LABORATORY FINDINGS IN SYMPTOMLESS CLONORCHIASIS*

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Clonorchiasis is an important human parasitic disease and widely prevalent in southern part of Korea. Since clinical and laboratory findings of clonorchiasis were reported in many countries by various workers (Yamagata, 1952; Ishikawa, 1958; Hou, 1956-1964; Yamaguchi et al, 1962; Strauss, 1962; Markell, 1966; Cho et al, 1966). Strauss (1962) pointed out that symptoms ascribed to *Clonorchis* infection are of a most nonspecific characters, and on the basis of an analysis of the complaints of 105 patients infected with *Clonorchis sinensis*, matched against an equal number of uninfected controls, concluded that the disease is generally benign without distinctive symptomatology. Markell (1966) reached the same conclusion as to the benign nature of the chronic infection.

In the present study, symptomless clonorchiasis patients who had been infected for 6 to 35 years were tested to ascertain the duration of infection, the frequency of eating raw fresh water-fishes, and a series of hepatic functions, and the differences between lightly infected persons without symptoms and uninfected controls were observed. The results of liver function tests were almost uniformly within normal limits.

METHODS

The study was begun in 1965. Persons harboring eggs of *Clonorchis sinensis* were selected by means

of routine stool examination from the out-patients, technicians, and physicians of Kyungpook National University Hospital. The duration of infection was calculated from the first year of eating raw fishes in the endemic area. The frequency of eating raw fishes was derived by a questionnaire to the patients. Each individual found to be infected was asked to bring two stool specimens for estimation of infection. The formalin-ether sedimentation and Stoll egg-counts techniques were performed in duplicates. Liver function tests were also examined. These include serum levels of total protein, albumin and globulin, alkaline phosphatase, bilirubin, icteric index, cholesterol/ester ratio, cephalin flocculation, thymol turbidity, bromsulfalein excretion, serum glutamic oxaloacetic transaminase (SGOT), and serum glutamic pyruvic transaminase (SGPT).

All persons were checked for complete physical examinations. The clonorchiasis patients who had cirrhosis, hepatoma, and gall bladder diseases were excluded, and 23 asymptomatic patients without cirrhosis were selected carefully in this study as the symptomless clonorchiasis patients.

RESULTS

Of the 23 symptomless clonorchiasis patients, all except two were males, and had been in endemic areas.

The duration of infection varied from 6 to 35 years; fourteen cases had been infected for 10 to

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Table 1. *Stoll egg-counts in symptomless cases with clonorchiasis*

Patient	Sex	Age (yr.)	Duration of infection (yr.)	Frequency of eating raw	Stoll counts
1	M.	30	12	Unknown	8,600
2	M.	46	17	10	2,600
3	M.	34	6	3-4	2,400
4	M.	30	17	Unknown	600
5	M.	39	30	30	3,400
6	M.	41	20	5-6	2,600
7	M.	35	8	20	1,200
8	M.	44	10	35	2,400
9	M.	44	18	Unknown	800
10	M.	41	7	8-10	2,800
11	M.	30	23	15	3,400
12	M.	56	35	20	3,200
13	M.	40	25	10	800
14	M.	19	12	2	2,200
15	F.	33	16	Unknown	1,800
16	M.	46	20	Unknown	5,800
17	M.	42	30	10	2,400
18	M.	56	10	Unknown	800
19	M.	51	20	8-10	1,600
20	M.	43	20	5-6	2,400
21	M.	52	32	35	2,800
22	F.	17	10	Unknown	1,000
23	M.	40	10	15	2,000

20 years with the highest percentage(60%), and two had been infected over 30 years. The frequency of eating raw fresh water-fishes ranged from 2 to 35 times.

The intensity of infection was estimated by the Stoll egg-counts (Table 1). The eggs per gram averaged approximately 2,800 eggs. Although patient No. 1 was heaviest in egg count with 8,600 egg per gram of feces, he had none of the symptoms with the exception of the slight icteric tinge to the sclera. There seems to be no relationship between frequency of eating raw fresh water-fishes and its intensity of infection.

A series of liver function tests are given in Table 2. When the synthetic function in liver were tested, the serum level of total protein, globulin, cholesterol, cholesterol/ester ratio, and thymol turbidity were within normal values in all persons tested, whereas albumin revealed the minimum

value of normal limits. Bromsulfalein retention test was abnormal in 5 out of 23(21.7%) in this study, and this result is the most strikingly unusual among the liver function tests. But the results were borderline. As the same time, the value of cephalin flocculation, such as a 3+ at 48 hours, was treated as borderline in this study.

The tests of excretion by the liver; the average value of total bilirubin showed within normal limits with 0.98 ± 0.36 mg per 100ml. of serum. However, direct bilirubin, the average value was somewhat higher than that of normal limits, with 0.33 ± 0.15 mg per 100ml. of serum.

In the tests of serum enzyme activity, the alkaline phosphatase was abnormal in 8 of 23(34.8%), and are of very questionable significance because no symptoms were revealed in this 8 cases. SGOT and SGPT in 23 cases were also examined, but abnormal values were not observed.

