長崎県中通島におけるつつが虫病に関する血清疫学的研究

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Seroepidemiology of Rickettsia Tsutsugamushi in Nakadori Island in Nagasaki Prefecture

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Abstract: During December 1984, blood samples were collected from 270, healthy inhabitants of five different areas in Nakadori Island of Nagasaki Prefecture. Rickettsia tsutsugamushi specific IgG and IgM antibody were determined by immune peroxidase method using the Gilliam strain as antigen. The positive rate of IgG antibody at four areas ranged from 51.8 to 76.0 percent and were similar to those reported for another endemic areas for Rickettsia tsutsugamushi in Japan. However these rates were not significantly different. Another area had a positive rate of 9.3 percent. This was significantly lower than the positive rates at the other four areas. The IgG antibody distribution in the samples from the five areas were significantly different by the Wilcoxon test. Our results show that four of the five localities investigated are endemic for Rickettsia tsutsugamushi. In addition, the results suggest that the endemic zone has been spreading with time and further spread to presently non-endemic areas is anticipated.

Key words: Rickettsia tsutsugamushi, Immune peroxidase method, Seroepidemiology

INTRODUCTION

The Nakadori Island, one of the Goto group of Islands, of the Nagasaki Prefecture is thought to be endemic for Rickettsia tsutsugamushi (R. tsutsugamushi). But for a period of 35 years there were no reports of disease due to R. tsutsugamushi from these islands or any other part of the prefecture (Health Department of Nagasaki Prefectural Government, 1983). Since 1982, however, documented cases of disease due to R. tsutsuga-
mushi have appeared sporadically not only in the Nakadori Island but also from several parts of the Nagasaki Prefecture, where the disease had never been reported before (Health Department of Nagasaki Prefectural Government, 1983). In the light of these recent developments we conducted a seroepidemiological survey to evaluate the prevalence rate, the distribution of antibody to R. tsutsugamushi and the pathogenic organism for the inhabitants of the Nakadori Island.

MATERIALS AND METHODS

Samples. In December 1984, during routine annual medical examination done for all inhabitants aged 40 years and above at Naname, Ota, Akao, Enohama in Arikawa town and Sone in Shinuonome Town (Fig. 1) blood samples were collected. A random selection of the samples obtained during the exercise was done. The number of samples thus obtained and the corresponding population ratio studied from each locality were as follows: 50 (9.1 percent) for Naname, 50 (5.4 percent) for Ota, 56 (13.4 percent) for Akao, 54 (17 percent) for Enohama and 60 (10 percent) for Sone. Sample source and structure of the population studied are shown in Table 1.

Occupation and residential environment. The inhabitants of the five localities from which the blood samples were collected are mainly involved in agriculture. At times however, some of them may do fishing or participate in road construction. The residential areas of the study population are separated from each other by small hills around which are stretches of waste lands.

Immune peroxidase method. Antibody to R. tsutsugamushi were examined for by the method described by Suto (1984). The Gilliam strain of R. tsutsugamushi was used.

Fig. 1. Map of Nagasaki Prefecture.
Table 1. Sample source and structure of the population studied

<table>
<thead>
<tr>
<th>Locality</th>
<th>Percent of population studied</th>
<th>No. of samples</th>
<th>Age in years mean</th>
<th>Sex M : F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arikawa town</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Naname</td>
<td>9.1</td>
<td>50</td>
<td>57</td>
<td>0.7 : 4.3</td>
</tr>
<tr>
<td>Ota</td>
<td>5.4</td>
<td>50</td>
<td>57</td>
<td>1.5 : 4.5</td>
</tr>
<tr>
<td>Akao</td>
<td>13.4</td>
<td>56</td>
<td>61</td>
<td>1.0 : 4.6</td>
</tr>
<tr>
<td>Enohama</td>
<td>17.0</td>
<td>54</td>
<td>62</td>
<td>1.7 : 3.7</td>
</tr>
<tr>
<td>Shinuonome town</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sone</td>
<td>10.0</td>
<td>60</td>
<td>68</td>
<td>2.3 : 3.7</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>270</td>
<td>61</td>
<td>40-88</td>
</tr>
</tbody>
</table>

as the antigen. The antigen was kindly supplied by Dr. Cho (Director, Institute of Virological Science, Denka Seiken Corporation). Peroxidase-labeled goat IgG and IgM fractions against human immunoglobulins were commercial preparations from Tago Inc. Salingame Ca. USA.

