, often leading inexorably to renal failure. A high mortality rate has also been reported.[1–3] Yet, despite the serious prognosis and regardless of the severity of the individual case, there is no recommended treatment beyond avoidance of unnecessary invasive vascular procedures, and discontinuation of anticoagulants, which actually aggravate the condition.[4]

Case reports have suggested that treatment with corticosteroids might be of value in managing the disorder.[2,5] The rationale for this intervention is the amelioration of the inflammatory reaction that occurs at the site of embolization in distal arteries, allowing host mechanisms to ultimately clear the microemboli and avoid progressive and irreversible ischemia.

In this case report, the successful treatment with corticosteroids of a patient with manifestations of atheroemboli is reported. The case offers hope that treatment with corticosteroids early in the course of atheroembolization can be of value in preventing irreversible ischemic manifestations.

Case Report

The patient, a white man, initially presented in 1993, at the age of 73 years, with recent onset hypertension, headache, shortness of breath, and edema. He was a nonsmoker, and had a serum cholesterol 215 mg/dL, with an HDL cholesterol of 65 mg/dL. Serum creatinine was 1.1 mg/dL.

Renal arteriography, performed at another institution, revealed a 99% ostial right renal artery stenosis; angioplasty was attempted unsuccessfully. Successful angioplasty, with stenting, was then performed at this institution and resulted in elimination of edema and shortness of breath. A 50% stenosis of the left renal artery was also noted but intervention was not believed indicated. The patient's blood pressure (BP) decreased from 190/100 mm Hg to 150/70 mm Hg after the procedure. The serum creatinine was 1.1 mg/dL.

In 1996, hypertension recurred and a renal scan now revealed reduced function in the left kidney (29% uptake *v* 71% in the right kidney) with delayed excretion. Left renal function deteriorated further on repeat scan with captopril. The serum creatinine was 2.0 mg/dL. There were no cardiovascular symptoms. On finasteride (5 mg), terazosin (2 mg), and amlodipine (5 mg), the patient's BP was 170/90 mm Hg. Arteriography revealed a tight left renal artery stenosis and left renal artery angioplasty, without stenting, was performed without complications. The stented right renal artery was noted to be widely patent. Blood pressure returned to normal and serum creatinine decreased to 1.6 mg/dL.

In November 1999, the patient's BP had increased from 110–140/70 mm Hg to 180/105 mm Hg. The patient was

Received November 30, 2000. Accepted December 19, 2000.

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0895-7061/01/$20.00
PII S0895-7061(01)02183-5

