Case Report

Irreversible chronic renal failure following jejunoileal bypass

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Hyperoxaluria and the presence of calcium oxalate stones are documented complications of intestinal bypass surgery. Renal failure secondary to interstitial calcium oxalate deposition is a rare complication of this procedure.[1] To our knowledge, three cases have been reported.[1-3] In two cases, intestinal continuity was reestablished and in one case urinary oxalate was reduced to normal and renal function was stabilized.[2] We describe another case of renal failure following intestinal bypass surgery and the clinical course after restoration of bowel continuity.

Case report

A 58-year-old white woman was first examined at The Cleveland Clinic Foundation in March 1970 with mild essential hypertension, exogenous obesity, 111 kg (245 pounds), 157 cm (5 feet, 2 inches), and mild Type IV hyperlipoproteinemia. Renal evaluation including intravenous pyelogram, creatinine, blood urea nitrogen (BUN), and urinalysis were within normal limits. In March 1974, the patient underwent an end-to-side jejunoileal bypass with incidental appendectomy at another hospital. She weighed approximately 114 kg (250 pounds). After surgery she began to experience hypogastric cramps, diarrhea (four loose stools per day), nausea, vomiting, and weakness, which continued unabated until she was seen at the Cleveland Clinic in September 1976. Over a 2½-year period she steadily lost weight and finally

reached a plateau of 59 kg (130 pounds). On September 28, 1975, she underwent cholecystectomy for chronic cholecystitis and cholelithiasis at another hospital. Her BUN was 35 mg/dl (*Table*). Except for a trace of protein, urinalysis was within normal limits. On February 6, 1976, the patient was again examined at another hospital; she complained of weakness, anorexia, diarrhea, and fatigue. Urinalysis showed 1+ proteinuria, pH 5, and numerous white blood cells. The BUN was 48 mg/dl and creatinine level was 4.0 mg/dl. Retrograde pyelograms failed to reveal any evidence of obstruction or nephrolithiasis. Nephrocalcinosis was noted for the first time. The size of the right kidney (12 cm) had not changed since 1970. The left kidney (11 cm) was 2.5 cm smaller than it was in 1970. The patient was again seen on May 27, 1976, for similar complaints. Her BUN was 106 mg/dl and creatinine clearance 0.5 ml/min. Urinalysis revealed 1+ proteinuria and white blood cells too numerous to count. There were 544 mg of urinary protein excreted in a 24-hour period. On June 19, 1976, the patient had presenting symptoms of acute pulmonary edema. Hemodialysis was instituted and maintained thereafter two to three times per week.

The patient was seen at the Cleveland Clinic for the first time since 1970 on September 30, 1976. At that time she complained of her usual symptoms as well as multiple arthralgias and was obviously depressed. She was chronically ill and had excessive skin folds over the abdomen indicative of weight loss. Her BUN was 75 mg/dl and her serum creatinine was 10.4 mg/dl. The blood oxalate was 1.1 mg/dl (normally none detectable). The patient was virtually anuric. Cultures of a few milliliters of urine revealed many organisms all less than 10^5 colonies per milliliter. Complement levels were within normal limits. Antinuclear factor, LE prep, and rheumatoid factor were also negative. A 72-hour fecal fat was indicative of malabsorption.

Tissues from two open kidney biopsies demonstrated the same findings. Each segment contained more than 25 glomeruli. Histopathologic assessment revealed normal glomeruli with extensive tubular atrophy, interstitial mononuclear inflammatory cell infiltrate, and mild interstitial fibrosis. Abundant intratubular birefringent crystals were present, which were morphologically consistent with calcium oxalate. Mild hyaline arteriolar nephrosclerosis was present. Direct immunofluorescence of fresh frozen air-dried kidney sections demonstrated focal granular deposition (1+) of IgA and C_3 in tubular basement membranes. Immunoglobulins and complement were not identified in the glomeruli. Tissue for electron microscopy was fixed in 2% glutaraldehyde, postfixed in osmium, Epon-embedded, and appropriate thin sections were stained with lead citrate and uranyl acetate for examination in the RCA-EMU4 electron microscope. Ultrastructural assessment revealed no glomerular changes. Electron-dense deposits were present within tubular basement membranes. The inflammatory cells in the interstitium consisted of lymphocytes and immunoblasts. Electron diffraction of the intratubular crystals present in 1-μ sections of Epon-embedded tissue was done using a Joel-100 B with an accelerating voltage of 100 kV. The resultant diffraction patterns and gold-calibrated d-spacings were compared to reference powders and were characteristic of calcium oxalate.

