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# A Clinical Study of Adult Japanese Encephalitis in the Chonnam District, Korea, During Summer of 1982

— A Difference between Improved and Expired Cases —

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*In the summer of 1982, we experienced a great number of patients with Japanese encephalitis compared with the previous years. We have studied 85 adult cases of Japanese encephalitis which were diagnosed clinically and/or serologically. A difference between improved and expired cases was also investigated.*

*We found that deteriorated mental state, elevated SGOT(AST) level, lower hemagglutination-inhibition(H-I) titer, and a more acute onset of the illness were associated with higher mortality.*

*The mortality rate in our cases was 35.3 percent.*

Key Words: *Adult Japanese encephalitis, Hemagglutination Inhibition test*

## INTRODUCTION

Japanese encephalitis, the only epidemic encephalitis in Korea[1,2], has shown a trend of an epidemic every 3 years and a great epidemic every 10 years since a great one in 1949. However, this trend has not been apparent since 1959. And since 1969, when there was a rapid reduction of occurrence, the incidence of Japanese encephalitis has been low[1,4].

In the summer of 1982, we experienced a great number of adult patients with Japanese encephalitis compared with the previous years. In this paper we present the results of a study of 85 adult cases of Japanese encephalitis which were diagnosed clinically and/or serologically in three general hospitals in the Chonnam District. We have observed clinical features, hematologic, chemical and serologic tests in blood and CSF, and also have investigated the difference between improved and expired cases.

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## METHODS

The subjects were 85 patients aged over 15 who were admitted to three general hospitals in the Chonnam District (Chonnam University Hospital, Chosun University Hospital, and Kwangju Christian Hospital) from late July to early October, and were diagnosed clinically and/or serologically as having Japanese encephalitis. We observed their clinical progress, and tested their blood for CBC, SGOT(AST), SGPT(AST), alkaline phosphatase, and their CSF for pressure, leukocytes with differential counts, concentrations of protein, sugar, and chloride. We also examined sera of patients for hemagglutination inhibition (H-I) tests on admission in 51 cases, and after one to two weeks in 9 cases for a follow-up exam. These H-I tests were done in the Korean National Institute of Health.

## RESULTS

### 1. Age and sex

Table 1. Age and sex distribution of adult Japanese encephalitis patients with the comparison of the improved patients with the expired ones

| Age group | Male | | | Female | | | Total | | |
|---|---|---|---|---|---|---|---|---|---|
| | Improved | Expired | Total | Improved | Expired | Total | Improved | Expired | Total(%) |
| 15 — 24 | 26 | 10 | 36 | 14 | 10 | 24 | 40 | 20 | 60( 70.6) |
| 25 — 34 | 8 | 4 | 12 | 3 | 3 | 6 | 11 | 7 | 18( 21.2) |
| 35 — 44 | 1 | 0 | 1 | 1 | 0 | 1 | 2 | 0 | 2( 2.3) |
| 45 — 54 | 0 | 2 | 2 | 1 | 0 | 1 | 1 | 2 | 3( 3.5) |
| 55 — 64 | 0 | 1 | 1 | 0 | 0 | 0 | 0 | 1 | 1( 1.2) |
| 65 — | 1 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 1( 1.2) |
| Mean ±SD | 23.6 ±8.8 | 27.6 ±13.6 | 24.9 ±10.6 | 23.3 ±9.5 | 21.6 ±5.4 | 22.6 ±8.0 | 23.5 ±8.9 | 25.0 ±11.1 | 24.0 ±9.7 |
| Total | 36 | 17 | 53 | 19 | 13 | 32 | 55 | 30 | 85(100.0) |

Age and sex distribution of both improved and expired patients are presented in Table 1. The male-to-female ratio was about 1.7 (male 53, female 32 cases). The age of patients was distributed from 15 to 65 (male 16-65, female 15-53) with a mean of 24.0±9.7. There was no significant difference in age and sex distribution between improved and expired patients. The number of expired patients was 30, so the mortality rate ran upto 35.3 percent.

## 2. Symptoms and signs

Major symptoms and signs on admission are presented in Table 2. Among them fever was most common (95.3%), followed by a deteriorated mental state (88.2%), headache (78.8%), nuchal rigidity (55.3%), and vomiting (37.6%). While 43 improved cases showed fever (98.1%), headache (86.8%), deteriorated mental state (81.1%), nuchal rigidity (58.5%), and vomiting (41.5%), those who expired (32 cases) showed deteriorated mental state (100%), fever (90.6%), headache (65.6%), nuchal rigidity (50%), and vomiting (31.3%).