Antibody positive level. Two fold serial dilutions (beginning with a dilution of 1:20) were prepared using phosphate buffered saline with 0.3 percent bovine serum albumin. Sera with antibody titers of 1:20 or more were considered positive.

RESULTS

Positive rate.

The IgG antibody rates were as shown in Table 2. The positive rate ranged from 9.3 percent at Enohama to 76 percent at Ota. The rate at Enohama was found to be significantly lower (by χ²-test) than the rates at the other four areas. On the contrary the
Fig. 2. Antibody distribution of Rickettsia tsutsugamushi at different areas in Nakadori Island. The number of parenthesis expresses percent. The level of antibody was expressed by the reciprocal in serum dilution.

*: significant at the level of 5%. **: significant at the level of 1%. Statistical calculation was done by the method of Wilcoxon test.
rates for Naname, Akao, Ota and Sone were not significantly different from each other. IgG antibody distribution.

Antibody level distribution in the samples from the four areas with high positive rates are shown in Fig. 2. Comparison of these data by the Wilcoxon test showed that the IgG antibody distribution was highest at Sone followed by Ota. The distribution at Akao and Naname were not significantly different from each other. Furthermore, antibody level distribution at Enohama was significantly lower than that at other four areas (data not shown).

IgM antibody distribution.

As shown in Table 2 R. tsutsugamushi specific IgM antibody were detected at Sone (16.7 percent) and Ota (16 percent) only. Whereas the reciprocal IgM antibody level for Sone ranged between 20 and 80, only titers of 20 could be detected at Ota, as shown in Fig. 2.

IgG antibody distribution and age.

Analysis of IgG antibody rate ($\chi^2$-test) and level (Wilcoxon test) by age decade at high prevalence areas (Akao, Naname, Ota and Sone) did not show any significant difference. As shown in Table 3, however, there was general trend for the antibody positive rate to increase with increasing age.

Table 3. Positive rate and antibody distribution of Rickettsia tsutsugamushi at each decade in high prevalence areas

<table>
<thead>
<tr>
<th>Age decade</th>
<th>cases</th>
<th>No. of positive cases (%)</th>
<th>Antibody distribution of positive cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>40</td>
<td>21 (52.5)</td>
<td>13 2 3 2 1 (32.5) (5.0) (7.5) (5.0) (2.5)</td>
</tr>
<tr>
<td>5</td>
<td>66</td>
<td>38 (57.6)</td>
<td>17 3 3 7 5 1 2 (25.8) (4.5) (4.5) (10.6) (7.6) (1.5) (3.0)</td>
</tr>
<tr>
<td>6</td>
<td>50</td>
<td>49 (66.0)</td>
<td>13 5 6 4 3 1 1 (26.0) (10.0) (12.0) (8.0) (6.0) (2.0) (2.0)</td>
</tr>
<tr>
<td>$\geq$ 7</td>
<td>60</td>
<td>44 (73.3)</td>
<td>18 6 5 7 3 (30.0) (10.0) (8.3) (8.3) (11.7) (5.0)</td>
</tr>
</tbody>
</table>

High prevalence areas of Rickettsia tsutsugamushi in Nakadori Island were Akao, Naname, Ota and Sone.

