THE MANAGEMENT OF ANURIA IN ACUTE MERCURIAL INTOXICATION

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February 22, 1947, a Kolff "artificial kidney" was acquired by the Mount Sinai Hospital through the courtesy of Dr. W. J. Kolff, Kampen, Holland, and Dr. A. Hyman, New York. Since then, patients with existing or impending uremia have been referred as potential objects for its use. In each instance, the oliguria or anuria was ascribed to reparable renal disease, usually of the "lower nephron nephrosis" type, where kidney damage is reversible and where restitutio of kidney function can be anticipated. Prior to admission to this hospital, each patient had received various types of treatment, but the primary purpose in all instances seemed to be directed at increasing the urinary output by administering large volumes of fluids intravenously.

It was only when this medical management had failed to increase the urinary volume that the patients were referred for the possible use of the artificial kidney. At this hospital a period of observation and study was instituted to determine whether the patient was to be subjected to the artificial kidney. It soon became evident to us that the conservative measures introduced in an preliminary period of study and observation could be continued to allow spontaneous resolution of the anuria. The stated purposes of these cases will be published at a future date. It is the purpose of this paper to present as a prototype a patient with acute mercurial intoxication sent to us for anurias by the artificial kidney, who recovered without the benefit of mechanical intervention.

Case Report

CASE 1.—M. W., a 52-year-old white man, was transferred to the Mount Sinai Hospital on May 1, 1947, thirty-six hours after the ingestion of seven tablets (3.5 Gm.) of mercurial chloride in attempted suicide. Vomiting had started approximately twenty minutes after the tablets were swallowed, but no tablets were identified in the vomitus. Diarrhea had started approximately one-half hour after vomiting; it persisted for about eighteen hours, then stopped abruptly. The patient was admitted to another hospital two hours after the tablets were swallowed, and emergency measures were instituted. Gastric lavage was employed using tap water and protein-containing fluids, and several saline irrigations were done. Saline and glucose solutions were administered intravenously to combat shock. A few cubic centimeters of bloody fluid were voided shortly after hospitalization, but for the twenty-eight hours prior to transfer to this hospital, no urine had been passed or obtained by catheter, and the nonprotein nitrogen of the blood rose to 78 mg. per cent. The previous personal history, family history, and habits were noncontributory. There was no history of previous renal disease.

Physical Examination.—The patient was a well-developed, well-nourished and cooperative white man, lying quietly in bed. His complexion was sallow. The skin and mucous membranes appeared pale. Slight periorbital edema was present. The tongue was dry. The heart and lungs were normal. The blood pressure in millimeters of mercury was 140/70. The abdomen was not distended or tender.

Laboratory Findings.—On admission a blood count showed the following: red blood cells 3,100,000 per cu. mm., hemoglobin 83 per cent (Sahli), and white blood cells 18,800 per cu. mm., with 73 segmented polymorphonuclear leukocytes, 8 mononuclear, 14 lymphocytes, 1 monocyte, 3 eosinophils, and 1 basophil. Catheterization of bladder failed to yield any urine. Two cubic centimeters of urine which were obtained on the second day contained epithelial debris, many white blood cells, 5 or 6 red blood cells, and 1 plus albumin. Subsequent findings are indicated on Fig. 1. The blood urea nitrogen on admission was 49 mg. per cent, and the carbon dioxide content of the blood was 31.2 volumes per cent.

Course.—The patient's physical and mental state deteriorated slowly with progressively worsening restlessness and confusion to the time of diuresis on May 8, 1947. A moderately severe stomatitis was noted on May 2 and responded slowly to local treatment. Sacral edema and a few fine moist rales appeared on May 4 (sixth day of anuria) and persisted until the day after the diuresis. Diarrhea started on May 7 and lasted for three days. The blood pressure rose to 150/90 from May 4 to 8 but then returned to normal.

The course of the patient in relation to treatment is indicated in Fig. 1. On the second hospital day, fluids were restricted to less than 1,000 cc., nearly all of which was administered by mouth. Small transfusions of whole blood were used to combat the anemia. A protein-free, salt-free, 1,500 to 2,500 calorie diet was given. Sodium chloride and sodium bicarbonate were administered in accord with duet-
The blood calcium value on May 3 was 11.0 mg per cent, and the phosphorus was 3.0 mg per cent. The stools remained guaiac positive until the seventeenth hospital day. The urine continued to show albumin, white blood cells, red blood cells, and epithelial debris, but no casts were identified until shortly before discharge. The specific gravity of the urine remained low, varying from 1.010 to 1.018 at the time of discharge.

