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W. Q. Sturner,[1] *B.S., M.D., D.M.J., F.A.C.P. and J. I. Coe,*[2] *M.D.*

Electrolyte Imbalance in Alcoholic Liver Disease

The forensic pathologist is confronted almost daily with instances of sudden and unexpected death in patients with an alcoholic history, who exhibit only disease of the liver at autopsy, often consisting solely of fatty metamorphosis, and whose blood contains little or no ethyl alcohol. The cause of death is usually certified as acute or chronic alcoholism or both, and on occasions includes the type of liver disease, but the exact mechanism(s) remain unknown. Some of those incriminated include hypoglycemia, subtle infection, seizures related to delirium tremens and various metabolic alterations from the diseased liver, including the "Hepatorenal Syndrome" [*1–5*].

With the advent of postmortem chemical determinations in the vitreous humor, it has become possible to support and confirm the diagnosis of a number of pathologic entities such as diabetes mellitus, and to establish conditions in which electrolyte imbalance has occurred [*6,7*]. It was felt that alcoholic patients should likewise be subjected to a vitreous analysis to determine if terminal chemical abnormalities may have contributed to their deaths.

Materials and Methods

Selected alcoholic patients dying suddenly were studied by Offices of the Medical Examiner in Dallas County, Texas and Hennepin County (Minneapolis), Minnesota. In the former group vitreous humor was withdrawn from eight cases for electrolyte and other studies using a Technicon 12 Channel Auto-Analyzer.[3] A separate chloride determination was performed on a Technicon Two Channel Auto-Analyzer.[3] Comparative blood studies were not undertaken, and a complete autopsy was performed in only two instances. In the latter group, twelve alcoholic patients were autopsied and postmortem serum and vitreous chemical analyses were performed by similar instrumentation. These were divided into groups in which hepatic failure evidenced by hyperbilirubinemia was noted (3 cases), renal failure alone indicated by an elevated urea nitrogen was determined (2 cases), and subjects in which neither was chemically confirmed (7 cases). In none of these instances was an obvious anatomic or toxicologic cause of death noted other than liver disease, with the exception of the patient in case #521-72 in which there was terminal massive gastrointestinal hemorrhage.

A separate group of alcoholic deaths from Dallas County, restricted to those dying from acute ethyl alcohol intoxication, were similarly studied for comparison purposes.

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[1] University of Texas Southwestern Medical School at Dallas and the Institute of Forensic Sciences, Dallas, Texas 75235.

[2] Office of the Medical Examiner, Hennepin County, Minnesota and chief, Department of Pathology, Hennepin County General Hospital, Minneapolis, Minnesota 55415.

[3] Technicon Instruments Corp., Ardsley, New York.

TABLE 1—*Vitreous analyses in alcoholics (Dallas County). Deaths with electrolyte imbalance.*

Case Number	Age	Sex	Race	Alc	Cause of death	History	P.M.I.	Vitreous						Blood Other Drugs
								Glu	Na	K	Cl	U.N.	SGOT	
2584-71	30	F	W	0.25	Fatty metamorphosis of liver	Heavy drinking	18	74	133	>10	103	37	250+	Isopropyl Alcohol
0401-72	56	M	W	0.11	Cirrhosis of liver	Heavy drinking	>5	38	138	7.4	104	4	34	None
0434-72	59	M	N	Neg	Hypertensive cardio-vascular disease; chronic alcoholism	Heavy drinking (4 days prior to death)	3	78	131	...	105	6	...	None
0990-72	62	M	N	0.17	Chronic alcoholism	Drinking	>15	66	143	9.2	102	24	18	None
0087-72	60	F	W	0.01	Acute and chronic alcoholism	Heavy drinking	>11	33	132	>10	103	20	218	Acetone and Isopropyl Alcohol
0004-72	64	M	W	0.11	Mild portal cirrhosis of liver	Heavy drinking	>24	24	130	>10	104	10	124	None
1087-72	64	M	W	0.01	Chronic alcoholism	Stomach pains	>5	12	126	9.3	101	17	24	None
2441-72	57	F	W	0.04	Chronic alcoholism	Drinking	>13	84	125	6.5	101	5	24	None

TABLE 2—*Vitreous analyses in alcholics (Hennepin County). Deaths with electrolyte imbalance.*