DISCUSSION

The antibody positive rate of 9.3 at Enohama was significantly lower than the rate at the other four areas. On the other hand the antibody rate for Enohama does not differ significantly with the rates of 2 to 8 percent reported from non-endemic areas in Nagasaki Prefecture (Suzuki et al. 1984). The present data, therefore, indicate that Enohama is a non-endemic area for R. tsutsugamushi. However, the possibility of low endemicity of R. tsutsugamushi at Enohama can not be ruled out by our data.
Akao, Naname, Ota and Sone had antibody positive rates of 51.8, 62.0, 76.0 and 60.0 percent respectively. These rates are higher than those reported for Yamanashi Prefecture (36.5 percent), Toshima Islands (23.5 percent) and Miyake Island (26.1 percent) areas known to be endemic for R. tsutsugamushi (Otsuru 1984). However, the rates at the four areas are similar to those reported for Hachijo Island of Tokyo-To (56.3 percent) another endemic area for R. tsutsugamushi (Otsuru 1984). Akao, Naname, Ota and Sone are therefore endemic areas for R. tsutsugamushi. However, the higher antibody level distribution and the presence of IgM antibodies in sera from Sone and Ota indicate recent infections. On the other hand infections at Naname and Akao were old as suggested by the lower IgG antibody levels and absence of IgM antibodies. It was, furthermore, assumed that the infection at Enohama was the oldest as evidenced by lower positive rate and antibody level distribution.

The similar positive rates for the samples from the four locations herein reported indicate that the pathogenic strain of R. tsutsugamushi endemic in these areas might be the same.

Following confirmed scrub typhus infection, the IgG antibodies to R. tsutsugamushi in most patients disappear within one year (Saunders et al. 1980). However persistence of IgG antibodies for over five years have been reported (Shishido 1962; Bozeman & Elieberg et al. 1963; Suto 1983). Also it is noteworthy that atypical, mild and subclinical infection by R. tsutsugamushi have been reported (Shishido 1962; Brown et al. 1983). Furthermore, inapparent infections with avirulent strains of R. tsutsugamushi are known to occur (Kawamura et al. 1980). The low IgG antibody levels detected in some inhabitants of Enohama could therefore have been due to either old infections of scrub typhus, avirulent strains of R. tsutsugamushi or both. It is interesting to note that the antibody level range of 1:20 to 1:80 at Enohama is similar to those for Miyake and Toshima reported by Kawamura and coworkers (1980). These researchers ascribed the antibodies found in their study population to inapparent infections with avirulent strains of R. tsutsugamushi.

In a given population, the seropositivity for R. tsutsugamushi is said to be influenced by the habitat, occupation, consumption of antibiotics (tetracycline, doxycycline and chloramphenicol) and the use of agricultural chemicals (Robinson et al. 1976; Cadigan et al. 1972; Sheehy et al. 1973; Olson et al. 1980; Twartz et al. 1982; Otsuru 1984). The occupation for the residents of the five areas studied are similar. We have no good reason to think that the antibiotic consumption or use of agricultural chemicals in these communities is different either. The fields around the residential areas were managed well until about ten years ago. Since then however, these fields have become waste land and therefore good for rodent habitation.

That in 1982 two patients from the Nakadori Island met both the clinical and serological criteria for scrub typhus could be a result of several factors. It is of note that none had been reported for 36 years in Nagasaki Prefecture. On the first place it has been reported that in endemic areas disease due to R. tsutsugamushi occurs every 15 to
25 years (Kawamura et al. 1980). Secondly atypical, mild or subclinical infections which escaped clinical attention could have occurred all along the years. Nonetheless the provision of good habitat for rodents during the last ten years favors persistence as well as increased risk of scrub typhus infections in these islands. Furthermore, results of the analysis of IgG and IgM antibody levels and distribution in the five areas suggest spreading R. tsutsugamushi infections from Akao and Naname to Ota and Sone. These results therefore, indicate that the change in the environment has been a major factor for the reappearance of scrub typhus disease in the Nakadori Island. That destruction of rodent habitat is mandatory for effective control and eradication of disease due to R. tsutsugamushi can not be overemphasized. Failure to do this simple but effective control measure will only encourage continued endemicity of R. tsutsugamushi and its consequences in the Nakadori Island.

REFERENCES


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Long-count islands in Japan and the research on blood film.