Carbon Tetrachloride Nephrosis

Report of Patient Treated Conservatively

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A CASE of anuria resulting from the inhalation of carbon tetrachloride fumes by a man who had been drinking alcoholic beverages in excess is reported to emphasize the dangers of carbon tetrachloride and to indicate the favorable prognosis when proper treatment is instituted. An unusual feature of this case, which we believe never to have been previously reported, was the marked kidney enlargement during the course of the disease, as demonstrated roentgenographically.

Incidence.—Until recent years, lower nephron nephrosis caused by inhalation of carbon tetrachloride fumes has not been considered a common entity. With increasing knowledge and awareness of the disease, however, particularly in the last 5 years, more case reports have been published. Farrier and Smith (2) recently reported a total of 12 cases with 5 deaths in 5,000 admissions over a 2-year period. This was twice the number of cases of subacute bacterial endocarditis, not a medical rarity, diagnosed during the same period of time in their hospital.

Etiology.—The inhalation of carbon tetrachloride fumes affects primarily the kidneys, whereas the ingestion of the liquid causes lesions in the liver (3). Damage to both the liver and the kidneys (the hepatorenal syndrome) has occasionally been reported (4). Konwaler and Noyes (5) list the factors which encourage poisoning by carbon

(1) Reese Air Force Base, Lubbock, Tex.

(2) Farrier, R. M., and Smith, R. H.: Carbon tetrachloride nephrosis; frequently undiagnosed cause of death. J. A. M. A. 143: 965-967, July 15, 1950.

(3) McGee, C. J.: Lower nephron nephrosis; carbon tetrachloride poisoning with report of 3 cases. Am. J. M. Sc. 218: 636, Dec. 1949.

(4) Dillenberg, S. M., and Thompson, C. M.: Carbon tetrachloride poisoning; report of 20 cases with one death. Mil. Surgeon 97: 39-44, July 1945.

(5) Konwaler, B. E., and Noyes, C. B., Jr.: Carbon tetrachloride poisoning; report of cases. California & West. Med. 61: 16-20, July 1944.

tetrachloride as (1) alcoholism, (2) excessive exertion, (3) the ingestion of a heavy meal prior to exposure, and (4) exposure to heat. They further state that alcoholics and those having nephritis, diabetes mellitus, myocardial degeneration, or high blood pressure should not be permitted to work with carbon tetrachloride.

Pathology.—Liver damage, when present, is evidenced by central necrosis. The lesions of the kidney are those of lower nephron nephrosis. Konwaler and Noyes (5) reported a fatal case with "large white kidneys," weighing 350 grams each. McGee (3) reported a case in which the microscopic renal lesions were pigment casts, degeneration of the ascending limbs of Henle's loop, interstitial inflammation at the cortico-medullary junction, and foci of venous thrombosis.

Symptoms.—Exposure to the fumes of carbon tetrachloride results in varying degrees of illness which cover a wide spectrum of clinical states. This spectrum encompasses the person who is stricken with influenzalike symptoms for a day or two, with or without albuminuria, and the person who develops complete anuria. Between these two extremes are many degrees of illness. The symptoms most commonly noted are severe headache, nausea, vomiting, prostration, giddiness, muscle pains, and diarrhea (4). The nausea and vomiting seem to be a universal problem, and, if accompanied by oliguria or anuria, constitute a complicating factor in fluid therapy. The vomiting is usually intractable. A hemorrhagic diathesis is also mentioned (3) (4).

Treatment of this disease must be predicated on the following fundamental considerations:

1. The kidney damage is reversible and the disease self-limited. According to Kugel (6), tubular regeneration begins on the third day after the injury and is complete on the fourteenth day. Spontaneous diuresis occurs by the eleventh or twelfth day.

2. Most patients who die during treatment for anuria or oliguria resulting from poisoning by carbon tetrachloride die as a result of overtreatment. The literature is replete with reports of patients who succumb in congestive heart failure as the result of overzealous fluid therapy (7).

3. Other patients die as the result of potassium intoxication (7) (8).

In general, then, the purpose of treatment is to keep the patient alive until the return of renal function. The patient is assumed to have

(6) Kugel, V. H.: Management of acute toxic nephrosis. Am. J. Med. 3: 188-205, Aug. 1947.