Follow-up.—The patient returned for re-examination and laboratory studies on November 5, 1947. He had no complaints and had resumed full activity. General physical examination was normal. He was able to concentrate his urine to 1.024 after an overnight thirst. The blood urea nitrogen was 11 mg per cent. The phenolsulfonphthalein test revealed that 85 per cent of the dye was eliminated in two hours. The urine was normal, acid, with no sugar, no albumin, and no formed elements on microscopic examination.

Comment

The treatment of acute mercurial intoxication resolves itself into the management of the immediate poisoning and the delayed toxic effects of the drug. The principles of emergency treatment are well established. Attention is initially directed toward combating shock and facilitating the elimination and neutralization of the proximal poison. Shock is combated by efforts to maintain an adequate circulating blood volume; whole blood and plasma are the most effective agents available at present. Rejection of the mercury is accomplished spontaneously by vomiting and diarrhea shortly after ingestion. Gastric lavage with protein-containing fluids is utilized to precipitate the mercury, and gastric irrigations are administered to aid removal of the poison from the large bowel. Peters has warned of the dangers to the water and electrolyte balance (inhomogeneous) in prolonged lavage and irrigation. The use of sodium formality or sulfapyridine to convert the mercuric ion to the insoluble mercuric ions has been advocated, but it is of questionable value and may be fatal if its administration is delayed.

If these measures are not promptly applied and are inadequate, then a significant amount of the drug is absorbed, and the mercury is concentrated at the sites of elimination, where the greater toxic action is consequently exerted. On this basis, the effects of the mercuric derivatives, such as the urticarial rash, collitis, and stomatitis result. Anuria is the dreaded complication of acute mercurial intoxication. In the series of Hull and Meeker of 40 patients who suffered anuria for two or four hours or longer died. No patient survived who was anuric for more than three days. Of the 72 fatal cases, the authors note that “marked shock, relatively few died without uremic manifestations.” The search for extrarenal factors in the production of anuria is essential through the period of anuria.
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period of anuria. However, distinction must
be made between the early anuria due to in-
trinsic circulating blood volume caused by
bleeding, diarrea, and shock, and the later
anuria which persists in the face of normal or
recovered circulating blood volume and is due to
injury of the renal tubules.16 Standard texts
often fail to distinguish between these two
classes of therapy, and the administration of large
amounts of fluid (up to 10 L per day) has been
tried.2 This distinction is therapeutically
important. Several months ago, a twenty-one-
year-old white man in acute anuria was received
here. He had been given 10 L of
intravenously in the forty-eight hours prior to
admission in an attempt to "open up" the
vasculature. Shortly after admission he died in
despite pulmonary edema. Bell notes that
on the histologist's point of view it is difficult
to see how any treatment could force necrotic
tissue to function. It is also clear that the forcing
fluids are of no value in any form of this disease.23
It was recognized in our case that the anuria
manifested at the time of admission to this
hospital was probably due to intrinsic renal
damage. Although it is understood that the
minimum time for administration of BAL is
three and one-half hours after the
injection, it was started forty-eight hours
thereafter in the alimentary tract or kidneys.12
The previously described toxic effects of BAL were
noted. The possibility that the BAL contributed
to the inhibition of the diuresis is not great.14 The
definitive effect of the BAL in this instance cannot
be evaluated. However, at this time, no purpose could be
seen in the use of the previously described
measures, which are directed primarily toward
neutering the toxic effects of lioctone and irrigation
and toward combating acidosis by the intravenous
administration of large amounts of sodium-
containing fluids.12 Our therapy was directed
instead toward the maintenance of electrolyte equilib-
rium and the avoidance of pulmonary edema.
The patient was placed on a protein-free, salt-
free diet (1,500 to 2,500 calories daily), which was
maintained up to the start of diuresis. The
freedom from exogenous protein was introduced
because of the anticipated short course of the
illness and the desire to use the endogenous
protein breakdown as a guide to the course of the
anaemia.11,19 The salt-free diet allowed the
administration of measured amounts of sodium chloride
and sodium bicarbonate to prevent severe acid-
oses. Fluids were restricted to less than 1,000
mL per day to replace the loss by insensible
perspiration.19 No evidence of hemococoncentration
was noted as manifested by the hematocrit.
The marked diuresis in the presence of diarrea
indicates that in the presence of anuria, small
amounts of fluids suffice to maintain an adequate
circulating blood volume. The slightly
increased serum potassium may indicate a release
of intracellular water to the extracellular
compartment. Under this regimen, diuresis occurred
on the eighth day following the onset of anuria.
With the establishment of diuresis, fluids were
increased to replace the output, chlorides were
administered in the form of sodium chloride to
replace the chlorides lost in the diuresis, and pro-
teins were gradually reintroduced into the diet.16,21
Despite the diuresis, the azotemia fell gradually,
and the specific gravity of the urine remained
fairly fixed in its resemblance to glomerular
filtrate.21,23 Examination of the patient six
months later revealed a normal blood urea nitrogen,
a normal phenolpthalein test, and good
urinary concentrating power.
On the basis of available prognostic criteria,
this patient's chances for recovery were
admittedly slight.13 The ingested dose was large,
vomiting delayed, and the initial shock was
followed by persistent anuria. It is to be noted
that the patient was relatively comfortable during
this period of anuria despite the progressive
azotemia. This is ascribed to the adequate
hydration maintained predominantly by oral
fluids, the prevention of severe acidosis, and the
freedom from circulatory embarrassment.
Fishberg cautions that the excessive administration
of fluid involves the danger of precipitating cardiac
failure.14 Kugel in his review of 15 patients with
acute anuria noted that nine showed clinical and
pathologic evidence of pulmonary edema.23 Only
one lived more than nine days. In Wol-
paw's and Adler's series, three patients died of
pulmonary edema, and the fourth died after
aspiration of gastric contents.12 All died before
the ninth day of anuria. Case 2 of Campbell
died of pulmonary edema on the seventh day.17
Ludere and others note the high mortality in the
early days of anuria.17,27

