Clinico—Immunological Studies of Filarial Chyluria

Keizo MATSUMOTO, Kimitoshi TAMAKI and Masashi YAMAMOTO

Department of Internal Medicine, Institute for Tropical Medicine
Nagasaki University

Abstract: Peripheral blood lymphocyte subpopulation counts, serum γ-globulin levels, serum immunoglobulin levels were measured, and skin tests with FST, PPD, PHA and DNCB were performed on filarial chyluria patients. T cell counts of the patients were reduced on an average to half of those of controls. However, there were no marked changes in B cell counts. Both T and B cell counts were significantly increased with the disappearance of urine protein. Changes in levels of serum immunoglobulins were examined. Positive reaction rates to PPD, PHA and DNCB were reduced. The presence of cellular immunodeficiency was suspected in chyluria on the basis of decreased T cell counts and reduced hypersensitivity tests.

INTRODUCTION

Wuchereria bancrofti infection, which had been prevalent in Japan in the past, was decreased markedly after World War II by mass treatment using diethylcarbamazine. It is now rare to see patients newly infected with the parasite, even in the Nagasaki prefecture, where there had formerly been a high incidence of filariasis. However, it is estimated that at least 250 million people are infected world–wide with *Wuchereria bancrofti* and *Brugia malayi* (7). This fact shows that filariasis is still an important infectious disease.

On the other hand, patients with chyluria, one of the prominent and specific complications of Bancroftian filariasis, are still present in Japan in fairly large numbers (3). We have studied chyluria, particularly the leakage of chyle into urine, to elucidate the clinico–immunological changes provoked by this abnormality. Herein we report several findings.

SUBJECTS AND METHODS

Subjects : The subjects of this study were 44 patients (male: 25, female: 19) diagnosed to have filarial chyluria on the basis of epidemiological findins. Other causes

of chyluria, such as malignancy, were ruled out by clinical examination. The patients were admitted to our department over a period of 5 years from Dec., 1974 to Nov., 1979. The total number of cases, which included multiple admissions of the same patient, was 57. Age distribution of the cases was from 18 years to 78 years old, and 95% of them were more than 40 years old. Almost all of them were born and/or living in the Nagasaki prefecture. Microfilaria was not detected in ear-lobe blood at midnight in any of the cases.

Methods : Urine protein was quantified by Esbach's method, serum protein fractions were measured by cellulose acetate electrophrophoresis, and immunoglobulins were identified by immunoelectrophoresis. Peripheral blood lymphocyte subpopulation counts were measured by means of the micro-method by Tachibana and Ishikawa (6) using a kit (JIMCO T-1, Japan Immunoresearch Laboratories Co., Ltd.). An intradermal skin test was done with the antigen FST (4) to check the presence of antibodies against filaria. Skin tests with purified protein derivative (PPD), phytohemagglutinin (PHA) (5) and 1-chloro-2, 4-dinitrobenzene (DNCB) were also performed to evaluate the cellular immunocompetence.

RESULTS

1) Peripheral lymphocyte subpopulations

T cell : Tcell counts of chyluria patients and controls are plotted in the left of Fig. 1. The mean value of T cell counts of the patients was 689 ± 406 (S.D.)/mm^3 and that of the controls was 1365 ± 387 /mm^3, i. e., the former was almost half of the latter (P < 0.0001). The left half of Fig. 2 shows T cell counts of the patients, which are plotted according to the presence or absence of urine protein. The mean value of T cell counts when protein could be detected in the urine was 587 ± 324 /mm^3. When no urine protein could be detected, there were 813 ± 461 /mm^3 T cells. The mean value of T cell counts
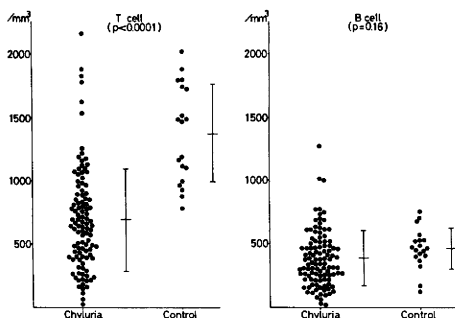