As was expected, the results of liver function tests in 12 uninfected controls were normal (Table 3).

DISCUSSION

The major part of laboratory and clinical studies of clonorchiasis have been studied in endemic area including China, Japan, and Korea, etc. In an excellent survey of Germer, et al.(1955) in Korea, they compared patients having clonorchiasis without cirrhosis with those having both diseases. Germer, et al. (1955) concluded that no increase in serum bilirubin was noted in any of 35 patients with pure clonorchiasis; whereas this value was elevated in 12 of 39 patients (30.8%) who had cirrhosis. Thymol turbidity was increased in 42.5 percent of patients with clonorchiasis, but in 78.8 percent of those who were cirrhotic. Bromsulfalein retention was abnormal in 32.4 percent and in 86.2 percent of cases respectively. In the present study, thymol turbidity and bromsulfalein retention were normal in all of 23 tested. Markell(1966)pointed out that the striking features of clonorchiasis is seen in the degree of eosinophilia. This is of questionable

significance because most of the Korean people were infected with more than one intestinal parasites. No attempt has been made to count eosinophilia in the present study, as none has found any significance of blood pictures which seemed related to their clonorchiasis.

Strauss(1962) indicated that there are no special symptoms due to the presence of clonorchiasis and there is also no group of symptoms that could be called clonorchiasis. His findings clearly indicated that no inference as to liver function in clonorchiasis is warranted; but it is obvious that normal values can occur in longstanding infections. Cho, et al. (1966) reported that the liver function tests were normal during pre and posttreatment except one case among 16. Serum alkaline phosphatase was high level before treatment in one case but recovered to normal level 3 weeks later of the drug

administrations. In the present study, the alkaline phosphatase was abnormal in 34.8 percent. As mentioned before, the significance of elevated alkaline phosphatase are of questionable in the present study. Serum albumin and globulin values were normal. Then results were the same as Huei, et al.(1955)'s conclusions that normal serum albumin and globulin values were observed in a series of 9 patients. No correlation can be seen among intensity of infection, frequency of eating raw fishes duration of infection, and abnormalities of liver function tests. Regarding clinical symptoms, Ishikawa(1958) reported that 138 (15.7%) were positive for *Clonorchis* eggs, out of 878 persons examined and no remarkable symptoms(fur and pressure point in liver) were found only in some cases. Increase in number of eosinophilia were recognized in 66.7 percent. Yamakata(1952) also

Table 2. Liver function tests in symptomless cases with clonorchiasis

Patient	Total protein (g%)	Albumin (g%)	Globulin (g%)	Alkaline phosphat. (Unit)	Bilirubin (mg/100ml.)			Cholesterol (mg%)	Cholesterol ester ratio	CCF	TTT	BSP	S-GOT	S-GPT
					Total	Direct	Indirect							
1	6.0	3.1	2.9	7.5	1.4	0.6	0.8	157	63	##	3.3	7	60	20
2	6.1	3.9	2.2	4.6	0.9	0.2	0.7	165	77	++	4.2	6	30	16
3	5.3	3.2	2.1	3.3	0.9	0.3	0.6	154	59	++	3.6	8	42	20
4	6.6	3.1	3.5	4.4	0.9	0.2	0.7	160	67	##	5.8	9	57	50
5	6.8	4.1	2.7	2.6	0.9	0.2	0.7	152	68	++	2.9	6	37	30
6	6.5	3.6	2.9	5.0	0.8	0.2	0.6	130	70	++	2.8	7	8	5
7	7.8	5.1	2.7	3.0	0.8	0.2	0.6	160	67	++	4.5	6	40	18
8	5.9	3.5	2.4	4.6	0.9	0.2	0.7	160	68	++	3.1	7	36	30
9	5.9	3.5	2.4	3.5	0.8	0.2	0.6	159	67	+	2.9	6	20	18
10	6.3	3.9	2.4	4.1	0.8	0.2	0.6	156	58	++	4.3	7	20	16
11	6.8	3.7	3.1	2.6	0.9	0.2	0.7	162	68	++	3.2	4	20	14
12	7.3	3.5	3.8	5.0	0.9	0.2	0.7	164	71	##	5.7	7	74	75
13	7.3	3.5	3.8	4.0	0.8	0.2	0.6	160	68	++	3.3	7	30	20
14	7.2	3.9	3.3	3.1	0.9	0.2	0.7	163	69	++	3.5	6	31	20
15	6.3	3.5	2.8	4.0	1.0	0.3	0.7	158	65	+	2.9	4	20	18
16	6.3	3.9	2.4	3.5	0.8	0.3	0.5	164	64	+	3.3	4	20	15
17	6.3	3.7	2.6	4.0	1.0	0.3	0.7	163	68	++	4.2	5	42	28
18	6.3	3.1	3.2	4.2	0.9	0.2	0.7	158	64	##	4.7	4	35	16
19	6.8	3.9	2.9	2.9	0.9	0.2	0.7	163	69	++	2.9	4	38	31
20	5.9	2.9	3.0	3.3	0.8	0.2	0.6	154	60	++	4.1	9	40	35
21	4.1	2.2	1.9	6.3	1.2	0.4	0.6	140	58	##	4.6	8	15	45
22	5.9	2.8	3.1	3.3	0.8	0.2	0.6	154	60	++	4.0	7	35	20
23	5.7	3.5	2.2	3.2	0.9	0.4	0.5	136	60	++	3.0	8	35	20