On November 11, 1976, the patient underwent an end-to-side restoration of bowel continuity after a short period of hyperalimentation and was discharged on November 24 after an uneventful postoperative course.

Thirty-six months after surgery the patient continues to be anuric and to require maintenance hemodialysis. Predialysis BUN and creatinine are in the range of 100 mg/dl and 10 mg/dl, respectively. Diarrhea and abdominal cramping have subsided and she has regained approximately 18 kg (40 pounds).

Discussion

An increased incidence of calcium oxalate urolithiasis occurs in patients with jejunoileal bypass.[4,5] Hyperoxaluria secondary to increased oxalate absorption

Table. Laboratory findings

	Date								
	3/70	3/74*	9/75	2/76	5/76	9/76	12/76	9/77	10/79
BUN	WNL†	WNL	35 mg/dl	48 mg/dl	106 mg/dl	75 mg/dl	45 mg/dl	133 mg/dl	97 mg/dl
Cr	WNL	WNL	...	4.0 mg/dl	13.5 mg/dl	10.4 mg/dl	5.8 mg/dl	11.4 mg/dl	9.6 mg/dl
U/A	WNL	WNL	Trace *protein*	1 + protein pH −5.0; *many* WBC	1+ protein; WBC‡	...	...	...	...
Hgb	WNL	WNL	...	8.3 g/dl	8.1 g/dl	6.1 g/dl	...	...	7.7 g/dl
Ca	WNL	WNL	...	WNL	7.5 mg/dl	WNL	...	...	5.1 mg/dl
P	WNL	WNL	...	WNL	8.0 mg/dl	WNL	...	...	8 mg/dl
Alb	WNL	WNL	...	...	2 g/dl	3.4 g/dl	...	...	...
Serum oxalate	...	...	...	...	...	1.1 mg/dl§	...	...	...
Na	WNL	WNL	...	...	155 mEq/L	138 mEq/L	141 mEq/L	137 mEq/L	140 mEq/L
K	WNL	WNL	...	...	6.2 mEq/L	4.2 mEq/L	5.0 mEq/L	6.0 mEq/L	7.1 mEq/L
CO_2	WNL	WNL	...	...	5.0 mEq/L	20 mEq/L	27 mEq/L	13.5 mEq/L	19.6 mEq/L
Cl	WNL	WNL	...	...	124 mEq/L	97 mEq/L	103 mEq/L	99 mEq/L	96 mEq/L
Ccr	...	...	...	...	0.5 ml/min	...	...	...	...

* Patient had jejunoileal bypass March 1974 and shunt restoration November 1976.
† Within normal limits.
‡ Too numerous to count.
§ No levels normally detectable.

