Long-Term Renal and Patient Outcome in Idiopathic Retroperitoneal Fibrosis Treated With Prednisone

Eric F.H. van Bommel, MD, PhD,[1] Claire Siemes, MD, MSc,[1] Liesbeth E. Hak, MD, PhD,[1] Sacha J. van der Veer, MD,[2] and Tadek R. Hendriksz, MD[2]

Background: Primary medical treatment of idiopathic retroperitoneal fibrosis (RPF) increasingly is accepted. However, the optimum treatment strategy is still unclear.

Study Design: Case series.

Setting & Participants: Single tertiary care referral center. 24 patients with idiopathic RPF treated with prednisone for 1 year, if needed, with (urgent) renal drainage from June 1991 through October 2006.

Outcome & Measurements: Clinical improvement, laboratory parameters, repeated computed tomographic (CT) scanning. Treatment was considered successful if the following criteria were met at the end of the 1-year treatment period: significant subjective clinical improvement, (near-)normalization of acute-phase reactants, improvement in renal function with disappearance of ureteral obstruction, and CT-documented mass regression. Recurrence is defined as need for retreatment because of return of signs and symptoms after the 1-year treatment period in patients with initial treatment success.

Results: 22 patients reported significant to complete resolution of symptoms after median treatment duration of 2.0 weeks (0.7 to 3.0). Follow-up showed decreases in erythrocyte sedimentation rate, C-reactive protein level (both $P < 0.0001$), and serum creatinine level ($P = 0.0230$) at 6 weeks, which persisted during the treatment period. Repeated CT scanning showed mass regression in 19 patients during the treatment period. Six patients were considered treatment failures, and there were 23 recurrences 10 months (7 to 14) after prednisone withdrawal in 13 of 18 patients with initial treatment success. At the end of follow-up (median, 55 months), 7 patients had impaired renal function; 1 patient reached end-stage renal disease. The mortality rate was 8%.

Limitations: There was no comparison with other treatments.

Conclusion: One-year treatment with prednisone is associated with a high rate of initial success, but a high recurrence rate. Despite frequent disease relapse, long-term renal and patient outcome was good.

Am J Kidney Dis 49:615-625.

INDEX WORDS: Idiopathic retroperitoneal fibrosis; prednisone; computed tomographic scan; gallium scan; renal outcome; patient outcome.

Retroperitoneal fibrosis (RPF) is an uncommon, but serious, disorder of unclear cause.[1,2] It is characterized by chronic nonspecific inflammation of the retroperitoneum that can entrap and obstruct retroperitoneal structures, notably the ureters.[1-3] RPF frequently is detected only after severe renal failure is present. However, advances in imaging techniques and increased awareness of the diagnosis have resulted in RPF being diagnosed in unobstructed patients at an earlier stage with increased frequency.[1,2,4]

The disease may be secondary to abdominal surgery, drugs (notably such ergot derivatives as methysergide, bromocriptine, and pergolide), chronic infection, malignancy, radiation therapy, and, possibly, asbestos exposure.[1-5] In the majority of patients, no causal factor can be identified, and the disease is considered idiopathic. In idiopathic RPF, an exaggerated inflammatory response to advanced atherosclerosis has been implicated in its pathogenesis. For this reason, some prefer the term chronic periaortitis to encompass idiopathic RPF and perianeurysmal fibrosis.[2-4]

From the [1]Departments of Nephrology and [2]Radiology, Albert Schweitzer Hospital, Dordrecht, The Netherlands.

Received November 13, 2006; accepted in revised form February 22, 2007.

Originally published online as doi:10.1053/j.ajkd.2007.02.268 on April 9, 2007.

Support: None. Potential conflicts of interest: None.

Address reprint requests to Eric F.H. van Bommel, MD, PhD, Department of Internal Medicine, Section Nephrology, Albert Schweitzer Hospital, PO Box 444, NL-3300 AK Dordrecht, The Netherlands. E-mail: e.f.h.vanbommel@asz.nl

0272-6386/07/4905-0008$32.00/0

doi:10.1053/j.ajkd.2007.02.268

Surgical ureterolysis, with or without postoperative corticosteroid treatment, has been the mainstay of therapy in patients with RPF, but does not always prevent recurrent ureteral obstruction and is associated with substantial morbidity.[1-3]

In recent years, the use of corticosteroids, with ureteral stenting if needed, has gained increasing acceptance as the preferred treatment strategy in patients with idiopathic RPF.[1-3] However, the optimum medical treatment is far from being established. Success rates with prednisone in small case series vary significantly,[6-11] and some investigators advocate the use of more aggressive treatment strategies.[12-15] It is unclear which factors determine the severity of disease or response to medical treatment. In addition, few data are available for long-term renal outcome in patients with this disorder.

