Acute Renal Failure Associated with Mannitol Infusion and Reversal with Ultrafiltration and Hemodialysis

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Mannitol 120g

eyes, 120 g of mannitol on day 2 and 240 g on day 3 were given intravenously. Urine output decreased to 10-15 ml/h following mannitol infusion and 5 kg of gain in body weight for 3 days was observed. On day 5, the patient was noted to be breathless. By then, the creatinine value had risen to 7.9 mg/dl and BUN to 71 mg/dl (fig. 1). Serum sodium was 113 mEq/l and serum os-

Dear Sir,

Mannitol is an osmotic diuretic agent widely used to reduce intracranial and intraocular pressures or to prevent acute renal failure (ARF), whereas the potential nephro-toxic effects of this drug have recently been reported when it is used unrestrictedly in patients with established renal failure [1,2]. The aim of this letter is to report an example of mannitol-induced ARF, successfully treated with ultrafiltration and hemodialysis.

Case Report

A 49-year-old man was admitted to our hospital for management of hemorrhagic glaucoma. The patient had type II diabetes mellitus for 10 years complicated by proliferative retinopathy. He had undergone treatment for hypertension and had been followed for mild chronic renal insufficiency due to diabetic nephropathy. Medications at the time of admission included benidipine and glibenclamide. Admission examination showed blood pressure 160/80 mm Hg, regular pulse rate 60/min, no pretibial pitting edema and mild impairment in vibration test due to diabetic peripheral neuropathy. Initial laboratory values showed proteinuria 2.4 g/day, blood urea nitrogen (BUN) 45.6 mg/dl, serum creatinine 2.6 mg/dl, serum protein 5.8 g/dl and serum albumin 3.0 g/dl. The serum sodium was 137 mEq/l, potassium 4.8 mEq/l and chloride 105 mEq/l. A fast blood glucose was 379 mg/dl. Chest roentgenogram revealed no cardiomegaly.

Because intraocular pressure measured on day 2 increased to 56 mm Hg in the left UF HD

7

6-

Ö 4 3

180 70 60 50

40

9 10

4 5 6 7 Hospital days

Fig. 1. Clinical course. UF = Ultrafiltration; HD = hemodialysis.

osmolality measured was 316 mosm/kg (calculated 252 mosm/kg). Intravenous furosemide (200 mg) was given without effect. Mannitol was discontinued. At this time physical examination showed a blood pressure of 210/100 mm Hg and a pulse of 85/min and there was no evidence of congestive heart failure. After giving his informed consent, 4 liters ultrafiltration for 4 h was insti-

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tuted on day 5, subsequently followed by intravenous furosemide (200 mg) which resulted in an increase in urine output to 100-120 ml/h by the next 12 h. Twelve hours later, hemodialysis was performed because of further rise in BUN levels inspite of a slight fall in serum creatinine levels. BUN and cre-atinine values thereafter fell to 33.9 and 1.96 mg/dl on day 28, respectively.

The close time relationship between mannitol infusion and acute deterioration of renal function in the absence of other recognizable causes implicates mannitol as the proximate cause of ARF in this patient described. ARF solely attributable to mannitol therapy has been reported [1-5]. The mechanisms by which mannitol can induce ARF are not clear. Swelling and vacuolization of tubular cells (osmotic nephrosis) with a substantial and reversible reduction in proximal tubular lumen diameter has been reported in animals given large doses of mannitol [6]. However, these morphologic changes are difficult to reconcile with the very prompt reversibility of this form of renal failure. Recently, hemodynamic alterations rather than substantial histologic alterations in the kidney are proposed to be involved in mechanisms of ARF secondary to mannitol therapy. Goldwasser and Fotino [3] postulated that the increased urinary solute excretion caused by mannitol may trigger an intense tubuloglomerular feedback (TGF) resulting in afferent arteriolar vasoconstriction and a fall in glomerular filtration rate. A recovery of renal function and urine output by treatment with low-dose dopamine [5] supports the contribution of functional alterations in renal hemodynamics in the pathogenesis of mannitol-induced ARF. We treated our patient with ultrafiltration not to change serum constituents including serum mannitol concentration and serum osmolality to preserve the postulated mannitol-induced intense TGF. Increased urine output after ultrafiltration in our patient indicated that mechanism(s) pertaining to functional alterations in renal hemodynamics other than mannitol-induced intense TGF mechanism may be involved in the pathogenesis of mannitol-induced ARF. A functional alteration in glomerular hemodynamics is proposed in the pathogenesis of ARF in minimal-change nephrotic syndrome [7], and reversal of such ARF with ultrafiltration and hemodialysis is reported [8]. Therefore, it is likely that a similar functional alteration in renal hemodynamics may be involved in mannitol-induced ARF.

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