Case Number	Age	Sex	Race	Alc	Autopsy Findings	History	P.M.I.	Vitreous					Blood		
								Glu	Na	K	Cl	U.N.	Na	Cl	Bilirubin
72-603	37	F	W	Neg	End stage cirrhosis and severe fatty metamorphosis	Chronic alcoholism	<2	25	100	5.1	87	3	100	68	11.0
72-1954	31	M	W	0.33	Cirrhosis and severe fatty metamorphosis of liver	Chronic alcoholism and hepatitis	<2.5	65	120	7.1	94	33	122	79	>10.0
72-2008	57	M	W	Neg	End stage cirrhosis, severe fatty metamorphosis, G. I. hemorrhage	Chronoic alcoholism	<1	31	125	4.0	...	97	120	80	>10.0
70-1534	34	F	Ind	Neg	Cirrhosis and severe fatty metamorphosis	Chronic alcoholism	<4	38	129	5.8	...	38	119	...	...
72-2034	66	F	W	Neg	Moderate fatty metamorphosis, chronis triaditis, chronic brain syndrome, ASHD	Chronic alcoholism	<12	40	128	6.6	89	126	...	...	1.4
72-521	56	M	W	0.32	Massive G.I. hemorrhage from varices, portal cirrhosis with fatty metamorphosis	Chronic alcoholism "Drunk all the time"	<8	45	132	7.7	100	12	121	71	1.4

72-243	49	F	W	Neg	Portal cirrhosis with fatty metamorphosis of liver	Chronic alcoholism "Went on wagon" two days before death	<8	35	130	6.0	104	10	128	81	3.3
71-1791	54	M	W	Neg	Severe emphysema, cirrhosis of liver, inanition	Chronic alcoholism with seizures and "asthma"	<1.5	57	115	5.4	93	11	118	76	1.2
71-1654	54	M	W	0.16	Severe fatty metamorphosis of liver	Chronic alcoholism	<8	26	130	7.0	102	11	120	88	1.1
72-1984	65	M	W	0.32	Early cirrhosis and mild fatty metamorphosis, chronic pancreatitis	Chronic alcoholism	<4	70	127	4.9	107	12	129	88	0.9
71-1534	50	M	W	0.15	Severe fatty metamorphosis of liver	Chronic alcoholism; 28 empty whiskey bottles in room	<10	30	124	7.7	104	15	...	...	...
72-1230	57	M	W	0.09	Fatty metamorphosis	Chronic alcoholism	<10	40	125	4.8	106	20	...	...	...

Results

The eight Dallas County deaths listed in Table 1 showed vitreous chloride values of 105 mEq/l or below in all instances (normal range 105–132 mEq/l, 3–10 h postmortem interval (P.M.I.), S.D. 6.1) [8]. Five of the vitreous sodium values were 131 mEq/l or below (normal range 131–151 mEq/l, 3–10 h postmortem interval, S.D. 4.7) [8]. Ethyl alcohol concentrations in the blood varied from negative (1 case) to moderately high (1 case). Toxicologic analyses revealed no drugs but detected a trace of other volatile substances in two cases. Fatty metamorphosis and moderate cirrhosis of the liver, respectively, were the only disease entities detected in the two cases which were autopsied. There were two other instances in which there was clinically documented cirrhosis of the liver. Death intervals varied from 3 h to more than 24 h, with the latter cases showing changes of early decomposition. One patient had a low glucose value, hypokalemia may have been present in the patient in case #2441-72 and the urea nitrogen was marginally elevated in the patient in case #2584-71.

The twelve Hennepin County deaths listed in Table 2 demonstrated similar abnormalities. Ten of the vitreous chloride values were below 105 mEq/l, and eleven of the vitreous sodium values were 131 mEq/l or below. All serum values obtained revealed corresponding hyponatremia and hypochloridemia. Serum bilirubin levels showed elevations of 10 mg percent or above in the three hepatic failure cases, and there were four cases, including two of the above, showing minimal to marked increases in urea nitrogen. The vitreous glucose concentration was depressed only in the patient in case #603-72. Ethyl alcohol values in the blood ranged from negative (6 instances) to moderately high concentrations (3 instances). Eight patients demonstrated cirrhosis of the liver varying from mild to severe, while four had moderate to severe fatty metamorphosis of the liver without accompanying cirrhosis. All cases were examined within 10 h of death. A toxicologic analysis for barbiturates and similar drugs was negative in eight cases.