Our experience is in keeping with others that
spontaneous resolution of acute toxic anuria
may be expected to occur from the eighth to the
twelfth days. Bell stressed the regeneration of
tubular epithelium after the first week.11
Consequently, it appears that the treatment of a
potentially reversible anuria is to maintain
the patient until renal repair from the toxic insult
can occur. By the same token, it is essential
that the precipitation of pulmonary edema and
severe electrolyte imbalance must be avoided.
It also becomes apparent that reports of cures
or improvement by mechanical measures should
be evaluated with caution. Kugel questions
two reported cases of "successful" unilateral renal decapsulation.22 In these instances, decapsulation preceded diuresis by several days. Diuresis occurred on the eleventh and twelfth days, when spontaneous diuresis may be anticipated.

A recent case report concerns itself with a patient who ingested a large dose of mercury with subsequent anuria.23 On the fourth day of anuria, following the administration of large volumes of intravenous fluids, peritoneal lavage was started. Prolongation of life, despite peritonitis and generalized edema, is ascribed to peritoneal lavage. Here as well, it is questionable how much prolongation of life can be attributed to the peritoneal lavage which was started in the "premature phase" of the anuria.25 Each of the measures available at the present time, including artificial kidney, intestinal loop perfusions, and peritoneal lavage, has inherent difficulties and dangers.26,27 We feel that these mechanical measures should be initiated only after an adequate period for spontaneous recovery has been permitted and that the need for them will often be obviated by judicious administration of fluids and careful attention to preservation of the normal electrolyte pattern.

Summary

A case of acute mercurocultural intoxication is used to illustrate the principles that have been found effective in aiding the recovery from reversible anuria. The tendency to spontaneous resolution of the anuria is stressed as well as the anticipated time of its occurrence. Because of the reversible nature of the kidney lesion, caution is advised in interpreting the efficacy of advocated mechanical means in the treatment of anuria.

Addendum

Since the preparation of this paper, we have successfully managed another case of anuria due to bichloride of mercury intoxication.

Case 2.—The patient, a 26-year-old Puerto Rican woman, attempted to induce an abortion by vaginal introduction of 2.5 Gm. of bichloride of mercury in tablet form on January 21, 1949. She was transferred to the Mount Sinai Hospital on January 26, 1949, on the fifth day of anuria with symptoms of severe ulcerative vaginitis, stomatitis, and colitis. She was treated with the Kolf artificial kidney for six hours shortly after admission. There was a drop in the blood urea nitrogen from 110 mg. per cent to 31 mg. per cent at the end of six hours. The blood creatinine, uric acid, and phosphorus levels fell from abnormally elevated to normal levels. However, the anuria persisted, and azotemia again became progressive. On February 4 the blood urea nitrogen had reached 115 mg. per cent, but the serum chlorides and carbon dioxide combining power were maintained within normal limits by means of oral administration of sodium chloride and sodium bicarbonate. Only minimal edema was noted during the entire illness. Twenty cubic centimeters of urine were obtained on the eight day following the onset of anuria, and by the twelfth day the urine output had increased to 1,200 cc. in twenty-four hours. Since then, the patient has continued to void large volumes of urine, up to 5,000 cc. daily, with specific gravity ranging from 1.010 to 1.012. The blood chemistries, including urea nitrogen, creatinine, uric acid, phosphorus, calcium, carbon dioxide combining power, were all normal.

The specific role of the artificial kidney in this instance will be discussed in a future publication. Resolution of anuria and oliguria occurred in approximately seven days after the artificial kidney had been applied. In this instance, recovery of the patient may be attributed to the use of the Kolf artificial kidney and to the meticulous care in controlling the fluid and electrolyte balance.

References