Successful strategy in diabetic nephropathy

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Scope of Problem

Diabetic nephropathy is the most prevalent known cause of irreversible uremia in the western world. The prevalence of uremia attributable to diabetic nephropathy in Japan, China, and the rest of Asia is about one third that reported in Europe. Approximately one in four new dialysis patients, and one in five renal transplant recipients in the United States are diabetic. Uremia therapy in the diabetic is less satisfactory than in age and sex matched nondiabetics mainly because of extrarenal disease in large and small arteries. Heart attack, stroke, limb amputation, and blindness plague otherwise "successful" diabetic renal transplant recipients, and preempt rehabilitation in long-term hemodialyzed diabetics. Despite their excess risk of medical catastrophe, an increasing proportion of type I diabetic kidney transplant recipients are returned to work, school, or home responsibilities. In the best reported experience with diabetic kidney transplantation, at the University of Minnesota, there was no difference in patient or graft survival of cadaveric donor grafts in diabetic and nondiabetic recipients. Other contemporary series of diabetic transplants, including our own, have not however been this successful. According to the first comprehensive report of the U.S. end-stage renal disease program only 38% of diabetics treated by dialysis will live for three years, while 82% of patients and 59% of grafts survive three years following living donor renal transplantation. Further emphasizing the extra risk of being diabetic when developing uremia is the experience of the University of Washington group in which none of 115 diabetics treated by kidney transplantation or maintenance hemodialysis lived longer than seven years. There is general agreement that a high level of overall care is vital to optimized maintenance hemodialysis, continuous ambulatory peritoneal dialysis (CAPD), or kidney transplantation. This paper proposes a strategy for treatment of the uremic diabetic.

Coincident Organ System Disease

Listed in Table 1 are the organ systems most likely to manifest coincident malfunction in a diabetic experiencing progressive renal insufficiency. Sufficient strides in the practice of defensive medicine have been made to minimize the probability that the success of a carefully implanted well tolerated kidney allograft will be lost, or the patient will die because of extrarenal disease.
Table 1 Organ systems likely to fail in the uremic diabetic.

1) Eyes  
2) Cardiovascular  
3) Vascular supply to brain  
4) Gastrointestinal tract  
5) Perfusion to extremities  
6) Peripheral motor nerves  
7) Bladder emptying  
8) Penile erection  
9) Psyche

Vision

Of the potential complications to which the uremic diabetic is liable, loss of vision is the most constant threat to rehabilitation. Diabetics risk blindness due to retinopathy, glaucoma, cataracts, and vitreous hemorrhage. At the time of initial evaluation for a kidney transplant, 97% of type I diabetics have retinopathy and 50% are blind or have lost vision. Proliferative retinopathy, a result of retinal hypoxia characterized by growth of new vessels on the retinal surface is present in 40 to 60% of type I diabetics after 20 years. Glaucoma occurs in about 5% of diabetics and is especially virulent when superimposed on proliferative retinopathy. Cataracts are present in at least one-half of type I diabetics who become uremic. It is evident that ophthalmologic consultation is vital for both transplant surgeon and nephrologist seeking to preserve sight in uremic diabetics under their care. Well timed laser photocoagulation, vitrectomy (with lensectomy if indicated for cataract extraction) to relieve light obstructing vitreous hemorrhage or fibrosis, and enhanced blood pressure and glycemic control, are components of a regimen likely to retain ambulatory vision in four out of five uremic diabetics managed by maintenance hemodialysis or kidney transplantation. Diabetics in renal failure can avoid blindness provided that the necessity for continuing management of the eye is appreciated by the patient’s principal physician.

Cardiovascular Performance

Normalization of high blood pressure is the most significant intervention accomplishable in diabetics with failing kidneys. In proteinuric type I diabetics, reduction of hypertensive blood pressures retards loss of creatinine clearance, and decreases urinary protein losses. Retinopathy accelerates in hypertensive diabetics and may be slowed by blood pressure control. Coronary artery disease, myocardial infarction, and congestive heart failure are known consequences of hypertension to which the diabetic is vulnerable. The impact of cardiac disease on survival of uremic diabetics can be gauged from the report of the first five thousand diabetics treated by dialysis and kidney transplantation in Europe in which 40 to 50% of deaths in each treatment group (peritoneal dialysis, hemodialysis, or kidney transplantation) were classed as caused by heart diseases. The diabetic heart is vulnerable to decompensation under the salt and water volume overload imposed by renal failure. Protection against heart failure is afforded by maintaining a “dry weight” during dialytic therapy by using ultrafiltration and by prescribing loop diuretics post-transplantation to counteract the salt retaining action of corticosteroids used for immunosuppression.
Cerebrovascular Integrity, Perfusion to Extremities

Strokes are second in prevalence to heart disease as the cause of death in treated uremic diabetics. Control of hypertension ought to reduce their incidence, which was about 15% of all deaths in European diabetics treated for E.S.R.D. through 1981. Key to blood pressure regulation in diabetics with failing kidneys is preemption of intravascular volume expansion due to retained salt and water. As was noted above for protection of cardiac compensation, diuretics for urine producing patients, and ultrafiltration during dialysis for functionally anephric patients, will minimize the quantity of vasodialator drugs required to normalized blood pressure.

