MEDICAL GRAND ROUNDS

Parkland Memorial Hospital

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"Cardiovascular Changes in Cirrhosis of the Liver"

by

F. A. Bashour, M.D.

Case 1, [redacted]

A 16 year old school girl was admitted to the hospital on [redacted], 1959 with an upper respiratory tract infection. This episode was believed to be viral in origin and was not related to her chronic illness.

The patient was apparently well until the age of 9 when she began complaining of exertional dyspnea and easy fatigability. At that time, her parents noticed that the child had some cyanosis of the lips and clubbing of the digits. At the age of 13, in 1956, she developed subjective fullness in the LUQ of the abdomen and abdominal swelling. A physician who was consulted found an enlarged liver and spleen. Exploratory laparotomy disclosed an enlarged nodular liver with microscopic evidence of portal cirrhosis, congestive splenomegaly, portal hypertension (portal vein pressure 310 mm of citrate). Splenectomy was performed. The spleen weighed 340 grams. X-ray studies revealed patent splenic and portal veins.

At the age of 15, she was readmitted to the same hospital with the diagnosis of conversion reaction and probable pulmonary arteriovenous fistula. Physical findings were essentially the same as on previous admission: marked clubbing of the digits, cyanosis of the lips and enlarged liver. Right heart catheterization demonstrated no intracardiac right to left shunt, normal right heart pressures and an arterial oxygen saturation of 89.6% on room air breathing and 90% on 100% O_2 breathing. The arterial CO_2 tension was 36 mm Hg and 39 mm Hg respectively. The liver function tests done at that time revealed a 10% BSP retention, a 4+ cephalin flocculation, 8 units Thymol turbidity, total protein 6.3 gm (albumin 2.6, globulin 3.7), SGOT 56 units/ml, and total serum bilirubin of 1.3 mg%.

When examined at [redacted], the patient was in no distress, her blood pressure was 126/60, pulse 120/min., respiratory rate 24/min. and an oral temperature of 102° F. The lips were cyanotic, moderate conjunctival injection and plethora of the face. The lungs were clear, several spider nevi were seen over the thorax. The heart was normal in size, loud M_1, P_2 was greater than A_2. No murmurs were heard. The liver edge was felt 3 fingers below the right costal margin. A transverse scar was present in the LUQ. Marked clubbing of the digits and minimal palmar erythema were noted. A trace of pretibial edema was present.

The pertinent laboratory findings were: hemoglobin blood level 14.8-15.3 gm%, hematocrit 43.7%, BSP retention 37%, serum bilirubin 0.8 mg%, cephalin flocculation 4+ in 48 hours, thymol turbidity 5.7 units, alkaline phosphatase 7.0 BU, total serum proteins 6.6 gm (albumin 2.8, globulin 3.8), prothrombin time 12 sec (control 12 sec), venous pressure 11-14 cm of citrate, circulation time 10 sec, total vital capacity 2.9 (85% of predicated). The cardiac series revealed a normal heart size, and no abnormal pulsations. The pulmonary vascular volume was within normal limits. Very small radiodensities were identified in the right lower lung field. The electrocardiogram revealed non-specific ST-T waves changes.

The patient was seen on several occasions in the emergency service and admitted to the hospital with pneumonia, upper gastrointestinal bleeding and drug intoxication. In [redacted], 1964, the heart was found to have increased in size and a pansystolic murmur was heard at the apex. The electrocardiogram at that time revealed diastolic overloading of the left ventricle. The patient refused further studies and later was transferred out of the city.

COMMENTS: The patient is believed to have had Juvenile cirrhosis.

Case 2, [redacted]

A 45 year old woman was admitted to [redacted] because of profuse G. I. bleeding. On [redacted] 1960 she had tarry stools, and experienced one fainting spell. On [redacted] 1960 she again noticed that her stools contained large quantity of fresh blood. When she was brought to [redacted], the patient was in hemorrhagic shock, for which she received several units of blood. Physical examination revealed an emaciated woman with slightly icteric sclera. The neck veins were flat, the lungs were clear. The heart was normal in size and an ejection systolic murmur was heard over the base. The blood pressure, after the transfusion, stabilized at 130/90. Palpable nodes were felt in both axillae. The liver edge was felt 7 cm below costal margin, but the liver appeared nodular and firm, and not tender. The spleen was not palpable. There was no peripheral edema. Spider nevi and palmar erythema were not seen.

Hemoglobin blood level was 9.5 gm% (after transfusion). The liver function tests performed on [redacted]/60 were: serum bilirubin 0.7 mg%, cephalin flocculation 1+, Thymol turbidity 2.1 units, alkaline phosphatase 24.7 B.U., and a prothrombin time 12.0 sec.