Fig. 1. Comparison of lymphocyte subpopulation counts between patients with chyluria and controls.
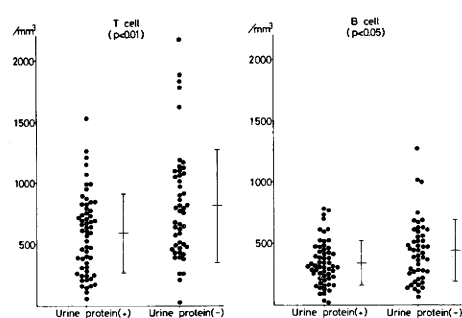
Fig. 2. Changes of lymphocyte subpopulation counts by tretament.

increased significantly (P<0.01) with the disappearance of protein from the urine.

B cell : B cell counts are plotted in the right half of Fig. 1 and 2 in the same way as T cell counts. The mean value of B cell counts of the patients was 386 ± 217 /mm³ and that of controls, 461 ± 157 /mm³. No significant difference was observed (P=0.16) between them. However, the mean value of B cell counts during the presence or absence of protein was 344 ± 178 /mm³ and 438 ± 248 /mm³, respectively. Therefore, the mean value of B cell counts also increased significantly (P<0.05) with the disappearance of protein from the urine.

2) Serum γ-globulin and immunoglobulins

In Fig. 3, 4, 5, 6 and Table 1, the results at the time of discharge represent data obtained when chyluria was cured or improved.

As shown in Fig. 3, the mean value of serum γ-gl increased significantly from 0.89 ± 0.34 g/dl on admission to 1.14 ± 0.29 g/dl on discharge. Almost all cases showed an increase after treatment.

As indicated in Table 1, the mean value of IgG increased significantly after treatment in both males and females. However those of IgM and IgA were not increased
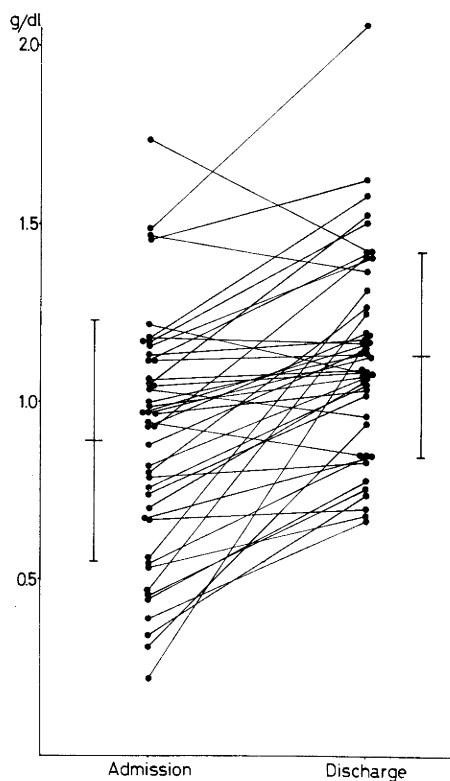

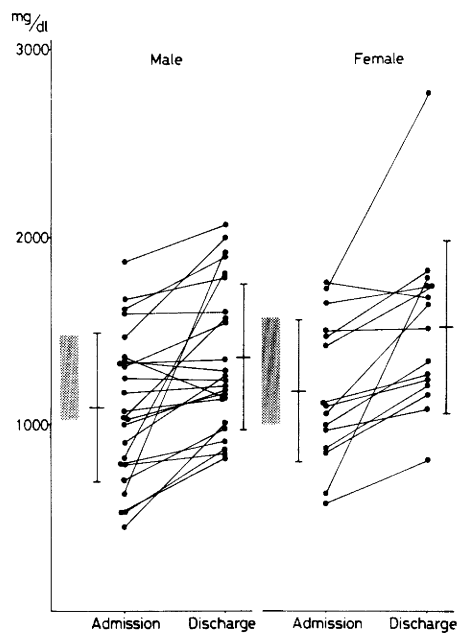Fig. 3. Changes of serum γ-globulin levels by treatment.

