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TREATMENT OF INTRACTABLE ASCITES FOR PATIENTS WITH A TERMINAL GYNECOLOGIC MALIGNANT TUMOR---REINFUSION OF CELL-FREE AND CONCENTRATED ASCITIC FLUID---

(gynecologic malignant tumor/cell-free ascites/reinfusion)

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We utilized the reinfusion technique developed for treatment of intractable ascites in liver cirrhosis for treatment of intractable ascites in three patients with terminal gynecologic malignant tumor. The re-infusion of the cell-free, concentrated ascitic fluid was effective and the BUN, uric acid and excessive minerals were removed from the serum and yet the total protein was unchanged. This treatment leads to symptomatic relief and prolongs the survival time.

Ascites is one sign of a terminal gynecologic malignant tumor and this fluid is intractable for treatment. Diuretics, steroids and anti-carcinomatous agents are usually prescribed for such patients. Withdrawal of the ascitic fluid is necessary when sensations and dyspnea are oppressive. When a rapid puncture is done, shock may occur due to an acute decrease in abdominal pressure and the loss of a large quantity of protein. We previously reported an effective system for reinfusion of sterilized, cell-free and concentrated ascitic fluid utilizing a therapeutic modality of intractable ascites in cases of cirrhosis of the liver (1).

We now report a new technique to treat intractable ascites in patients with a terminal malignant tumor of the reproductive organs.

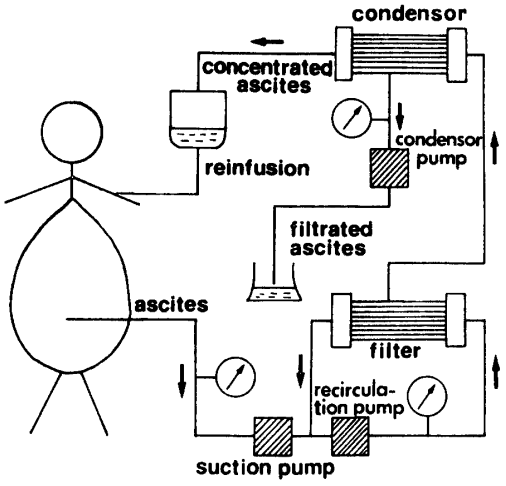

Fig. 1. Flow chart of our apparatus for the treatment of intractable ascites.

METHODS

The apparatus used for the treatment is KURASCIT (KM 6000, KURARAY, Co. LTD.), consisting of a polyvinyl alcohol hollow fiber filter (PVAHF) and a cellulose hollow fiber ultrafilter (CHF). Removal of malignant cells and bacteria is obtained by filtration through the PVAHF with a pore size of 0.2 μ and an effective surface area of 0.6 M^2.

Ascitic fluid filtrated through the PVAHA is concentrated with the CHF having a pore size of 0.003 μ and an effective surface area of 2.0 M^2 at a desired concentration of total protein, by regulation of the negative pressure.

The concentrated ascitic fluid is continuously reinfused into the vein. 3 volume-limited pumps enable the withdrawn ascitic fluid to circulate throughout the system. The first pump is positioned to allow a flow of ascitic fluid from the peritoneal cavity to the PVAHF, the second pump allows flow from the PVAHF to the CHF, and the third pump is concerned with the flow from the CHF to the filtered ascitic fluid.

The velocity and concentrating ratio of the fluid can be regulated.

A flow chart of the apparatus is shown in Fig.1. Three patients with intractable ascites were treated with 5 re-infusions.

The diagnoses were as follows: embryonal carcinoma of the

Table I. DURATION OF TREATMENT SESSIONS AND THE VOLUME OF ASCITIC FLUID

	Duration (mins)	Volume (ml) total filtrated fluid	Volume (ml) condensed fluid
Range	125–240	2600 – 4285	400 – 1285
Mean	180	3398	798

Fig. 2. Pap. smear; left: adenocartinoma cells on the inner surface of the PVAHF. right: no cells in the filtrated ascites.

ovary, Krukenberg's tumor, carcinomatous peritonitis of a uterine cervical cancer.