(7) Friedberg, C. K.: Congestive heart failure of renal origin; pathogenesis and treatment in 4 cases of carbon tetrachloride nephrosis. Am. J. Med. 9: 164-174, Aug. 1950.

(8) Hicks, M. H.; Crutchfield, A. J.; and Wood, J. E.: Intestinal lavage in potassium intoxication of lower nephron nephrosis. Am. J. Med. 9: 57-61, July 1950.

lost about 1,000 cc. of fluid per day by respiration and perspiration. If this amount of fluid, plus the amount of fluid lost by emesis and urination is replaced, and the amount of sodium and potassium administered is rigidly restricted, most of the pitfalls of overzealous therapy can be avoided (9). A semblance of nutrition is maintained and ketosis is minimized by the liberal administration of dextrose and vitamins. Serial electrocardiographic studies are made for detecting the occurrence of hyperpotassemia. If hyperpotassemia should occur, such methods as the use of the artificial kidney (7), intestinal lavage (8), peritoneal lavage (10), or replacement transfusions (7) become necessary.

After diuresis has begun, urination may be excessive and the patient may pass in excess of 10,000 cc. in 1 day (9). At this time, hyponatremia, hypopotassemia, hypocalcemia, and dehydration must be avoided by proper replacement therapy. It is conjectured that the diuresis is caused by the poor concentrating power of the convalescing tubules and/or to the previous overhydration.

CASE REPORT

A 27-year-old white male cook presented himself at the dispensary on the morning of 6 October 1950 complaining of sore muscles, nausea and vomiting, and a cough with the production of "yellow phlegm." Physical examination at this time revealed nothing of significance except a markedly reddened pharynx, slight epigastric tenderness, and a temperature of 102° F. He was admitted to the hospital with the diagnosis of influenza and therapy with aureomycin was begun. That evening, the nurse reported that the patient had not voided since admission. Catheterization was attempted, but was unsuccessful. Several hours later the patient spontaneously voided 60 cc. of dark red urine. Urinalysis revealed a specific gravity of 1.021, acid reaction, 4 plus albumin, 6 to 8 erythrocytes and an occasional leukocyte per high power field. No casts were seen at this time, but several days later granular casts appeared in the urine.

Further questioning of the patient revealed that he apparently had not urinated for the previous 48 hours. He stated that he was perfectly well until 30 September 1950, at which time he consumed, over a period of several hours, about a quart of whiskey and an unknown quantity of beer. He was able to drive to work the next morning. He drank an unknown quantity of beer daily up to and including 3 October. On 4 October, at 0800, a repairman cleaned the motors of the refrigerator units in the kitchen in which the patient was working. A 1-gallon pail of carbon tetrachloride, which was open to the air, was used for this purpose. The patient was seated several yards away in front of an open window

(9) Muirhead, E. E.: Lecture on the Treatment of Lower Nephron Nephrosis. South Plains Medical Society Meeting, Lubbock, Tex., September 1950.

(10) Odel, H. M.; Ferris, D. O.; and Power, M. H.: Peritoneal lavage as effective means of extrarenal excretion. Am. J. Med. 9: 63-77, July 1950.

for the hour and a half that the work was in progress. That night the patient drank several more cans of beer. He began to feel sick the next day and reported to the dispensary about 48 hours after exposure to the fumes of carbon tetrachloride. He had no insight as to the relation of the carbon tetrachloride fumes to his illness and it took 2 days of persistent probing into the history before he remembered that he was in the vicinity of carbon tetrachloride fumes.

