Short reports


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Anuria due to sulphadiazine

While acute oliguria due to precipitation of sulphonamide crystals in the urinary tract is well recognized it is now uncommon, and standard textbooks give little detailed information on its treatment. We report the case of a child who became anuric while being treated with sulphadiazine for purulent meningitis.

Case report

History. A previously healthy boy weighing 17 kg, aged 3 years, was admitted with purulent meningitis. There was a purpuric eruption and Neisseria meningitidis was considered to be the likely pathogen, though cultures of his blood, CSF, urine, and throat swab were subsequently reported to be sterile. He appeared moderately dehydrated but blood urea level was 35 mg/100 ml and serum electrolytes were normal. His urine contained no cells or protein. He was treated with intravenous fluids, benzyl penicillin 1 megaunit, chloramphenicol 250 mg, sulphadiazine 750 mg, and hydrocortisone, all given 6-hourly intravenously, and oral phenytoin. He responded well, and 24 hours later the intravenous therapy and phenytoin were stopped. Treatment was continued with oral sulphadiazine 750 mg 6-hourly and intramuscular penicillin and chloramphenicol.

On the fourth day he developed a mild facial and oral herpes simplex eruption accompanied by occasional vomiting. On the sixth day of therapy he was noted to have frequency of micturition but there was no fever, pain, or dysuria. The following morning he passed 20 ml of heavily blood-stained urine containing protein and a few white cells, but no casts or crystals. His blood urea had risen to 98 mg/100 ml. There was no haematological evidence of intravascular coagulation. The sulphadiazine was stopped, but in spite of an intravenous infusion of 32 mEq sodium bicarbonate in 660 ml of 5% dextrose, and 1150 ml oral fluids over the next 12 hours, he remained totally anuric. There was no response to 60 ml of 20% mannitol intravenously, frusemide 50 mg intravenously, or to a bladder washout with warm 0-5% sodium bicarbonate. He was transferred to this hospital for management of his renal failure.

On admission he was clinically well with no oedema, blood pressure 120/80 mmHg, no enlargement or tenderness of his kidneys, and no abnormal neurological signs despite 24-hour anuria.

Investigations. Hb was 11 g/100 ml, platelets 208,000/mm³, urea 120 mg/100 ml, sodium 129 mmol/l, potassium 4-9 mmol/l, uric acid 5-2 mg/100 ml, calcium 9-2 mg/100 ml, phosphate 6-7 mg/100 ml, albumin 3-5 g/100 ml, antistreptolysin 0 titre <20 Todd units/ml, antinuclear factor negative, serum β₂ globulin 80 mg/100 ml. Analysis of the last urine specimen passed before the child became completely anuric revealed numerous red cells, sodium 66 mmol/l, potassium 6 mmol/l, urea 82 mg/100 ml, albumin 100 mg/100 ml, proteinuria poorly selective (θ = 34°). The urine-plasma urea ratio was 0-86 (normally >5 in children with physiological oliguria).

Cystoscopy showed an oedematous left ureteric orifice with cellular debris but no crystals in the bladder. On bilateral retrograde pyelography using sodium diatrizoate 25% w/v solution (Hypaque) there was dilatation and inactivity of both ureters, renal pelves, and minor calyces (Fig. 1) but no organic obstruction could be shown. A needle renal biopsy (Fig. 2) was obtained which contained 24 normal glomeruli and showed fairly uniform tubular dilatation and epithelial degeneration with moderate interstitial oedema and two small foci of interstitial mononuclear cells. There was no arterial abnormality, and crystals were not seen.

Six hours after ureteric catheterization the child passed 150 ml blood-stained urine and thereafter maintained an adequate urine flow rate. The following day, after having received no sulphadiazine for 48 hours, his urine contained crystals with the characteristic 'wheat sheaf' appearance of acetyl sulfadiazine. This specimen also gave a positive Bratton-Marshall (Varley, 1967) test for sulphonamides. 7 days after onset of anuria his creatinine clearance was 71 ml/min per 1·73 m² (plasma creatinine 0·6 mg/100 ml), and the haematuria and proteinuria had ceased. Intravenous pyelography on the tenth day showed normal kidneys and ureters.

Discussion

Sulphonamides may cause renal damage by crystallization and obstruction in the urinary tract or more rarely by toxic acute tubular necrosis, acute interstitial nephritis, or a generalized necrotizing angiitis (More, McMillan, and Duff, 1946). In our patient the renal biopsy appearances were similar to those described in necropsy material from patients dying of obstructive uropathy due to sulphonamide crystallization (Murphy et al., 1944).