Discussion

This series of twenty cases reveals a mixed pattern of alcoholism and its disease ramifications in the liver, but demonstrated a terminal sodium or chloride depletion or both in each instance. While severe cirrhosis of the liver with accompanying hepatic failure was documented at several autopsies, some cases revealed only fatty metamorphosis of the liver and no other significant anatomic disease or toxicologic finding sufficient to cause death.

The reason for the electrolyte imbalance is not clear. It is probably not related to ethyl alcohol itself, as many cases have none or minimal amounts detected in the blood. Furthermore, most patients dying from acute alcohol intoxication have demonstrated a relatively normal postmortem vitreous electrolyte pattern (see Table 3). Although hypoglycemia may be operative in other cases of sudden death in the chronic alcoholic, seven of the eight Dallas County cases (1087-72 the exception: 12 mg percent, > 5 h P.M.I.) with electrolyte imbalance had relatively normal glucose concentrations (normal 27–180 mg percent, 3–10 h P.M.I.; 18–106 mg percent, 10½–29 h P.M.I.) [8]. Similar findings in the Hennepin County cases were documented with a single instance of a decreased glucose noted (72-603: 25 mg percent, <2 h P.M.I.). It is known that alcoholics vomit in the postinebriation state, and the loss of gastric juices such as HCl during excessive or prolonged vomiting might influence the fluid and electrolyte status in their system. Changes varying from focal hemorrhagic gastritis to upper gastrointestinal lacerations (Mallory-Weiss Syndrome) have been documented at autopsy in the alcoholic, and even a small and

TABLE 3—*Vitreous analyses in alcoholics (Dallas County). Deaths from acute alcohol poisoning.*

Case Number	Age	Sex	Race	Alc	History	P.M.I.	Vitreous					Blood Other Drugs
							Glu	Na	Cl	U.N.	SGOT	
0433-72	50	F	W	0.61	Heavy drinking	12	35	148	118	11	59	None
0009-72	45	M	W	0.48	Alcoholic	20	30	145	115	23	129	None
1031-72	50	M	W	0.38	Heavy drinking	18	60	145	120	18	118	None
0341-72	61	M	W	0.43	Heavy drinking	20	37	145	123	12	54	...
1073-72	59	F	W	0.42	Dead in bathtub	20	26	140	120	14	...	None
0982-72	46	F	W	0.48	Depressed	6	35	148	124	7	50	0.01 mg% Darvon®
1358-72	52	M	W	0.36	Heavy drinking	4	40	152	129	25	35	...
2365-72	39	F	W	0.36	Heavy drinking	4	36	149	131	5	10	0.2 mg% Phenobarbital

unsuspected loss of blood prior to death could tip a previously existing delicate chemical balance of the body.

Cirrhosis of the liver is known to have accompanying hyponatremia, frequently even without evidence of renal failure; and a decrease in the concentration of chloride, with or without an accompanying azotemia, has received clinical documentation. However, it is not clear if one or more such alterations exist in the alcoholic patient with only fatty metamorphosis of the liver, and without hepatic or renal failure or both. The present study would indicate that such an electrolyte imbalance can develop in alcoholics showing severe fatty metamorphosis alone, without evidence of cirrhosis or the "Hepatorenal Syndrome." It may, moreover, be significant in the terminal mechanism of death in these patients.

Summary

Twenty alcoholic patients dying suddenly and unexpectedly exhibiting a variety of liver disease and sub-lethal concentrations of ethyl alcohol in the blood were selected from two jurisdictions. Postmortem vitreous chemical analyses were performed and some corroborative serum studies were obtained. A marked depletion of sodium or chloride or both was demonstrated in each of the cases, indicating that electrolyte imbalance was present at the moment of death. These included four instances of liver disease consisting solely of fatty metamorphosis and in which there was no chemical evidence of hepatic or renal failure. Various factors, alone or in combination, may be responsible for this alteration, but it probably is not directly related to acute ethyl alcohol intoxication, carbohydrate dysfunction resulting in terminal hypoglycemia, or the severity and extent of the liver disease.

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Department of Pathology
University of Texas Southwestern Medical School at Dallas
5323 Harry Hines Boulevard
Dallas, Texas 75235