These questions prompted us to review in detail our experience with a relatively large group of patients with idiopathic RPF who were treated with prednisone monotherapy and had extended follow-up.

METHODS

Patients

Twenty-four patients with idiopathic RPF treated with prednisone monotherapy for first presentation of disease from June 1991 through October 2006 are the subject of this retrospective study. All patients were followed up by our nephrology team at a single tertiary-care referral center. Fourteen study patients were referred to us from other departments (general internal medicine, gastroenterology, and vascular surgery).

All study patients had a clinical and radiological diagnosis of RPF in the absence of any sign of malignancy.[1-3] In 6 patients, the diagnosis was histologically confirmed. No patient had a history of infection or use of drugs associated with RPF. Therapy consisted of initial high-dose prednisone (60 mg once daily for 6 weeks), which usually was tapered within the next 2 to 3 months to a maintenance dose of 10 mg/d and continued for 1 year. If tapering the dose within the treatment period led to recurrent signs and/or symptoms, prednisone dose was increased temporarily. Patients also were administered omeprazole, 20 mg/d, and alendronate, 10 mg/d, plus calcium, 500 mg/d, for gastric mucosal and bone protection, respectively.

Ureteral management depended on the presence and severity of hydroureteronephrosis at presentation. Prior experience[1,3] suggested that normal diuresis usually returns within 7 to 10 days and sometimes as early as 24 to 48 hours after starting prednisone treatment. Therefore, percutaneous nephrostomy was used for emergency decompression in cases of severe obstructive renal failure. Response to treatment was evaluated by means of anterograde ureterography through the nephrostomy tube and subsequent clamping of the tube, which was removed as soon as the ureter was found to be patent. Less severe obstructive renal failure not improving within 2 weeks of prednisone treatment was considered an indication for ureteral stenting. Ureteral stents were changed every 3 to 4 months until definitive removal.

Patients in whom treatment failed were administered prolonged courses of steroids, either alone or in combination with azathioprine or cyclophosphamide. Patients who experienced recurrence were treated with combination immunosuppressive therapy or tamoxifen, either alone or in combination with azathioprine. Choice of treatment regimen was at the discretion of the treating physician. When there was diagnostic uncertainty during follow-up, histological examination of specimens from a computed tomographic (CT)-guided biopsy was performed.

Follow-Up

Follow-up included repeated clinical evaluation and laboratory measurements and serial CT scanning. All baseline and follow-up CT scans were reviewed independently by 1 experienced radiologist who was unaware of the patient's status. For all CT scans, the presence or absence of hydronephrotic kidneys was documented and categorized as absent, unilateral, or bilateral. The number of atrophic kidneys, defined as kidney diameter of 8.5 cm or less, also was documented. The amount of mass regression after treatment was categorized as none, moderate ($<$50%), significant ($\geq$50%), or complete (ie, no identifiable mass) compared with the CT scan at presentation. In 15 patients, gallium 67 (^{67}Ga) scintigraphy also was performed. Enhanced ^{67}Ga uptake in the paravertebral midline at the same position as the CT-documented retroperitoneal mass is considered indicative of the active inflammatory stage of the disease (positive gallium scan result).[16,17] Absence of uptake in this region (negative gallium scan result) did not influence the decision to start prednisone treatment in these patients. In patients with a positive gallium scan result at presentation, follow-up ^{67}Ga scanning was performed after 12 weeks of prednisone treatment.

Measurements

Age, sex, clinical signs and symptoms, duration of symptoms, laboratory parameters (erythrocyte sedimentation rate [ESR], C-reactive protein), serum creatinine, hemoglobin, white blood cell count, and serum albumin and gallium and CT scan findings were documented at baseline. Follow-up measurements included clinical improvement, time to substantial resolution of symptoms (weeks), changes in laboratory parameters, and follow-up gallium and CT scan findings. Primary outcome measurements were success rate of therapy, rate of recurrence, time to first recurrence, and long-term renal and patient outcomes. Treatment was considered successful if the following criteria were met at the end of the prescribed 1-year treatment period: significant subjective clinical improvement according to the patient, (near-)normalization of acute-phase reactant levels, improvement in renal function with disappearance of ureteral obstruction, and CT-documented mass regression. If all 4 criteria of