has been observed in many of these patients.[6] Until recently, impairment of renal function was not observed in the absence of urinary tract obstruction or infection. Vainder and Kelly[3] described a case of renal tubular deposition of oxalate with concomitant tubular dysfunction. Renal tubular acidosis (Type II) developed in their patient. No mention was made of the creatinine clearance, and it is not apparent from their report whether renal function improved after intestinal reanastomosis. Cryer et al[2] reported a case of renal insufficiency with biopsy-proven interstitial nephritis and calcium oxalate deposition occurring 1½ years after jejunoileal bypass. After intestinal reanastomosis there was stabilization and slight improvement of renal function and reduction of urinary oxalate excretion to normal. Creatinine clearance never fell below 13 ml/min, and it does not appear that the patient ever required dialysis. Gelbart et al[1] described a case of chronic renal failure secondary to calcium oxalate deposition developing approximately 1½ years following intestinal bypass surgery. Earnest et al[7] reported that 12% of a large series of patients undergoing jejunoileal bypass had mild degrees of azotemia over a mean follow-up period of 2½ years. Two of their patients with azotemia were followed up by serial creatinine clearances. Both had disproportionately low serum creatinine concentrations relative to their creatinine clearances. This observation was believed to be compatible with the reduction of muscle mass known to occur after the jejunoileal bypass.

The patient described here had progressive renal insufficiency during a 2-year period following jejunoileal bypass. Thirty-six months after intestinal integrity was reestablished, there was essentially no change in renal function. There is little doubt that the renal failure was secondary to interstitial nephritis and calcium oxalate deposition. There is good documentation of the absence of preexisting renal disease. Retrograde pyelography performed during the progression of renal insufficiency failed to reveal any evidence of obstruction or lithiasis, and there was no evidence of pyelonephritis. At the time of referral the patient was virtually anuric, and thus it was impossible to measure urinary oxalate. The patient's blood oxalate value was unquestionably elevated and there was laboratory documentation as to the nature of the crystals in the renal tubules.

When monitoring the renal function of patients with jejunoileal bypass, it is important to realize that the serum creatinine level may be within the normal range until the glomerular filtration rate (GFR) is reduced at least 50%. In patients with loss of body muscle mass as a result of jejunoileal bypass, the serum creatinine can be more misleading. Advanced renal failure as demonstrated by our patient represents the other end of the spectrum. Fuller awareness of calcium oxalate interstitial nephritis should prompt monitoring the renal function of these patients with serial GFR preferably by iothalamate I 125 (inulin clearance), which will not overestimate the true GFR in renal failure as the creatinine clearance might do.[8] Progressively worsening function should prompt a vigorous search for reversible conditions, especially infection and obstruction. The effect of intestinal reanastomosis on renal function is speculative because of the limited number of case reports, although Cryer et al[2] reported that early reanastomosis may lead to improved renal function and prevent end-stage renal disease. Drenick et al,[9] in a study of 18 patients after

intestinal bypass, recommended dismantling the bypass for patients with oxalate interstitial nephritis proved by biopsy and progressive renal dysfunction. Drenick et al also suggested a possible immune complex mechanism in addition to mechanical damage caused by direct oxalate deposition in the kidney tubules.

Finally, it is of interest to review briefly the mechanisms involved in increased oxalate absorption. It has been shown that not only patients with jejunoileal bypass, but also those with ileal disease or ileal resection have an enhanced absorption of dietary oxalate via the colon. The presence of increased fatty acids secondary to malabsorption results in increased complex formation with calcium ions. Decreased free calcium ions intraluminally result in oxalate combining into more soluble sodium oxalate, which because of an increased colonic permeability secondary to the presence of unabsorbed bile salts and fatty acids, is absorbed leading to hyperoxaluria.[10-12] Management calls for a low oxalate, low-fat diet plus the cations (calcium, aluminum), which form insoluble oxalate salts intraluminally. Cholestyramine can also be used to bind excess fatty acids, thereby making more calcium available intraluminally.

Addendum

The patient died suddenly following dialysis on January 7, 1980. Postmortem examination revealed histopathological changes consistent with end-stage renal disease. These changes included a diffuse generalized glomerular hyalinization and/or fibrosis, diffuse interstitial fibrosis and tubular atrophy, and arterial and arteriolar sclerosis. Numerous crystals, most likely calcium oxalate, were also detected in the renal tubules with polarized light microscopy. Direct immunoflorescent studies were negative. Ultrastructural findings were nonspecific and consistent with end-stage renal disease.

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