The patient was extremely ill for 2 weeks. Each day he passed more urine until the tenth day after exposure when the amount reached 1 liter in 24 hours. On the eleventh day, he voided 2,900 cc. and on the fifteenth day, 4,800 cc. of very dilute (sp. gr. 1.007) urine, at which time vomiting ceased. The vomiting had been intractable and had lasted 2 weeks. He failed to respond to atropine, sedation with seconal given rectally, pyridoxine and vitamin B complex intramuscularly and intravenously, or to intramuscular injections of liver extract. During the greater part of these 2 weeks, he complained almost constantly of pain in the left upper abdominal quadrant. The abdomen was extremely tender to palpation and there was marked left costovertebral tenderness to deep percussion. A flat film of the abdomen taken on 9 October revealed the left kidney to be enlarged to about twice the normal size, with the lower pole reaching almost to the transverse process of the fourth lumbar vertebra. The right kidney could not be definitely visualized. Neither kidney was palpable. Serial roentgenograms revealed no decrease in the size of the left kidney until 23 October, 19 days after exposure. An intravenous pyelogram on 6 November, 1 month after admission, revealed a normal urinary tract. The kidneys at this time appeared to be of normal size.

On the eighth, ninth, and tenth days of illness, periorbital edema appeared, apparently the result of excess sodium administration. At no time, however, was there any respiratory distress. Neither were rales in the lung bases ever noted nor was ankle edema demonstrated. About this time swelling of the salivary glands also appeared. The parotids were slightly enlarged and the submaxillary glands markedly so. The orifices of the ducts were not inflamed and the patient had no fever. This swelling disappeared spontaneously after a few days. The blood pressure on admission was 118/88. At no time during the illness did it rise above 140/90. The patient's weight was recorded daily in order to detect hidden edema. It remained stationary during the first 10 days of illness and then gradually fell off until after 3 weeks he had lost a total of 20 pounds. (He then weighed 154 pounds.)

Some of the laboratory findings are shown in table 1. The serologic tests were negative. The cephalin-cholesterol flocculation test was negative on 10 October. On this date also the total protein was 8.2, albumin 5.3, globulin 2.9, icteric index 8, and direct van den Bergh zero. Because of the lack of facilities the carbon dioxide combining power was determined only once, when on the eighth day of illness, it was found to be 47. A concentration dilution test 5 weeks after the

TABLE 1.—*Laboratory findings*

October	6	7	8	9	10	11	12	13	14	15	16	17	18
Day of illness	2	3	4	5	6	7	8	9	10	11	12	13	14
Nonprotein nitrogen (mg. per 100 cc.)	31	31	120	145	100	108	96	100	96	99	95	95	99
Plasma chlorides (mg. per 100 cc.)	.....	.....	.....	.....	346	462	528	495	462	495	501	495	428
Erythrocyte count (millions)	5	.....	.....	4.7	.....	4.5	.....	4.9	.....	5.0	4.9	4.9	4.9
Leukocyte count (thousands)	14	.....	.....	11.0	.....	15.6	16.2	10.2	.....	17.2	13.6	18.2	13.2
Urine:													
Specific gravity	.....	1.021	1.020	.....	.....	1.010	1.008	1.008	1.007	1.005	1.006	1.008	1.007
Albumin	.....	++++	+++	+++	.....	+ +	++	+	+	trace	trace	+	+
Erythrocytes per highpower field	.....	6-8	6-8	6-8	.....	occ*	4-6	occ*	occ*	0	0	0	0
Leukocytes per highpower field	.....	occ*	occ*	2-3	.....	4-6	occ*	occ*	occ*	occ*	occ*	occ*	occ*
Hyaline and granular casts	.....	0	0	.....	.....	+++	+++	0	++	++	0	rare	0

October	19	20	21	22	23	24	25	26	27	28	29	30
Day of illness	15	16	17	18	19	20	21	22	23	24	25	26
Nonprotein nitrogen (mg. per 100 cc.)	99	.....	110	80	66	.....	70	.....	39	.....	.....	25
Plasma chlorides (mg. per 100 cc.)	495	.....	545	520	577	.....	561	.....	653	.....	.....	610
Erythrocyte count (millions)	5.0	4.4	4.3	.....	4.6	.....	4.5	4.6	.....	.....	.....	4.7
Leukocyte count (thousands)	16.8	14.0	14.0	.....	14.1	.....	14.2	7.2	.....	.....	.....	10.6
Urine:												
Specific gravity	1.007	1.007	1.016	1.016	1.007	1.010	1.010	1.008	1.010	1.010	.....	1.007
Albumin	trace	trace	0	0	+	0	0	0	trace	0	.....	0
Erythrocytes per highpower field	0	0	0	rare	0	0	0	0	0	0	.....	0
Leukocytes per highpower field	occ*	occ*	0	occ*	rare	occ*	occ*	occ*	occ*	0	.....	0
Hyaline and granular casts	0	0	0	0	0	0	0	0	0	0	.....	0

*occ = occasional

onset of illness produced a specific gravity ranging from 1.003 to 1.015, indicating continued impairment of tubular function. The phenolsulfonphthalein test was normal at the time. Electrocardiograms taken during the oliguric phase of the illness revealed no evidences of hyperpotassemia.