Table 2. Major clinical features of the improved and the expired cases of adult Japanese encephalitis patients on admission

| Symptoms and signs | Number of cases (%) | | |
|---|---|---|---|
| | Improved | Expired | Total |
| Fever | 52( 98.1) | 29( 90.6) | 81( 95.3) |
| Change of mental state | 43( 81.1) | 32(100.0) | 75( 88.2) |
| Headache | 56( 86.8) | 21( 65.6) | 67( 78.8) |
| Nuchal rigidity | 31( 58.5) | 16( 50.0) | 47( 55.3) |
| Vomiting | 22( 41.5) | 10( 31.3) | 32( 37.6) |
| Others | 7( 13.2) | 6( 18.8) | 13( 15.3) |
| No. of patients | 53(100.0) | 32(100.0) | 85(100.0) |

The duration of illness before admission in these patients is shown in Table 3. Their symptoms developed acutely in most cases, so the duration of illness before admission was less than 5 days in most

Table 3. Duration of illness before admission in the improved and the expired cases of adult Japanese encephalitis patients

| Days | Number of cases (%) | | |
|---|---|---|---|
| | Improved | Expired | Total |
| 1 | 3( 5.5) | 3( 10.0) | 6( 7.1) |
| 2 | 5( 9.1) | 8( 26.7) | 13( 15.3) |
| 3 | 13( 23.6) | 9( 30.0) | 22( 25.9) |
| 4 | 13( 23.6) | 7( 23.3) | 20( 23.5) |
| 5 | 12( 21.8) | 2( 6.7) | 14( 16.5) |
| 6 | 2( 3.7) | 0 | 2( 2.3) |
| 7 | 4( 7.3) | 0 | 4( 4.7) |
| — | — | — | — |
| 10 | 1( 1.8) | 1( 3.3) | 2( 2.3) |
| — | — | — | — |
| 14 | 1( 1.8) | 0 | 1( 1.2) |
| Uncertain | 1( 1.8) | 0 | 1( 1.2) |
| Mean ± SD | 4.2±2.2* | 3.1±1.7* | 3.8±2.1 |
| Total | 55(100.0) | 30(100.0) | 85(100.0) |

*$p<0.01$

cases (88.3%) with a mean of 3.8±2.1 days. The number of days of illness before admission was much greater in the improved group (4.2±2.2 days) than in the expired group (3.1±1.7 days) (P<0.01).

### 3. Laboratory findings

Peripheral blood leukocyte counts with their differentiation, SGOT (AST), SGPT (ALT), and alkaline phosphatase levels are presented in Table 4. The mean leukocyte count showed no difference between the improved and the expired cases (11,910.9±5,168.5/mm³ in the total, 12,175.1±5,179.6/mm³ in the improved, and 11,412.5±5,203.3/mm³ in the expired). A differential count of leukocytes also showed no difference between the two groups. The mean percent of neutrophils was 78.0±13.1% (76.6±13.9% in the improved, 80.5±11.4% in the expired), that of lymphocytes was 18.8±11.2% (19.4±10.9% in the improved, 17.9±11.9% in the expired), and that of monocytes was 1.4±2.6% (1.5±2.8% in the improved, 1.2±2.1% in the expired). But there was a significant difference of SGOT between the two groups in the serum level. The SGOT level of the improved patients (34.8±23.4 Karmen units) was much lower than that of the expired ones (55.8±44.2 Karmen units). The mean was 42.2±33.4 Karmen units. Whereas the serum levels of SGPT and alkaline phosphatase showed no difference between the two. The mean of SGPT was 30.5±19.2 Karmen units (30.9±20.7 Karmen units in the improved, and 29.8±16.5 Karmen units in the expired), and that of alkaline phosphatase was 1.9±1.0 Bessay-Lory (B-L) units (1.9±0.9 B-L units in the improved, 1.8±1.0 B-L units in the expired).