The sudden onset of frequent or painful micturition in a patient receiving sulphonamides should arouse the suspicion of crystalluria. Characteristically these symptoms are followed within 24 hours by oliguria with crystalluria, heavy proteinuria, and haematuria. However, the urine at this stage may contain no crystals (Murphy et al.,
Fig. 1.—Retrograde pyelogram showing dilatation of both ureters and pelves during the anuric phase.

Fig. 2.—Renal biopsy showing flattening of the tubular epithelium, moderate tubular dilatation, and interstitial oedema. Glomeruli are normal. (PAS. x64.)

1944), as in our patient, presumably because of their precipitation in the upper urinary tract and a low urine flow rate.

The treatment of oliguria due to sulphonamide crystalluria has been reviewed by Dorfman and Smith (1970). In the early stages oliguria may be reversed by alkalinization of the urine with intravenous sodium bicarbonate and forced diuresis initiated by hypertonic mannitol (e.g. 0.75 g/kg body weight as a 20% solution). For established
anuria, the treatment of choice is immediate retrograde catheterization of the ureters and irrigation of the renal pelves with warm 5% sodium bicarbonate solution. However, the mechanical effect of irrigation may be of greater importance since our patient developed a massive diuresis within a few hours of retrograde pyelography. Occasionally it has been necessary to perform nephrostomy when the ureters were completely blocked by crystals. Conservative management of the condition by administration of intravenous sodium bicarbonate without irrigation of the renal pelves will allow ultimate recovery in most patients (Arneil, 1958). However, they are likely to be subjected to the risks of unnecessarily prolonged anuria and of severe hypertension with encephalopathy.

The incidence of this serious complication of sulphonamide therapy is low, but it should be lower still. Sulphadiazine is one of the least soluble sulphonamides (18 mg/100 ml urine at pH 5.5) and without alkalinization of the urine it may cause crystalluria in 25 to 30% of patients (Weinstein, 1970). Administration of sodium bicarbonate to maintain a urine pH of 7.5 will increase the solubility of sulphadiazine to 200 mg/100 ml, but routine alkali therapy is unnecessary if a fluid intake of at least 700 ml/m² per day is given and the maximum dose of 100 mg/kg per day is not exceeded (Weinstein, 1970). Sulphadiazine has long been recommended for use in meningococcal meningitis because of the high CSF levels (60–80% of the blood level) which it achieves. However, sulphadimidine is much more soluble in urine (100 mg/100 ml at pH 5.5) and also achieves adequate CSF levels for the treatment of meningitis (Black, 1970). If a place still exists for sulphonamides in the treatment of acute bacterial meningitis in children (Wehrle, Mathies, and Leedom, 1969) then a soluble compound such as sulphadimidine should be the drug of choice.

Summary

A 3-year-old boy developed anuria due to sulphadiazine crystalluria. Bilateral ureteric catheterization and irrigation of the renal pelves was followed by the restoration of a normal urine flow rate. The use of sulphadimidine rather than sulphadiazine in the treatment of bacterial meningitis is recommended.

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References


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Down’s syndrome with diabetes mellitus and hypothyroidism

We report a girl with Down’s syndrome, who has been shown to have both diabetes mellitus and hypothyroidism.

Case report

The patient was born in August 1966, a normal delivery after 38 weeks’ gestation, birthweight 2·5 kg. Her mother was aged 23 years and had undergone subtotal thyroidectomy some time before pregnancy. Apart from a maternal uncle who is retarded and epileptic, there is no relevant family history. There is one normal older sister.

The child showed typical features of Down’s syndrome which was confirmed by chromosome studies showing regular trisomy 21, with a total of 47 chromosomes. Her developmental progress was subsequently recorded as being slow.

In November 1967, at 15 months of age, she was admitted to this hospital in coma. She was found to have diabetic ketoacidosis with an initial blood sugar of 2000 mg/100 ml, which was successfully managed, though her diabetes later proved to be brittle and difficult to control.

In June 1972, progressive enlargement of the child’s abdomen was noted and her diabetes again became unstable. She was readmitted to hospital where examination showed the presence of ascites and hepatomegaly (Fig.). Investigations showed Hb 12·1 g/100 ml, erythrocyte sedimentation rate raised to 75 mm/hr, with the rest of the blood count normal. Liver function tests showed