Esophagoscopy and gastroscopy revealed large varices in the lower third of the esophagus and over the posterior wall of the stomach. Injection of some of the large varices with a sclerosing substance was performed. A splenogram was done on [redacted]/60, and revealed obstruction of the portal vein. The portal vein ended abruptly in the porta-hepatis forming a serpinginous, tortuous collection of dilated veins. A liver scan revealed a grossly nodular liver pattern.

In 1957, the patient had a left mastectomy and bilateral oophorectomy for a duct-cell carcinoma of the left breast. In [redacted], 1960, a right mastectomy, removal of axillary lymph nodes and radiation of the axillary regions were accomplished.

The condition of the patient progressively worsened with evidence of further liver cell dysfunction and metastasis. On [redacted]/60, the

patient became markedly icteric and had multiple mestastatic lesions throughout the chest wall. Her serum bilirubin rose to 13.4 mg%, alkaline phosphatase to 41.3 B.U., Thymol turbidity to 15.8 units, with 1-3+ cephalin flocculation.

COMMENTS: The patient had complete obstruction of the portal vein at the porta-hepatis with the development of esophageal and gastric varices. The patient bled profusely from these varices. Most probably the portal venous obstruction was caused by metastatic process to the lymph node in the porta-hepatis with secondary thrombosis of the portal vein.

PULMONARY AND PERIPHERAL GASEOUS EXCHANGE

IN CASES 1 AND 2

	SaO_2	Peripheral Δ AV O_2		A-a gradient (mm Hg)	
		(%)	mm Hg	Room air	100% O_2
Case 1	89	4	8	64	577
Case 2	95	26	76	5	69
Normal	94.9 ± 2.6	41.7 ± 12.8	49 ± 7	13 ± 6	48 ± 16

Case 3, [redacted]

A 30 year old colored man was apparently well until a year prior to admission ([redacted] 1962), when he began noticing some ankle swelling, after being up all night drinking Vodka and Bourbon. Four months PTA, he started complaining about some exertional dyspnea, which was followed by orthopnea and paroxysmal nocturnal dyspnea. For 3 weeks PTA, he has had dark-tea colored urine.

The patient began drinking at the age of 17, consuming one-fifth to one pint of whiskey daily. His protein intake was probably deficient, as he did not eat when he drank. He denied any previous episodes of jaundice or symptoms referable to the liver or heart.

Physically, he appeared emaciated and dyspneic. His blood pressure was 130/108 on admission, his pulse rate was 140/min. and his respiratory rate 28-32/min. The sclera were slightly icteric, and he had early arcus senilis. Visual fields revealed a right

homonymous hemianopsia. The lungs were clear. The heart was enlarged, a ventricular gallop and an apical systolic murmur (grade i) were heard. The P_2 was greater than A_2. There was no paradoxical pulsations. The liver edge was felt 2 fingers below the costal margin, the spleen was not palpable. A marked wasting of the shoulder muscles and moderate clubbing of the digits were noted. A hyperactive knee jerk was present.

The hemoglobin blood level was 11.8 gm%, hematocrit 28%, serum bilirubin 2.2 mg%, BSP retention 29%, cephalin flocculation 2+, alkaline phosphatase 13 B.U., Thymol turbidity 4 units, total serum protein 6.4 gm% (albumin 4.2, globulin 2.2), prothrombin time 12.5 sec, SGOT 65 units/ml.

On [redacted]/62, the venous pressure was 26 cm and circulation time 50 sec. After one week of treatment ([redacted]/62), his venous pressure fell to 11 cm and CT to 21 sec. Similarly his body weight dropped from 137 lbs. on admission to 123 lbs. on [redacted]/62, and to 115 lbs. on [redacted]/62. The therapeutic regime consisted of bed rest, hospital diet with supplement of Vit. B_1, and B complex, Digitalis and diuretics.

On his discharge from the hospital, the patient had only a moderate cardiomegaly and a blood pressure of 100/75. Both the ventricular gallop and the apical systolic murmur had disappeared. His cardiac status was stable from discharge to [redacted], 1964. From that date to [redacted], 1965, he was in and out of cardiac decompensation.

The patient was thought to have "Nutritional Heart Disease", cerebral embolism and cardiac decompensation.

Table 1. Study on arterial oxygen during the breathing of room air and the breathing of 15 per cent O_2 in patients with cirrhosis of the liver.

	Room Air		15% O_2	
Case	O_2 saturation (%)	A-a gradient (mm Hg)	O_2 saturation (%)	A-a gradient (mm Hg)
1	94	25	90.6	15
2	92	24	89	9
3	92	31	90	18
4	80	50	72	22
5	89	46	78	28
Mean	89	35	84	18

Table 2. Pulmonary venoarterial admixture, using the 100% oxygen method (subject is at rest).

		A-a gradient (mm Hg)	
	n	range	mean
A. Cirrhosis of the Liver	20	14-466	146.4
B. Clubbing of Digits	17	159-597	369
C. Normal Digits	11	31- 86	48.1

A-a gradient = Alveolar-arterial O_2 tension gradient in mm Hg.

