Acute Renal Failure Following Intravenous Cholangiography*

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SUMMARY

A case of acute renal failure following the diagnostic administration of a tri-iodinated compound is reported. The clinical findings and course are presented, with particular emphasis on the fact that there appeared to be no underlying or associated disorder which may have cause the renal failure, other than possible mild dehydration.

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Tri-iodo compounds are widely used, both orally and parenterally, in order to outline the gall bladder, the biliary tree, the renal collecting system, and blood vessels. They have been implicated in the causation of acute renal failure in a number of cases,[1] although, in relation to the number of investigations performed, the incidence of this side-effect is probably low. There have been a number of cases reported in the American literature.[2-9] It is our purpose to add another case report, in order to emphasize this rare but serious side-effect of a group of drugs in common use today. In addition, some of the postulated pathogenetic mechanisms will be reviewed.

CASE REPORT

Nine days before admission a 34-year-old male suddenly developed rigors and fever, with nausea, vomiting and abdominal pain. Investigations, including a barium meal and intravenous cholangiogram, were done. For the latter he received 20 ml of a 50% solution of methylglucamine iodipamide (Biligrafin Forte, Schering A.G.), and a normal biliary tree was outlined. The barium meal showed 'evidence of gastritis', but no ulcer was demonstrated. The following day the patient complained of severe headache and pain in the back of the neck, and 24 hours later he had an epileptiform seizure.

He had repeated fits at frequent intervals over the next 4 days. During this period he was hypertensive, with blood pressure readings in the region of 185/115 mmHg. He was confused, with dilated pupils, which were not reactive to light. Phenytoin, diazepam and phenobarbitone failed to control his seizures. On the ninth day of his illness, before transfer to this hospital, laboratory investigation results were as follows: blood urea 336 mg/100 ml; serum sodium 127 mEq/litre; potassium 4·7 mEq/litre; chloride 79 mEq/litre and CO_2 content 15 mEq/litre.

Examination on admission showed him to be stuporose. He was extremely restless and was hyperventilating. Uraemic frost was present on his face, and there was dried blood in his mouth. The pupils were equal in size and reacted to light, directly and consensually. Papilloedema was present, and the vessels of both retinae showed generalized arteriolar narrowing, but no evidence of longstanding hypertension. Tendon reflexes were brisk, more so on the right than on the left, and the plantar responses were flexor. The blood pressure was 200/120 mmHg, and the pulse rate was 104/min. An atrial gallop was present. The veins in the neck were distended 4 cm above the sternal angle; the liver was enlarged 3 cm below the costal margin and was tender, and fine crepitations were present at both lung bases. There was mild oedema.

Urinalysis revealed 2+ proteinuria, and microscopy showed moderate numbers of erythrocytes, leukocytes, tubular cells, hyaline, granular, pigment and red cell casts. A lumbar puncture yielded clear cerebrospinal fluid under normal pressure; cell count was normal and protein 69 mg/100 ml. The haemoglobin concentration was 12·6 g/100 ml; white cell count 9 100/mm^3; ESR 40 mm in 1 hour (Westergren); blood urea 450 mg/100 ml; serum sodium 127 mEq/litre; potassium 7·8 mEq/litre; chloride 77 mEq/litre; CO_2 content 14 mEq/litre. Serum creatinine was 16 mg/100 ml; calcium 4·8 mEq/litre; inorganic phosphorus 10·2 mg/100 ml; SGOT 63 units; SGPT 39 units; LDH 550 units; alkaline phosphatase 6·4 King-Armstrong units; and total bilirubin 0·4 mg/100 ml.

Peritoneal dialysis was instituted and was continued for 110 hours. There was a progressive improvement in the patient's clinical state. His course, as measured by haemoglobin, blood urea and urinary volume is depicted in Fig. 1. Blood pressure control was achieved initially with intramuscular hydralazine, and subsequently with decreasing amounts of oral α-methyldopa. With the onset of a diuresis, there was a rapid return to normal. At the time of discharge from hospital, the blood urea was 26 mg/100 ml, serum electrolytes were normal, and the serum creatinine was 3·0 mg/100 ml. At a subsequent follow-up, the serum creatinine was 1·3 mg/100 ml.

A needle biopsy of the kidney was performed on the tenth hospital day (i.e. 16 days after the intravenous cholangiogram). The histological features were tubular cell damage, with evidence of tubular necrosis. A mild lymphocytic and polymorphonuclear infiltration was present in the interstitium around areas of tubular damage. Hyaline and haemoglobinuric-type casts were present in tubular lumens (Figs. 2 and 3). There was mild hyaline arteriosclerosis.

DISCUSSION

In 1968 the Council on Drugs of the American Medical Association published a review of adverse reactions to contrast media.[1] Bethyl-glucamine iodipamide was cited as a cause of these in 10 cases. Reactions were acute and explosive, and included acute renal failure, hepatotoxic manifestations, convulsions and anaphylaxis. Other iodinated compounds had previously been reported to produce renal failure, including iopanoic acid[2] and bunamiodyl.[3-5] The latter has since been removed from the market. In 1965 Setter *et al.*[6] reported a series of 9 patients with renal failure developing after administration of contrast media.

*Date received: 30 April 1971.

Again bunamiodyl was the drug implicated; however, 4 of these patients, of whom 2 died, were also given methylglucamine iodipamide. In our patient the only preparation given was methylglucamine iodipamide, and it is not possible to attribute the clinical course to any other drug.