All patients were prescribed rest and diuretics, and as these measures proved to be ineffective, we attempted a rapid control of the ascitic fluid and symptomatic relief, using this reinfusion system.

RESULTS

This reinfusion method was effective in all cases and the amount of ascitic fluid was reduced. The volume of ascitic fluid removed and duration of treatments are shown in Table I.

As the PVAHF has a pore size of 0.2 μ, all cells, bacteria and substances with a molecular weight of more than 3,000,000 were removed from the drained ascites. Adenocarcinoma cells were present on the inside surface of PVAHF but not in the filtrated ascites (Fig.2).

Table II. BIOCHEMICAL DATA ON ASCITIC FLUID OF A PATIENT WITH EMBRYONAL CARCINOMA

Ascites	1 st			2 nd		
	original	filtrated	concentrated	original	filtrated	concentrated
Volume (ml)	3645	2300	745	4385	2500	1285
T-protein (g/dl)	3.5	0	6.0	3.2	0	10.7
Alb (%)	60.0	—	58.3	58.5	—	56.8
a_1-gl. (%)	4.3	—	4.5	6.3	—	6.6
a_2-gl. (%)	6.7	—	7.8	6.6	—	7.5
β-gl. (%)	5.9	—	6.4	9.8	—	10.6
γ-gl. (%)	23.1	—	23	18.6	—	18.4
BUN (mg/dl)	33.1	28.5	13.5	8.4	7.7	0.3
Crea. (mg/dl)	1.2	1.3	0.6	0.5	0.4	0.1
Na (mEq/L)	138	137	144	136	137	152
K (mEq/L)	4.6	3.6	1.8	2.9	2.9	0.1
Cl (mEq/L)	96.8	110.4	123.7	101.8	108.4	130.6
Ca (mEq/L)	4.0	2.5	2.2	4.2	3.1	0.6
T-cholesterol(mg/dl)	68	3	120	65	2	178
Uric acid (mg/dl)	7.7	6.1	3.5	2.0	2.1	0.9
t-bil. (mg/dl)	0.59	0.13	0.71	0.58	0.11	1.92
d-bil. (mg/dl)	0.15	0.22	0.18	0.18	0.21	0.67

As the CHF has a pore size of 0.003 μ and removes substances with a molecular weight of less than 13,000, the concentrated fluid after passage through the CHF was shown to contain a higher concentration of total protein and albumin than was present in the ascitic fluid, and a lower concentration of BUN, uric acid and potassium in the serum than was present before treatment.

The results of biochemical data are shown in Tables II and III.

All patients tolerated the re-infusion and there was an improvement in general physical condition.

The duration of re-infusion ranged from 3.5 to 5 hrs (mean about 4 hrs). The volume of concentrated ascites was from 400 ml to 1285 ml (mean about 800 ml). In patients with malignant ascites, the protein contents in the ascitic fluid were higher

Table III. BIOCHEMICAL DATA ON ASCITIC FLUID OF A PATIENT WITH KRUKENBERG'S TUMOR

Ascites	1 st			2 nd		
	original	filtrated	concentrated	original	filtrated	concentrated
Volume (ml)	3780	2300	880	2980	1700	680
T−protein(g/dl)	4.5	0	9.6	4.5	0	10.4
Alb. (%)	60.4	—	58.8	61.5	—	59.5
α_1−gl. (%)	7.5	—	7.5	6.4	—	8.0
α_2−gl. (%)	9.7	—	10.4	9.5	—	10.9
β −gl. (%)	14.7	—	13.3	13.7	—	11.6
γ −gl. (%)	7.5	—	9.7	8.6	—	10.1
BUN (mg/dl)	27.0	25.0	25.0	7.0	8.0	7.0
Crea. (mg/dl)	0.9	0.6	1.2	0.8	0.6	1.2
Na (mEq/L)	140	143	137	139	143	139
K (mEq/L)	4.0	3.9	3.8	3.7	3.3	3.4
Cl (mEq/L)	103	109	98	101	113	92
Ca (mEq/L)	7.4	5.0	10.9	7.3	4.8	11.0
T−cholesterol (mg/dl)	75	0	190	62	0	174
Uric acid(mg/dl)	3.2	2.8	3.7	2.3	2.0	2.8
t −bil. mg/dl	0.5	0	1.4	0.3	0	1.5
d −bil. mg/dl	0.2	0	0.3	0.1	0	1.2

than those noted in patients with benign ascites. Therefore, the ascitic fluid was concentrated by ultrafiltration 2 to 3 times and the duration of re-infusion was prolonged.