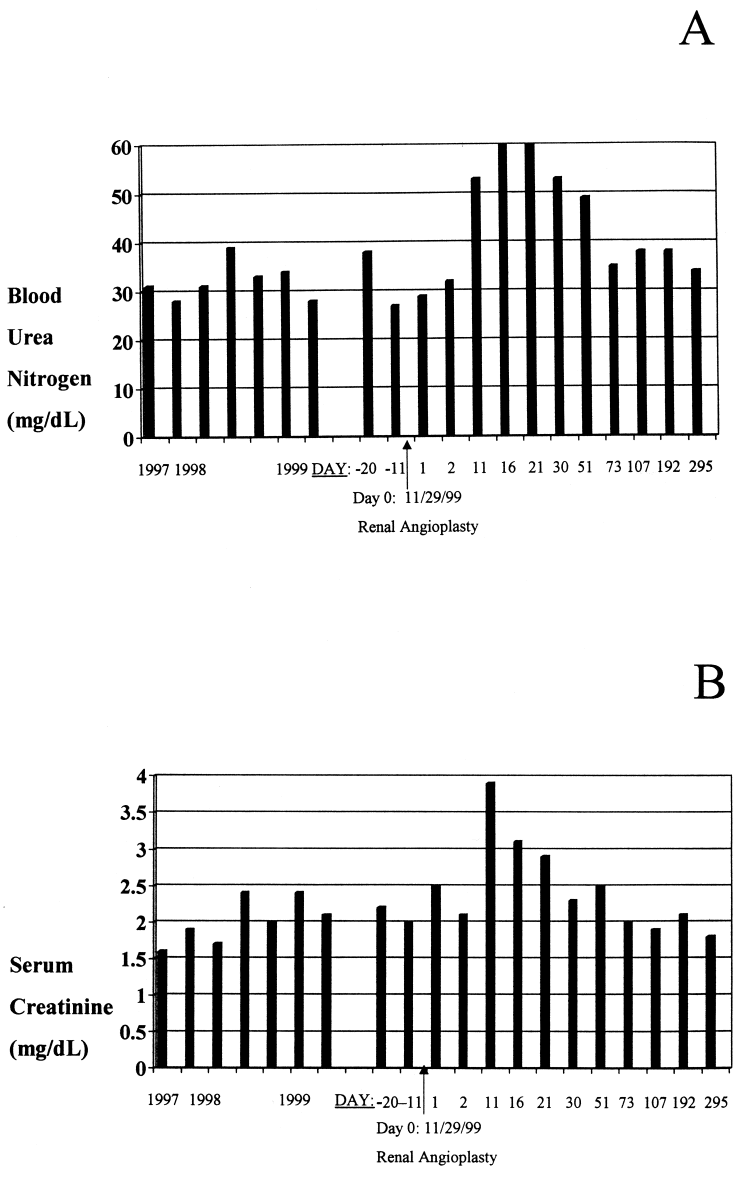

FIG. 1. Blood urea nitrogen level (**A**) and serum creatinine level (**B**) before and after renal angioplasty.

taking 7 mg daily of terazosin and was asymptomatic except for chronic nocturia. The serum creatinine had been in the range of 2 mg/dL (Fig. 1).

Repeat arteriography on November 29, 1999, revealed bilateral renal artery stenosis, with a 100 mm Hg and 60 mm Hg gradient in the right and left renal artery, respectively. Atheromatous lesions were noted in the abdominal aorta. Bilateral angioplasty, with stenting of the left renal artery, was performed without difficulty or complication. The serum creatinine increased to 2.5 mg/dL the day after the procedure, and returned to 2.1 mg/dL the next day (Fig. 1).

On revisit on December 10, 1999, the patient complained of new bilateral two block calf claudication and a slightly diminished appetite. On examination, the BP was 150/90 mm Hg. A petechial rash was noted on the dorsum of both feet. The serum creatinine was 3.9 mg/dL and the blood urea nitrogen (BUN) was 53 (Fig. 1). There was 6% eosinophilia, and the sedimentation rate was 6 (normal).

Because of the new claudication, petechial rash of the feet, marked increase in serum creatinine, and eosinophilia, a presumptive diagnosis of atheroembolization was made. Given the marked and rapid increase in serum creatinine, the high risk of progressive renal failure, and the absence of any proven effective therapy, the decision was made to offer the patient a trial of oral prednisone therapy, and a daily dose of 50 mg was prescribed.

The patient was seen 5 days later and reported improvement in the claudication and appetite. He complained of persisting pain in the sole of his left foot, where an ecchymotic lesion was noted. His BP was 146/90 mm Hg. The pedal rash was slightly improved. The serum creatinine had fallen to 3.2. The BUN was 60. Amlodipine (5 mg daily) was added to the terazosin.

The prednisone was continued and slowly tapered as summarized in Fig. 1. The petechial rash, claudication, and pain on the sole of his foot all resolved. Pain in the first digit of the left foot resolved over a period of 2 months. The BP remained 115/70 mm Hg and the amlodipine was stopped.

One year after the angioplasty, the patient remains asymptomatic with a BP of 135/80 mm Hg, a serum creatinine of 1.8 mg/dL, and a BUN of 34 mg/dL.

Discussion

The atheromatous aorta is ulcerated, crystal-laden or lined by friable atheromatous debris.[2] The risk of atheroemboli increases in proportion to the severity of the atherosclerosis.[6] Macroemboli may arise from thrombus originating in atheromatous ulcers, or from dislodgement of atheromatous plaque.[2] Microemboli are platelet–fibrin emboli or cholesterol crystals.[2] Interstitial inflammation and generalized vasculitis have been postulated to occur,[3] with large crystals surrounded by neutrophils, eosinophiles, macrophages, and platelets, and small crystals engulfed by macrophages.[1] By 2 to 4 weeks, crystals are embedded in multinucleated giant cells and smooth muscle cells. At 1 to 2 months crystals may become extruded out of the vessel lumen and buried in the adventitia, or remain in the lumen embedded within organized thrombus that may recanalize.[1] Crystals have been shown to persist for up to 9 months.[7]

Arterial lumina are eventually occluded by accumulation of cells and other material.[6] In the kidney, atheroembolization leads to ischemia in glomeruli, ultimately with hyalinization and sclerosis, and interstitial fibrosis.[6]

The natural history of this atheroembolic process is characterized by considerable morbidity and mortality. In one review, 179 of 221 patients had a fatal outcome.[3] Even excluding cases from pathologic series, the survival rate was only 27%.[3] In another review of 52 patients with creatinine increase attributable to biopsy-documented atheroemboli, 33 (63%) eventually required hemodialysis, and 38 (73%) died within 6 months.[1] Six patients experienced improvement in renal function after a period of 42 to 122 days.[1] Another review of 22 patients reported elevation in serum creatinine in 14, with 8 progressing to dialysis, and 6 ultimately experienced improvement in their renal function.[2] One patient was able to discontinue hemodialysis.[2] Fourteen of the 22 died.[2] Another review reported that 80% of patients with the disorder progress to renal failure.[8]

It is likely that reported cases are biased in terms of selection of more severe patients. Suggestive of this, in one small series of 6 patients, renal function improved in 5.[9] However, even in this report, renal function failed to return to its baseline level in 5 of the 6 patients.[9] Nevertheless, even with such a bias, it is clear that the morbidity and mortality associated with atheroembolization is high.