Treatment.—An attempt to limit the total fluid intake to 1,000 cc. plus the output was made as shown in figure 1. Only 21 grams of sodium chloride was administered intravenously during the oliguric

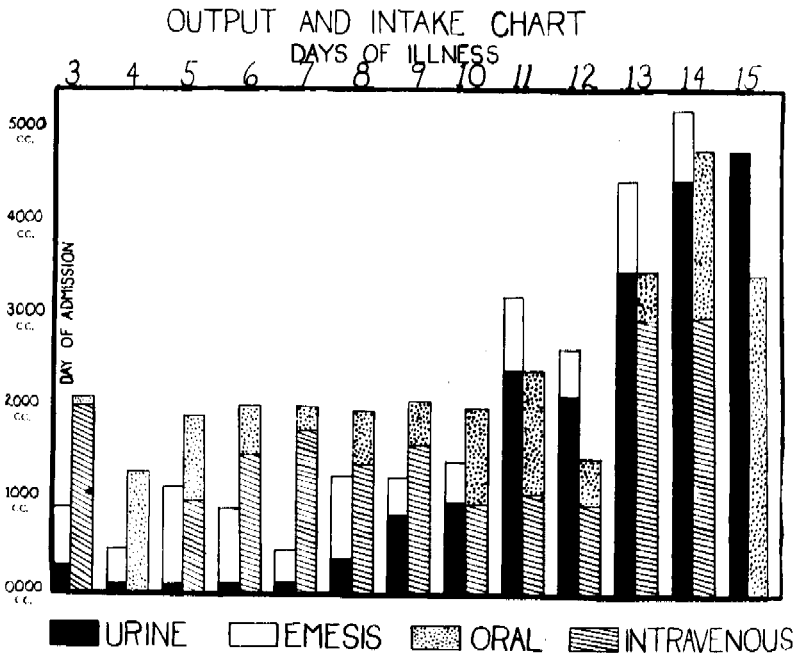

Figure 1.

phase of the illness. The first 9 grams of sodium chloride was administered because of dehydration caused by vomiting. The second and third administrations were for the correction of presumed blood sodium deficiency as evidenced by low blood chlorides. The fourth dose, given intravenously, was to correct an episode of hyperpnea, presumed to have been on the basis of acidosis. Sodium chloride intravenously was administered afterwards during the first days of excessive diuresis when the patient was still vomiting.

Dextrose, in 5 to 50 percent solution comprised the remainder of parenteral fluids. Parenteral vitamins in generous amounts and 1 cc. of liver extract were given daily throughout treatment. Penicillin intramuscularly and aureomycin rectally were given to combat the bron-

chitis which was present on admission and as prophylaxis against intercurrent infection. Seconal suppositories were administered for sedation. The patient was put on a rice diet (Kempner) in addition to other carbohydrate foods. Orange juice, because of its potassium content (even though low), was avoided. He did not tolerate solids or liquids very well until after diuresis had begun. Eight weeks after the onset of illness, the patient was clinically well and had regained the 20 pounds he lost during the first 3 weeks of his illness.

SUMMARY

A patient with lower nephron nephrosis following the inhalation of carbon tetrachloride fumes was treated conservatively and survived. An unusual feature of this case was the kidney enlargement as seen by roentgenograms. For the best results in carbon tetrachloride nephrosis, one should bear in mind that the renal tubules return to function in about 11 days and the mortality of the disease is largely caused by (1) congestive heart failure arising from overtreatment and (2) hyperpotassemia.

Because of the patient's lack of insight concerning the relation of carbon tetrachloride to the possible cause of his illness it is important to probe the history carefully.