The biochemical data on the serum was little changed before and after each treatment. The total protein did increase slightly and uric acid and BUN levels decreased to some extent. (Tables IV-VI)

The clinical course in one patient with embryonal carcinoma is summarized in Fig.3.

On the 22nd day after the first treatment, she complained of an oppressive sensation and on the 25th day the treatment was repeated. Thereafter, the abdominal girth increase was decreased. The oppressive sensation next appeared on the 73th day after the second treatment. Thus, this method is effective in decreasing the production of ascitic fluid.

Fever of a mild degree occurred in all with re-infusion, but subsided when antipyretics were injected into the peritoneal cavity. Pulmonary edema and infection never occurred.

Table IV. LABORATORY DATA OF A PATIENT WITH EMBRYONAL CARTINOMA BEFORE AND AFTER TREATMENT

serum		1 st		2 nd	
		before	after	before	after
RBC	$\times 10^4/mm^3$	290	272	368	333
Hb	g/dl	10.0	9.3	13.0	11.0
Ht	%	28.9	27.1	36.4	32.8
WBC	$/mm^3$	8400	7100	8100	8400
Na	mEq/L	138	136	140	137
K	mEq/L	4.9	5.5	4.1	3.6
Cl	mEq/L	98	104.0	99.4	96.7
Ca	mEq/L	4.6	5.1	4.5	5.2
Uric acid	mg/dl	7.9	7.6	3.5	2.2
T-cholesterol	mg/dl	173	198	152	177
T-protein	g/dl	6.4	7.0	6.4	7.0
GOT	U	8	12	22	19
GPT	U	3	5	15	10
ALP	KU	5.9	6.1	6.1	4.8
t-bil	mg/dl	0.36	0.49	0.74	1.04
d-bil	mg/dl	0.04	0.03	0.18	0.34
LAP	GR/ml	100	110	83	97
LDH	U	214	218	231	310
CHE	PH	0.61	0.79	0.51	0.50
γ-GTP	U	4	5	15	16
BUN	mg/dl	32.1	27.5	11.3	9.7
Crea.	mg/dl	1.3	1.3	0.6	0.6

Table V. LABORATORY DATA OF A PATIENT WITH KRUKENBERG'S TUMOR BEFORE AND AFTER THE TREATMENT

serum		1 st		2 nd	
		before	after	before	after
RBC	$\times 10^4/mm^3$	443	401	449	408
Hb	g/dl	12.9	11.5	12.7	11.6
Ht	%	38.5	34.2	39.1	35.3
WBC	$/mm^3$	4800	5500	6600	7100
Na	mEq/L	139	142	137	135
K	mEq/L	4.6	4.2	4.4	4.2
Cl	mEq/L	99	103	108	93
Ca	mEq/L	8.6	8.1	8.5	8.0
Uric acid	mg/dl	3.3	2.2	3.5	2.2
T-cholesterol	mg/dl	137	109	126	137
T-protein	g/dl	5.2	5.8	5.1	5.5
GOT	U	14	16	19	18
GPT	U	10	9	13	13
ALP	U	26	23	25	27
t-bil	mg/dl	0.4	0.3	0.3	0.2
d-bil	mg/dl	0.1	0.2	0.2	0.1
LAP	U	37	31	37	32
LDH	U	265	281	330	285
CHE	U	552	449	662	552
γ-GTP	U	8	6	7	6
BUN	mg/dl	26	20	8	16
Crea	mg/dl	0.9	0.9	0.9	0.9