Limb loss, like blindness, is in large part preventable in diabetics undergoing dialysis or given a kidney transplant. The diabetic foot is in jeopardy because of its poor perfusion (atherosclerosis), and diminished sensation (neuropathy). Uncontrolled studies indicate that electrical conduction in motor nerves of the lower extremities will improve once euglycemia is established. Rausher et al. outlined a rational approach to foot care and preservation in kidney transplanted renal diabetics. Amputation can be avoided in a significant proportion of transplant recipients (no experimental data substantiates this conjecture) by frequent visits to a podiatrist for removal of calluses, prescription of sensible shoes, cutting nails straight across, and regarding every ulcer, abrasion, or injury to the foot as potentially serious.

Gastrointestinal Manifestations

Nausea, vomiting, and anorexia are constant components of untreated uremia. Uremic diabetics, in addition, may suffer intermittent explosive nocturnal diarrhea, and continuous gastroparesis. No satisfactory explanation for the pathogenesis of the often embarrassing diarrhea has been proffered. In our experience, provision of a functioning kidney transplant abruptly ends this complaint. Management of the stomach dilatation is more troublesome. Delayed and inconstant stomach emptying results in erratic absorption of food, which in turn causes fluctuating blood glucose control and repeated episodes of hypoglycemia. A diet divided into four small meals plus an evening snack, coupled with treatment with metoclopramide 10 mg before each feeding improves gastric function in nearly all diabetic transplant recipients who have experienced "bloating" and impaired motility.

Cystopathy

Kidney transplant recipients with diabetic cystopathy have impaired bladder sensation, increased bladder capacity, decreased detrusor contractility and incomplete emptying. Urinary retention due to diabetic cystopathy may be easily missed, if not kept in mind, leading to the incorrect diagnosis of intrinsic renal disease rather than functional urinary outflow obstruction. Cystopathy post-transplantation may mimic renal allograft rejection by raising serum creatinine concentration. Of 12 patients with advanced diabetic nephropathy studied by Norlen, Blaivas, and Gabel, 11 had evidence of cystopathy, while four
complained of poor bladder emptying. This nearly universal presence of cystopathy in diabetic kidney transplant recipients is reason to encourage frequent voiding and prompt treatment of urinary infection. A trial of phenoxybenzamine 10–20 mg 1–4 times daily increases effectiveness of detrusor muscle contraction in most symptomatic patients. For those with more than 200 ml of infected residual urine who are unresponsive to this regimen, a program of clean intermittent self-catheterization as devised by Lapides et al. many obviate the necessity to divert the upper urinary tract into a bowel conduit.

**Psychosocial Impact**

Azotemic diabetics and their families face intense stress during the seemingly inexorable downhill course of the diabetic renal-retinal syndrome. Once uremia supervenes, a psychosocial crisis encompassing patient and family is usual. Depression, panic, resort to drug abuse, alcohol, and active or passive suicide were observed in the 29 diabetic renal failure patients studied by D'Elia and associates at the Joslin clinic. As noted by these workers, “Profound visual impairment was the major handicap leading to loss of independence and self-esteem for the group that refused further therapy”. Amongst our diabetic transplant recipients, support by a spouse appears to be the key to weathering the long storm of endured by the type I diabetic in renal insufficiency. Sequential changes in body image prior to and after a kidney transplant are distressing to most patients, particularly young women. Starting with nephrotic anasarca and a weight gain of 10 to 40 pounds, the typical patient then decreases in size during uremic cachexia, only to subsequently expand in girth as a consequence of adrenocorticosteroid immunosuppression. Such radical transformations in physical condition occur at a time when nearly simultaneous complications in multiple organ systems are occurring. We have treated uremic diabetics for concurrent vitreous hemorrhages, foot ulceration, nocturnal diarrhea, gastroparesis, hypertension, heart failure, and peripheral vascular insufficiency. The burden of apparently unending new medical complications may induce despair, futility, and hopelessness impacting on spouse and family.

No simple answer to the needs for emotional support of diabetics with failed kidneys is known. Patients at our institution have formed a “Diabetic Kidney Transplant Self Help Group”. By meetings with selected empathetic staff members, and visits to hospitalized members, the group succeeds in counseling newly referred uremic diabetics while sustaining long-term patients. Despite our awareness of the need for psychosocial support, divorces, admission to psychiatric wards, and depression accompany serious medical reverses such as irreversible kidney rejection or leg amputation.

**Summary**

Planning treatment for the diabetic with progressive renal insufficiency requires allowance for the high probability that coincident multisystem disease will develop. By establishing a team approach, the patient is protected from the stress of having conflicting treatment protocols prescribed by physicians concerned with only one organ or system.
The majority of uremic diabetics can survive at least the first three years of dialysis or renal transplantation with preserved sight and intact limbs. It may be anticipated that the proportion of nephropathic diabetics who attain rehabilitation will continue to increase.

References