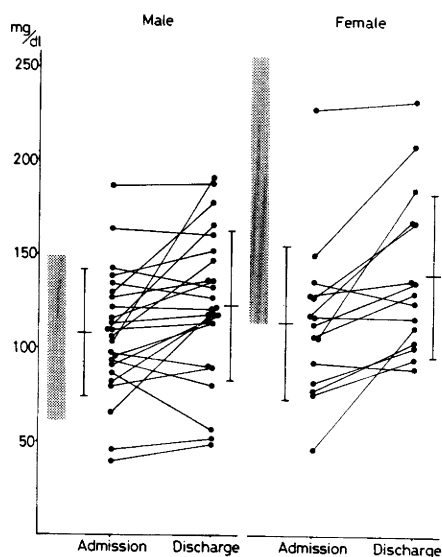Fig. 4. Changes of serum IgG levels by treatment.
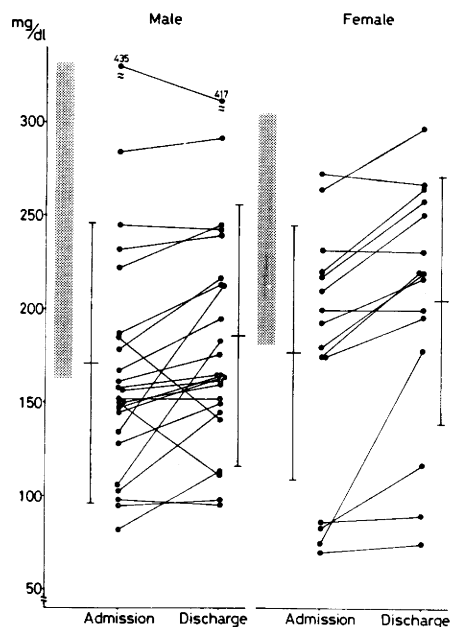
Fig. 5. Changes of serum IgM levels by treatment.

Fig. 6. Changes of serum IgA levels by treatment.

Table 1. Changes of IgG, IgM and IgA by treatment

	Male			Female		
	IgG	IgM	IgA	IgG	IgM	IgA
M ± S.D. (mg/dl) on admissisn	1094.6±395.7	107.8±33.9	170.9±74.8	1181.3±384.5	113.9±41.5	176.9±67.7
M ± S.D. (mg/dl) on discharge	1357.6±389.9	123.2±39.7	185.8±70.0	1518.7±457.4	140.5±42.5	20.5±65.9
P−values	p<0.05	p=0.16	p=0.48	p<0.05	p=0.10	p=0.25

S.D.: Standard Deviation.

significantly.

Abnormally low IgG values were observed on admission in 41.7% of male cases and in 33.3% of female cases, as indicated in Fig. 4. 8.3% of male cases and 53.3% of female cases showed abnormally low IgM values on admission (Fig. 5). 62.5% of male cases and 46.7% of female cases revealed low IgA values on admission (Fig. 6). Relatively large numbers of patients did not respond to treatment by the time of discharge.

3) Skin tests

Results of skin test are presented in Table 2. Those tests were not necessarily conducted in all of the cases. That with FST was performed on 31 patients, and those with PHA, PPD and DNCB on 38, 46 and 19 cases respectively.

Table 2. Results of skin tests

	Positive	Negative
FST	3(9.7%)	28(90.3%)
PHA	29(76.3%)	9(23.7%)
PPD	21(45.7%)	25(54.3%)
DNCB	10(52.6%)	9(47.4%)

DISCUSSION

It was reported by several research workers that serum protein, γ-globulin and peripheral blood lymphocyte counts were decreased in patients with chyluria (1). In this paper, it was shown that serum T cell counts of chyluria patients were reduced on an average to half of those of healthy people, and that there were no marked changes in B cell counts. The fact that both serum T and B cell counts were significantly increased concomitantly with the disappearance of urine protein after treatment seemed to indicate that decreased cell counts before treatment may have been due to the leakage of cells into urine. It is not known why B cell counts remained unchanged. However, T and B cells in the urine could not be measured directly.