Clinical experience suggests a spectrum of severity of this disorder. In some patients, a gradual decline in renal function is observed, which resolves spontaneously in some, and progresses inexorably to renal failure in others. In other cases, particularly those with more rapid decline of renal function or with manifestations of systemic embolization affecting lower extremities, gastrointestinal tract and kidneys, the prognosis appears particularly poor.

Despite the poor outcome associated with this disorder, the current standard of care consists of watchful waiting. There have been no controlled trials of any therapeutic intervention. Case reports have suggested that cholesterol-lowering drugs might be helpful,[10] whereas anticoagulation, which favors dissemination of cholesterol crystals from aortic plaque into the peripheral circulation, is harmful and is therefore, contraindicated.[4]

Another intervention that has been considered is corticosteroid therapy, based on the ability of corticosteroids to reduce vascular inflammatory reactions. In a report of 2 patients, prednisone (60 mg daily) or methylprednisolone (80 mg daily), given for 5 days resulted in rapid and dramatic improvement in manifestations of peripheral embolization.[2] Another case report describes improvement in renal function enabling the patient to discontinue dialysis within 20 days of initiating corticosteroid therapy, with eventual restoration of his baseline creatinine of 2.8.[11] In another case report, prednisone given at 50 mg daily also resulted in improvement in renal function.[12]

Others, however, have reported no benefit.[13,14] In these reports, 7 patients received corticosteroids, but died shortly afterward. These appear to be cases of massive embolization, with treatment given late in the course of the disease. Dosage and duration of treatment were not reported. Although these case reports suggest that treatment at a late stage may be futile, they don't preclude the potential benefit of corticosteroid therapy at an earlier stage.

In the patient presented in this report, the diagnosis of atheroemboli was based on the marked and sustained increase in serum creatinine, the petechial rash, persisting ischemic pain in the foot and toe, the eosinophilia and the antecedent arteriographic procedure. Given the rapid increase in the patient's serum creatinine, rapid progression to renal failure was a major concern, prompting the decision to perform an n-of-1 experiment and administer prednisone. The rapid response observed argues for greater consideration of this intervention.

The alternative diagnosis of contrast nephropathy was considered but was believed to be unlikely for several reasons. First, the patient's creatinine was at baseline 2 days after the procedure, at a time when the effect of contrast nephropathy on renal function is usually evident. Furthermore, azotemia due to contrast nephropathy usually remits within 2 weeks,[15] whereas in this case, it persisted for more than 6 weeks. Finally, the total dose of contrast injected during arteriography and angioplasty was 60 mL of iodinated contrast with the concentration of 160 mg of iodine/mL (30%), which is equivalent to 30 mL of

320 mg of iodine/mL (60%) contrast, a dose highly unlikely to produce contrast nephropathy.[16]

A controlled trial of corticosteroid therapy has never been performed, and unfortunately is unlikely to be performed in the near future. In the meantime, given the high morbidity and mortality of the disorder and the absence of known effective treatment, cases such as this suggest that the risk of an empiric trial of prednisone is warranted. Even in the absence of a biopsy, a presumptive clinical diagnosis can be made based on variables that include cutaneous manifestations, eosinophilia, elevated sedimentation rate, and otherwise unexplained deterioration of renal function in a setting suggestive of atheroemboli, such as arteriography.[1,2] The drug could be discontinued after 2 or 3 weeks in nonresponders, minimizing the potential adverse effects of failed treatment. In responders, treatment could be tapered more gradually, over several weeks or months. Optimally, a registry could be formed to which the results of such trials could be communicated, to document the responses and to help determine if a multicenter controlled trial is warranted.

In conclusion, a patient has been presented in which oral corticosteroid therapy led to rapid improvement in manifestations of systemic atheroembolization, including, most notably, restoration of baseline renal function. Because a controlled trial is not likely to be performed in the near future, empiric n-of-1 trials might be the only means to test the efficacy of corticosteroid therapy in this otherwise grave but untreated vascular complication.

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