The findings of cerebrospinal fluid (CSF) are presented in Table 5. CSF was grossly transparent with a few exceptionally turbid cases. There was no difference between the improved and the expired groups in CSF findings on admission. In the improv-

Table 4. CBC, SGOT, SGPT and alkaline phosphatase of the improved and the expired cases of adult Japanese encephalitis patients on admission

| | Mean±SD | | |
|---|---|---|---|
| | Improved | Expired | Total |
| WBC(/mm³) | 12,175±5,179.6 | 11,417.5±5,203.3 | 11,910.9±5,168.5 |
| Differential count (%) | 76.6±13.9 | 80.5±11.4 | 78.0±13.1 |
| Neutrophil | 76.6±13.9 | 80.5±11.4 | 78.0±13.1 |
| Lymphocyte | 19.4±10.9 | 17.9±11.9 | 18.8±11.2 |
| Monocyte | 1.5±2.8 | 1.2±2.1 | 1.4±2.6 |
| SGOT (Karmen units) | 34.8±23.4* | 55.8±44.2* | 42.2±33.4 |
| SGPT (Karmen units) | 30.9±20.7 | 29.8±16.5 | 30.5±19.2 |
| Alk-Pase (B-L units) | 1.9±0.9 | 1.8±1.0 | 1.9±1.0 |

B-L units: Bessay-Lory units, *p<0.01

Table 5. Comparison of CSF findings between the improved and the expired cases in adult Japanese encephalitis patients

| CSF findings | Mean±SD | | | |
|---|---|---|---|---|
| | Improved | | Expired# | Total |
| | (On admission) | (At discharge) | (On admission) | (On admission) |
| Pressure ($mmH_2O$) | 197.6±71.5 | 142.8±37.6** | 197.0±78.3 | 197.4±73.4 |
| Leukocyte (/mm³) | 303.6±821.8 | 35.5±23.8*** | 229.0±259.0 | 277.8±680.6 |
| Lymphocyte (%) | 52.6±26.8 | 78.1±16.0** | 51.7±22.1 | 52.3±25.1 |
| Protein (mg/dl) | 92.2±57.4 | 64.6±29.6** | 84.7±36.4 | 89.6±51.0 |
| Sugar (mg/dl) | 71.3±15.5 | 68.1±16.5* | 71.6±17.1 | 71.4±16.0 |
| Chloride (mEq/L) | 121.2±15.2 | 120.2±4.9* | 122.7±8.3 | 121.7±13.1 |

*not significant **p<0.05 ***p<0.01

#Follow-up examination was not performed.

Table 6. Titers of H-I antibody in the improved and the expired cases of adult Japanese encephalitis patients

| H-I antibody Titers | Number of cases (%) | | |
|---|---|---|---|
| | Improved | Expired | Total |
| 1:20 | 5(16.1) | 8( 40.0) | 13( 25.5) |
| 1:40 | 4( 12.9) | 4( 20.0) | 8( 15.7) |
| 1:80 | 8( 25.8) | 4( 20.0) | 12( 23.5) |
| 1:160 | 6( 19.4) | 0 | 6( 11.8) |
| 1:320 | 5( 16.1) | 3( 15.0) | 8( 15.7) |
| 1:640 | 3( 9.7) | 1( 5.0) | 4( 7.8) |
| Total | 31(100.0) | 20(100.0) | 51(100.0) |

ed group, we underwent follow-up examinations of CSF at discharge, but in the expired group we could not follow up because of their poor conditions or sudden deaths. The mean of CSF pressure on admission was 197.0±73.4 $mmH_2O$ (197.6±71.5 $mmH_2O$ in the improved, 197.0±78.3 $mmH_2O$ in the expired). But the CSF pressure of the improved patients diminished significantly at discharge (142.8±37.6 $mmH_2O$ at discharge; $P<0.05$). The mean number of leukocytes was 277.8±680.6/$mm^3$ on admission (303.6±821.8/$mm^3$ in the improved, 229.0±259.0/$mm^3$ in the expired), and that of the improved group diminished significantly at discharge (35.5±23.8/$mm^3$; $P<0.01$). The mean percent of lymphocytes among leukocytes was 52.3±25.1% on admission (52.6±26.8% in the improved, 51.7±22.1% in the expired), and that of improved patients at discharge elevated significantly (78.1±16.9% at discharge; $P<0.05$). The mean protein content of CSF on admission was 89.6±51.0 mg/dl (92.2±57.4 mg/dl in the improved, 84.7±36.4 mg/dl in the expired), and that of improved cases diminished significantly at discharge (64.6±29.6 mg/dl; $P<0.05$). Mean concentrations of sugar and chloride in CSF on admission were 71.4±16.0 mg/dl (71.3±15.5 mg/dl in the improved, 71.6±17.1 mg/dl in the expired), 121.7±13.1 mEq/L (121.2±15.2 mEq/L in the improved, 122.7±8.3 mEq/L in the expired). And those of sugar and chloride in the improved group at discharge showed no difference (68.1±16.5 mg/dl, 120.2±4.9 mEq/L, respectively).