Looking over the changing pattern of immunoglobulins, IgG responded well to treatment both in males and females. In contrast with IgG, IgM and IgA showed a slightly different patterns, i. e., their variation during, before, and after treatment was small. Besides, almost all cases which showed abnormally low IgA values on admission revealed low values on discharge as well. It is not clear what causes the differences among these immunoglobulin levels. The reduction of T cells, which are important in B cell activation, may have affected levels of antibody production.

The fact that the number of positive reactions to FST was low, and that microfilaria was not found in the blood in any of the cases may reflect the effectiveness of diethyl-carbamazine administration.

45.7% of those tested had a positive reaction to PPD, as compared to an average of 79.2% in 1968 (2). Considering our subjects' age distribution, the rate for them would be almost the same as that in 1968. Consequently, it can be said that their responses to PPD were reduced. 52.6% of the subjects had a positive reaction to DNCB, which was about the same as that to PPD. The positive reaction rate to PHA was also low.

Decreased T cell counts and reduced response in delayed hypersensitivity tests seem to indicate a cellular immunodeficient state in chyluria. Further studies need to be conducted to determine whether cellular immunodeficiency in chyluria, if present, affects protection mechanisms against infection.

We hope this study will be useful for the investigation of chyluria, which developing countries in the tropics will be faced with in the future.

REFERENCES

1) Katamine, D. (1966): Progress of medical parasitology in Japan. Vol III, 440−466, Meguro Parasitological Museum, Tokyo.

2) Muranaka, T. (1969): Tuberculosis prevalence survey in Japan in 1968. Kekkaku, 44(10), 325−332 (In Japanese with English summary).

3) Okamoto, K. (1976) : Personal communtication.

4) Sawada, T. et al (1968) : Intradermal skin test with antigen FST (FSCD1) on individuals in endemic area. Japan. J. Exp. Med., 38(6), 405−414.

5) Sone, S. et al (1975): Phytohemagglutinin skin test: Diagnostic value for showing immunodeficiency in patient with cancer. Gann, 66(6), 645−648.

6) Tachibana, T. and Ishikawa, M. (1973): A new micro-method for quantitation of human T-and B-lymphocytes. Japan. J. Exp. Med., 43(3), 227−230.

7) WHO Expert Committee on Filariasis (1974) : Third report. WHO. techn. Rep. Ser., No. 542.

フィラリア性乳糜尿症の臨床免疫学的研究
松本慶蔵, 玉置公俊, 山本真志（長崎大学熱帯医学研究所, 内科）

フィラリア性乳糜尿症と診断された患者44名, 57症例を対象として, 末梢血リンパ球サブポピュレーション, γ-グロブリン, 免疫グロブリンを測定し, 治療前の値の正常コントロールとの比較をすると共に, 治療による変動をみた. また, FST, PPD, PHA, DNCB による皮膚反応を実施した. 本症患者の T 細胞数平均値は正常コントロールに比較して半減していたが, B 細胞数平均値は正常コントロールとの間に有意の差を示さなかった. 尿蛋白の陰性時, 陽性時でこれらの細胞数平均値の変動をみると, 両者共尿蛋白の陰性化により有意に増加していた. γ-グロブリン値は治療によく反応し, 有意に増加した. IgG 平均値は男性, 女性双方で有意に増加したが, IgM, IgA 平均値は治療による差を認めなかった. また, 治療前後で個々の変動をみると, IgG は治療前に異常低値を示したものも治療によく反応して増加したが, IgA では治療前低値を示す症例が多く, かつ, 治療による改善は遅延した. FST 陽性率は低く, また, PPD, PHA, DNCB に対する反応性も低下していた. 以上の成績から, 主として本症の細胞性免疫能について考察した.