Table VI. LABORATORY DATA OF A PATIENT WITH CARCINOMATOUS PERITONITIS OF UTERINE CERVICAL CANCER BEFORE AND AFTER THE TREATMENT

serum		before	after
RBC	$\times 10^4/mm^3$	238	190
Hb	g/dl	8.4	6.7
Ht	%	25.2	20.8
WBC	$/mm^3$	31900	15300
Na	mEq/L	136	135
K	mEq/L	3.5	3.4
Cl	mEq/L	98	99
Ca	mEq/L	10.2	10.6
Uricacid	mg/dl	3.4	2.4
t-cholesterol	mg/dl	96	85
t-protein	g/dl	4.5	4.7
GOT	U	25	25
GPT	U	21	18
ALP	U	63	62
t-bil	mg/dl	1.4	0.8
d-bil	mg/dl	0.7	0.5
LAP	U	44	44
LDH	U	233	526
CHE	U	226	130
γ-GTP	U	17	17
BUN	mg/dl	18	16
Crea	mg/dl	0.7	0.9

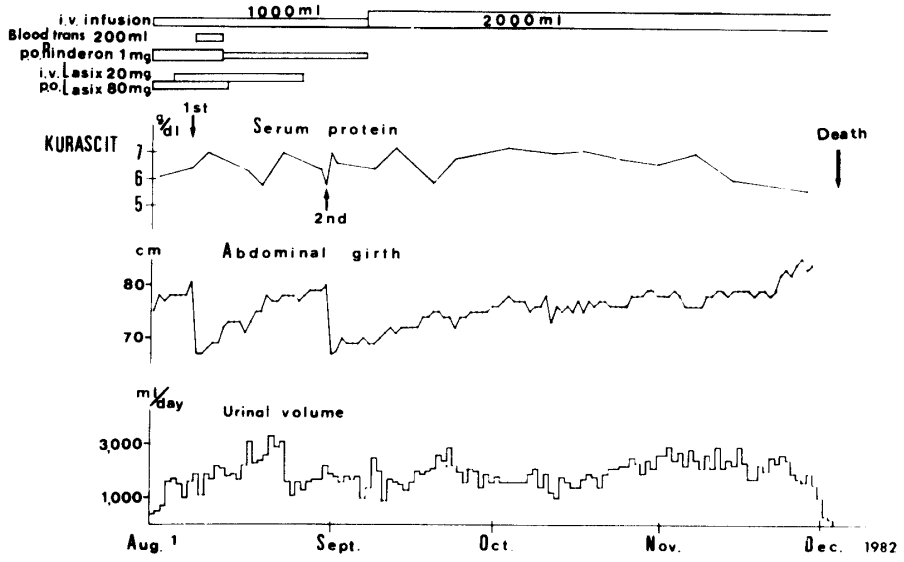

Fig. 3. The clinical course of a patient with embryonal carcinoma.

DISCUSSION

Ascites re-infusion is effective for the treatment of intractable ascitic fluid in patients with liver cirrhosis (2-6). Nevertheless, this approach is not practical as cancer cells are present in the malignant ascitic fluid.

To reinfuse this carcinomatous ascites, the cancer cells must be removed. The apparatus which will remove these cells consists of a cellulose asetate hollow fiber filter (CAHF) and a polyacrylonitrile hollow fiber ultrafilter (PANHF) (7,8), and of PVAHF and an ethylenvinyl alcohol hollow fiber ultrafilter (EVAHF) (9). Our apparatus consisted of PVAHF and CHF.

This method can be utilized with no danger of dissemination of the cancer cells. Cancer cells were present on the inside surface of PVAHF but not in the concentrated ascitic fluid, as determined by Fig.2. This therapy leads to the removal of BUN, uric acid and excessive minerals and is effective in retaining the total protein in the plasma. Reinfusion of the ascites is a rational approach to utilize self-albumin and this treatment will have a diuretic effect due to an increase in blood volume and renal plasma flow (RPF).

Malignant ascites contains a large amount of cells and other tissues. Consequently, function of this apparatus is not smooth because of fibrin, cells and substances present on the inside surface of PVAHF. Therefore, we injected 10,000 I.U. Heparin into the circuit and 5,000 I.U. Heparin into the peritoneal cavity.

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