Table 3. Liver function tests in uninfected controls

Control	Total protein (g%)	Albumin (gm)	Globulin (g%)	Alkaline phosphat. (Unit.)	Bilirubin(mg/100ml.)			Cholesterol (mg%)	Cholesterol ester ratio	CCF	TTT	BSP	S-GOT	S-GPT
					Total	Direct	Indirect							
1	6.5	4.5	3.0	4.0	0.8	0.2	0.6	165	65	+	4.2	6	20	30
2	7.1	4.0	3.0	3.0	0.9	0.2	0.7	160	63	++	3.6	4	18	12
3	6.5	4.5	2.5	5.0	0.9	0.3	0.6	130	68	+	3.6	4	30	15
4	6.3	4.0	3.5	4.5	0.8	0.2	0.6	165	62	+	4.2	8	28	26
5	7.5	5.0	3.0	2.6	0.9	0.2	0.7	150	65	++	3.0	4	30	25
6	7.0	4.5	3.0	3.5	0.8	0.2	0.6	150	63	+	3.0	5	15	10
7	7.8	5.0	3.5	3.0	0.8	0.2	0.6	160	65	+	4.0	4	50	20
8	6.5	4.5	3.0	3.3	0.9	0.2	0.7	140	68	++	3.0	5	30	15
9	7.0	4.5	2.5	2.6	0.8	0.2	0.6	160	65	+	3.0	4	20	20
10	7.0	4.5	3.0	3.0	0.8	0.2	0.6	140	62	+	4.0	6	55	25
11	6.5	4.0	2.5	2.9	0.9	0.2	0.7	130	63	+	3.2	4	15	10
12	7.3	4.5	3.0	4.1	0.8	0.2	0.6	160	70	++	4.2	5	40	50

reported absence of recognizable symptoms of infection. However, Hou(1956) concluded that at least 15 percent of primary hepatoma are induced by *Clonorchis* infection. This conclusion was based on the findings that 30 cases of precancerous changes were associated only with *Clonorchis* infection. Hou, et al.(1964) reported an incidence of 65.6 percent in Hong Kong residents with more than one year of age, and a maximum egg count was 67,400 per g of feces. In the present study, the most heavily infected person had about 8,600 eggs per g of feces, with average value of approximately 2,800 eggs. Thus, the laboratory findings varied by the investigators. The most consistent laboratory abnormality were the presence of *Clonorchis* eggs in the stool, eosinophilia, retarded BSP excretion, and deranged urinary urobilinogen. It has been emphasized that clonorchiasis cannot be studied without considering the etiologic and statistical association with Laennecis cirrhosis, hepatoma and gall bladder disease, The cirrhotic patients were excluded in this study.

SUMMARY

The duration of infection, frequency of eating raw fresh water fishes, and a series of liver function tests were studied in a group of 23 Korean symptomless cases with *Clonorchis sinensis*, and

compared with those in a control group of uninfected persons. Of 23 lightly infected cases, 11 cases who had been infected for 10 to 20 years was found the highest in percentage (47.8), and 2 had been infected for over 30 years. The frequency of eating raw fresh water fishes ranged from 2 to 35 times. The range of Stoll egg-counts in 23 cases varied from 600 to 8,600 eggs per g of feces and the average value was approximately 2,800 eggs. A series of liver function tests examined showed normal value in all cases. These results showed no difference in either infected group and its control group.

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== 초 록 ==

무증상 간디스토마 보충자의 임상검사 소견

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무증상 간디스토마 보충자 23명(남 21명, 여 2명)에 대해 각자의 생식후 경과기간, 생식회수, 및 Stoll 씨 충난계산(EPG)을 검사함과 아울러 간기능검사로써 혈청중의 total protein, albumin 및 globulin, alkaline phosphatase, bilirubin (total, direct, indirect), cholesterol, cholesterol/ester ratio, cephalin flocculation, thymol turbidity, bromsulfalein excretion과 serum glutamic oxaloacetic transaminase (SGOT), 및 serum glutamic pyruvic transaminase (SGPT)량을 대조군인 12명의 비보충자와의 임상검사소견을 비교검토하였다.

보충기간에서 무증상보충자 23명중 11명(47.8%)는 10~20년으로서 가장 많았고 2명은 30년 이상 보충자였다. 생식회수는 2~35회였고 Stoll 씨 충난계산에서는 최저 600개, 최고 8,600개, 평균 2,800개였다. 보충자에 대한 간기능검사소견은 모두 정상치내에 있어 비보충자와의 사이에 유의적차를 인정할 수 없었다.