Titers of H-I antibody of 51 cases on admission are presented in Table 6. Twenty-one cases (41.2%) showed a titer below 1:40, 12 cases (23.5%) 1:80, and 18 cases (35.3%) over 1:160. Among 9 cases who underwent a follow-up examination one to two weeks later, 7 patients showed a 4 fold increase in their titer, and the other 2 showed the same titers are as in the primary examination (1:320, 1:80). It was found that the lesser the H-I titer, the poorer the prognosis.

## DISCUSSION

In the summer of 1982, there were a great many Japanese encephalitis patients, expecially adult ones, as compared with the previous years. It had been predicted more or less, however, because of a reduced ratio of antibody possesion resulting from decreased incidence of Japanese encephalitis during the preceeding 20 years. In addition, severe heat which lasted from a short rainy spell in late July to late August was regared as one of the causes.

As previous reports had pointed out,[1,5,6,7] the male-to-female ratio was about 1.7:1. And there was no difference in the age and sex distribution between the improved and the expired cases.

The major clinical features manifested were in the sequence of fever, deteriorated mental state, headache, nuchal rigidity, and vomiting. These features were very similar to those noted in the report of Kwon et al,[8] but somewhat different from those of Lee et al.[9]. In the expired cases, deteriorated mental state was dominant as compared with the improved ones, however, the other features were similar in the two groups. This might indicate a more extensive cerebral damage in those who expired.

The duration of illness before admission was much longer in the improved cases as compared with that of expired ones ($P<0.01$). It could be suggested by the fact that the more acute the disease process the poorer the prognosis. But we could not exclude the possibility of heterogeneity in provinces, and cultural or economic status.

It was reported that the peripheral leukocyte count was elevated in Japanese encephalitis patients, while it was diminished in those with an Arbo virus infection[10]. Our data also revealed this point.

There was no change in serum concentrations of SGOT, SGPT, alkaline phosphatase in these patients except a significant elevation of SGOT in the expired cases ($P<0.01$) which might reflect a leakage of GOT from brain tissue to serum due to marked cerebral damage[11].

As previous investigators had reported[11,12], pressure, number of leukocytes, and protein concentrations in CSF in these patients were also elevated. In the improved group, the number of leukocytes ($P<0.01$), pressure ($P<0.05$), protein concentration ($P<0.05$) in CSF were diminished significantly at

discharge as compared with those on admission. On the contrary, the percent of lymphocytes in CSF was higher at discharge ($P<0.05$) than that on admission. It might indicate that during the early phase of the disease the percent of leukocytes increased, and that as the disease improved the percent of lymphocytes increased. CSF concentrations of sugar ad chloride were not changed at all. The number of leukocytes and protein concentrations in CSF were slightly higher without statistical significance in the improved group than those in the expired group.

The hemagglutination inhibition (H-I) test which Sabin first used as a diagnostic tool of Japanese encephalitis in 1950 is regarded as a simple and economical test, hence it has become very popular now[13,14,15]. So we also tested it in 51 cases on admission, and in 9 cases after one to two weeks as a follow-up. The result of the H-I test is regarded as suspicious when it is 1:80, and diagnostic when it is over 1:160 or it rises over 4 fold on a followup examination[16]. In our patients, 12 cases (23.5%) showed 1:80, 18 cases (35.3%) showed over 1:160 on the primary examination, and 7 or 9 who underwent a follow-up test showed over 4 fold increase. Our data also confirms previous reports saying that the lower the H-I titer, the higher the mortality rate.[9,14]

The mortality rate of Japanese encephalitis in Korea was 40-48% from 1949 to 1957, but it declined slowly to 30% after 1958, and it declined further after 1969, so the mortality rate in 1973 was 20.4%[1,17,18,19,20]. In our case, however, 30 of 85 patients expired, so the mortality rate ranked as high as 35.3%. It is much higher than 2% or 10.6% in the reports of Lee *et al.*[9] or Kwon *et al.*[8] of the same year.

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