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NEPHROLOGY BOARD REVIEW MANUAL

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Chronic Allograft Nephropathy

Series Editor:

Stanley Goldfarb, MD, FACP

Professor of Medicine

Interim Chairman

Department of Medicine

University of Pennsylvania School of Medicine

Philadelphia, PA

Contributor:

Alden Doyle, MD, MS, MPH

Instructor of Medicine

Penn Transplant Center

Kidney/Pancreas Program

University of Pennsylvania School of Medicine

Philadelphia, PA

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Cover Illustration by Scott Holladay

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Chronic Allograft Nephropathy

Alden Doyle, MD, MS, MPH

INTRODUCTION

Renal transplantation has assumed an increasingly central role in the treatment of end-stage renal disease (ESRD). With the advent of the first preparations of cyclosporine by Calne in 1978, 1-year graft survival rates rapidly improved, ushering in the modern era of transplantation. In the past 2 decades, incremental advances have been made in understanding and managing immunosuppression, resulting in further improvements in 1-year graft survival rates and an expansion of the potential patient population eligible to receive an allograft (Figure 1).

The real challenge in renal transplantation for the next few years is prolonging the functional life span of transplanted kidneys. Multiple factors such as hypertension, drug toxicity, and glomerular hyperfiltration conspire to decrease the function of renal allografts after the first year, but how these factors work remains incompletely understood. Initially, the primary emphasis was put on immunologic mechanisms. As a result, progressive loss of function of renal allografts was most commonly referred to as *chronic rejection*. It has become clear, however, that classic immune-mediated rejection accounts for no more than 15% of the clinical spectrum of deteriorating allograft function. This is not to say, however, that immunologic processes do not play an important role, but rather that they interact with other clinical processes in ways that are less understood. More recently, the term *chronic allograft nephropathy* (CAN), which more accurately reflects the diverse nature of the insults, has been favored.¹

Because the management of transplant patients is becoming an increasingly integral part of clinical nephrology, nephrologists must have an understanding of current approaches to managing the factors that contribute to CAN. This manual discusses (1) factors that the practicing nephrologist can modify to prolong the life span of renal allografts, (2) an approach to diagnosing CAN and excluding other diagnoses in the differential, and (3) strategies to attenuate the effects of CAN once the diagnosis has been made.

PROLONGING THE LIFE SPAN OF RENAL ALLOGRAFTS

CASE PRESENTATION

A 45-year-old woman with a 25-year history of insulin-dependent diabetes who underwent a successful cadaveric renal transplant 7 years ago presents to clinic for routine follow-up. The patient had been diagnosed with ESRD at age 37 after a 4-year history of progressive diabetic nephropathy. She received a cadaver kidney transplant after spending 9 months on dialysis. During post-operative week 3 she experienced an explosive rise in her serum creatinine level. Biopsy of the transplant kidney revealed acute rejection, and the patient was admitted to the hospital for treatment. After treatment with OKT3, the patient improved and her creatinine level stabilized around a baseline of 1.5 mg/dL. Since that admission, she has done well. She has been maintained on a 3-drug immunosuppressive regimen including tacrolimus, mycophenolate mofetil, and prednisone. In addition, she currently takes the β -blocker atenolol and the calcium channel blocker felodipine for control of hypertension, and continues with twice daily dosing of subcutaneous 70/30 insulin to control her diabetes.

The patient reports being increasingly sedentary but has been well otherwise. She states that she makes a general effort to restrict dietary sodium and has been compliant with her medication regimens. The patient notes, however, that she has taken a variety of antihypertensive medications in the past and “nothing seems to work.” She points out that, if anything, her blood pressure became even harder to control after renal transplantation. Recently, her blood pressure levels have ranged from 145/80 to 168/88 mm Hg. At present, her blood pressure is 155/84 mm Hg with a pulse of 65 bpm. In addition, she has 1–2+ pitting edema in her lower extremities bilaterally. Cardiac examination reveals a faint S₄ but no murmurs, rub, or S₃. Her graft is nontender. Urinalysis shows 1+ proteinuria but no blood. Review of the patient’s chart reveals that her creatinine has been stable, but her blood pressure and weight have been rising slowly since 1 year post-transplantation.