Table 3. The effect of exercise on the pulmonary venoarterial admixture in patients with cirrhosis of the liver (using 100% O_2 breathing).

		A-a gradient (mm Hg)					
		Rest		Exercise		Δ Ex - R	
	n	mean	(range)	mean	(range)	mean	(range)
Cirrhosis	20	146.4	(14-466)	207.6	(27-610)	+61.2	(-5 to 201)
Normal	11	48.1	(31-86)	58.1	(18-93)	+10	(-13 to 36)

A-a gradient = Alveolar-arterial O_2 tension gradient in mm Hg.

Table 4. Pulmonary gaseous exchange in patients with cirrhosis of the liver after portacaval anastomosis.

	Room Air Breathing				100% O_2 Breathing		100% Breathing and Exercise		Δ Ex-R
Case	SaO_2 (%)	PaO_2 (mm Hg)	$PaCO_2$ (mm Hg)	A-a gradient (mm Hg)	Pa O_2 (mm Hg)	A-a gradient (mm Hg)	PaO_2 (mm Hg)	A-a gradient (mm Hg)	A-a gradient (mm Hg)
23a.	83	49							
23b.	86	57	37	59	311	363	110	564	+201
24b.	90	73	31	49	308	371	287	394	+ 23
25b.	94	80	31	43	293	384	---	---	---
26a.	--	--	--	--	635	35	---	---	---
26b.	95	78	24	43	627	54	617	62	+ 8

a: Preoperative b: Postoperative SaO_2: Systemic arterial O_2 saturation

Δ Exercise-rest = Change in A-a gradient after exercise

Table 5. Peripheral gaseous exchange in patients with cirrhosis of the liver.

	Systemic Arterial O_2 Saturation (%)	Arteriovenous difference across the hand		
		Oxygen Saturation (%)	O_2 Tension (mm Hg)	CO_2 Content (vol %)
1*	93	1.6	0	+0.29
2*	89	4.0	8	-1.42
3*	88	16.0	19	+2.59
4**	90	7.0	16	+1.03
5	90	22.0	20	+4.18
6	94	29.0	44	+6.18
7	93	39.0	44	+3.14
8	81	21.0	14	+2.78
9	92	30.0	48	+3.86
10	94	47.0	37	+2.92
11	98	53.0	72	---
12	95	64.0	--	+2.73

* Clubbed Digits

** Marked Palmar Erythema

Table 6. Blood gas measurements under ambient conditions*.

	Normal	Clubbed fingers No.	Clubbed fingers Mean
Arterial O_2 saturation (%)	94.9 ± 2.6	23	85.7 ± 9.5
Arterial O_2 tension (mm Hg)	85 ± 13	18	59 ± 15
Arteriovenous O_2 saturation difference (%)	41.7 ± 12.8	23	7.5 ± 4.6
Arteriovenous O_2 tension difference (mm Hg)	49 ± 7	18	8 ± 5.5
Arterial CO_2 content (M/ML)	20.4 ± 1.4	17	21.9 ± 4.1
Arteriovenous CO_2 content difference (volume %)	2.03 ± 1.59	17	0.46 ± 0.78
Alveolar-arterial O_2 tension (mm Hg)	13 ± 6	9	44 ± 18

*At room temperature (24 to 25° C.) ambient oxygen averages 20.85%.

Arteriovenous differences are measured across the hand [brachial artery to cephalic vein].

Table 7. Alcohol and the heart: Historical events.

Walshe	1873	Fibrosis in the Myocardial Wall
Bollinger	1884	"Munchen Bierherz": Cardiac dilatation, hypertrophy
Aufrecht	1895	"Alcoholic Myocarditis"
Mackenzie	1902	"Alcoholic Heart Disease"
Graham Steell	1906	Similarity of Alcoholic Heart Disease to Beriberi
Aalsmer-Wenckebach	1929	Beriberi Heart Disease
Laubry	1930	"Myocardie"
Keefer	1930	Hyperkinetic State in 1/3 of Beriberi H. D.
Weiss-Wilkins	1937	Occidental Beriberi
Blankenhorn	1946	Alcoholic with Poor Response to Vitamin B
Eliaser-Giansiracusa	1952	Electrocardiographic Changes
Evans	1959	Specific T Waves

Table 8. Cardiac findings in 50 patients with Cirrhosis of the Liver. (Studied at Parkland Memorial Hospital).

Age = 38-82 years Sex M/F = 31/19

Weight of the Heart: 200-560 gm.

Weight of the body: 75-200 lbs.

Evidence of Cardiac Hypertrophy: in 21 patients

Microscopic findings:

A. interstitial edema in 9 (18%)

B. myocardial fibrosis in 19 (38%)

C. endocardial thickening in 3

D. mural thrombi in 2

E. Fatty invasion and degeneration in 10 (20%)

Clinical and Pathological evidence of heart failure in 4 (or 8%)

(in absence of known forms of heart disease).

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