Other factors may have contributed to the production of acute renal failure in our patient. He had been vomiting and sweating, and was pyrexial before undergoing the intravenous cholangiogram. Although not documented, it is possible that some degree of dehydration had been present. Dehydration has been incriminated as a major factor in the production of renal failure following intravenous pyelography in myelomatosis, rather than a direct nephrotoxic effect of the contrast media used.

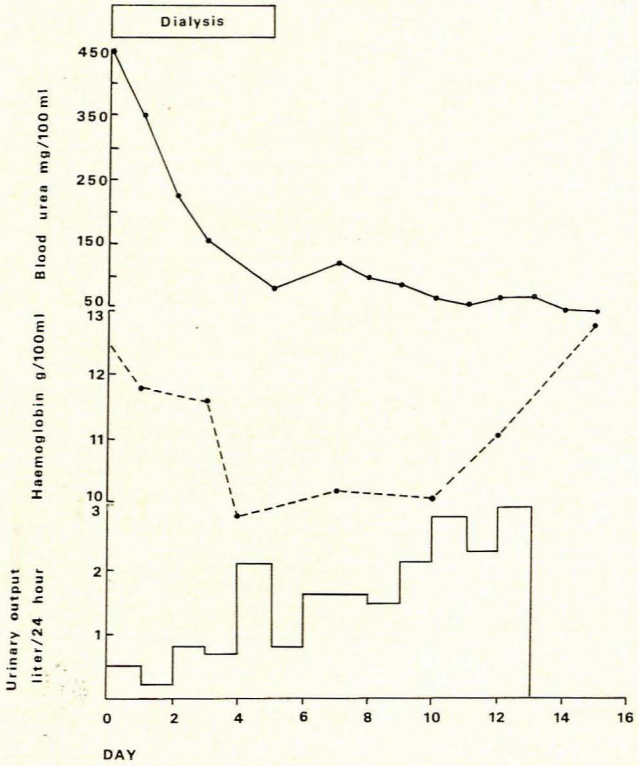

Fig. 1. Clinical course of patient as demonstrated by level of blood urea, haemoglobin and daily urinary volume, from admission to recovery.

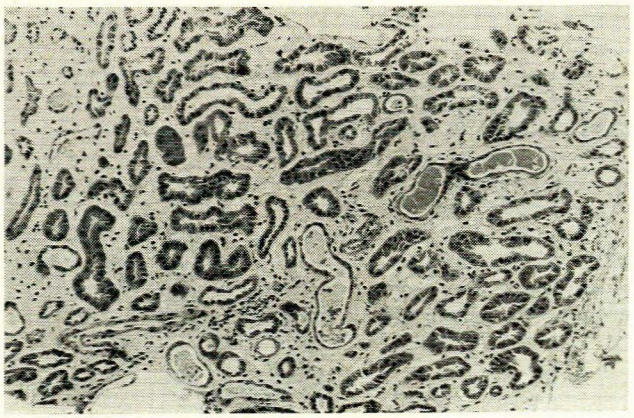

Fig. 2. Low-power view of a needle biopsy specimen of the kidney. There is tubular cell degeneration, necrosis and inflammatory cell infiltrate. Note also haemoglobinuric casts (H. and E. × 95).

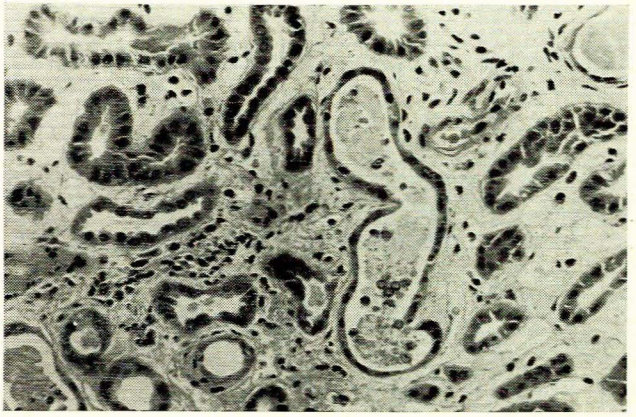

Fig. 3. High-power view of the same specimen showing necrotic tubules, interstitial oedema and round-cell infiltrate (H. and E. × 240).

Setter *et al.*[6] suggested that underlying renal disease predisposed to acute renal failure in a large proportion of their 9 patients, but the blood urea had been recorded as being normal in 6 patients before administration of the drug. In the patient reported here, routine investigation, including an intravenous pyelogram done some months before his present illness, showed no evidence of renal disease.

Another factor which has been considered of importance is excessive dosage or multiple doses at short intervals, of the same or different, related compounds. This could not be implicated in our patient. Other than the possibility of dehydration, there was no evidence of underlying disease, including hepatobiliary disease, which may have impaired excretion of the drug. Thus, the renal failure appears to have been related to a direct toxic effect of the compound used.

Collateral evidence for the condition being due to a direct toxic effect of the drug was the clinical presentation, suggesting an encephalopathy, with headache followed by fits shortly after administration of the contrast medium. This could not be attributed to uraemia at that time. Such a presentation corresponds with other reported cases[1] and could be on the basis of a direct toxic or sensitivity reaction to the drug.

Histological changes present were non-specific, but compatible with tubular necrosis from any cause. The histological changes reported in the literature, in patients with renal failure attributed to contrast media, were similarly non-specific.

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