

Sexually-transmitted amoebiasis: Epidemiology and serodiagnosis **CH-87-22**

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Introduction

Amoebiasis, caused by a parasitic protozoon Entamoeba histolytica, is still one of the major public health hazards in the tropical zone. According to the recent data by WHO, there are approximately 500 million infected people and 75 thousands deaths due to this parasite every year. Most of these cases seem to be localized in developing countries in the tropical zone. In the developed countries, the incidence of amoebiasis had been decreasing since World War II, and this enteric infection was regarded to be of no more importance in the public health; indeed, amoebiasis was one of the "great neglected diseases". Apparently, this was true of other oral infections in the western countries including Japan, and primarily attributed to improvement of our hygienic environment. However, from the end of seventies, the incidence of amoebiasis suddenly started to increase in the developed countries including Japan. Subsequent studies on this increment demonstrated quite a novel fact about transmission of the pathogen; E. histolytica was transmitted by sexual intercourse among male homosexuals. Such observations have certainly opened a new scope about amoebiasis. Now, it is one of the sexually-transmitted diseases of homosexual males, which is called sexually-transmitted amoebiasis. The present communication deals with recent epidemiological aspect of sexually-transmitted amoebiasis in the developed countries and summarizes some progress in the diagnostic techniques of this infection.

Current epidemiology of sexually-transmitted amoebiasis

Initially, sexually-transmitted amoebiasis was recognized as a few case reports from large cities in the United States^(1, 2). It was not until 1981 that some epidemiological analyses on sexually-transmitted amoebiasis were performed^(3, 4). According to these reports, cyst of E. histolytica was detected at more than 20% of the male homosexuals examined. Similar data were also reported by Quinn et al.⁽⁵⁾ on the basis of their investigation in Seattle. However, the most detailed parasitological data were presented by Markell et al.⁽⁶⁾ in San Francisco in 1984. They examined 508 homosexual males using questionnaire and stool examination and found high prevalence rates of intestinal protozoa. For example, they reported 37.8% and 28.5% of the homosexual males were infected with Endolimax nana and E. histolytica, respectively. Cyst of Giardia lamblia was detected at 5.7%. Moreover, the correlation of amoebic infection with the number of sex partners and also with the frequency of oral-anal sex contact was confirmed.

In the United Kingdom, an epidemiological study on sexually-transmitted amoebiasis was attempted in Edinburgh. McMillan et al.⁽⁷⁾ selected 35 subjects with amoebic infection from 350 male homosexuals, and carried out clinical and serological investigations. They suggested that E. histolytica was detected more frequently than other protozoa. The Toronto study by Keystone et al.⁽⁸⁾ showed that 30% of the homosexual males they examined were

infected with E. histolytica.

These studies clarified some interesting features of sexually-transmitted amoebiasis. First of all, it should be pointed out that the homosexual males examined in these studies had a surprisingly high incidence of syphilis and/or gonorrhoea. For example, Markell et al.⁽⁶⁾ reported that 67% of the biased males they examined had history of at least either of these venereal diseases. They also found that the frequency of positive history of these venereal diseases increased in proportional to the number of sex partners, indicating the same property as sexually-transmitted amoebiasis. Another interesting observation was that most strains of E. histolytica transmitted sexually among homosexual males in the western countries seemed low- or avirulent. This is compatible with the finding that the biased males with sexually-transmitted amoebiasis seldom develop symptoms due to amoebic infection⁽⁶⁾. In addition, McMillan et al.⁽⁷⁾ reported that the isoenzyme patterns of some glycolytic enzymes of E. histolytica strains isolated from 35 biased males with sexually-transmitted amoebiasis belonged to zymodeme I of Sargeant et al.⁽⁹⁾ which stands for the avirulent amoeba. Moreover, they isolated sera from 20 of the 35 cases, but none of them were positive on IHA indicating the absence of production of detectable amounts of anti-amoebic antibody. All of these data suggest that the cases with sexually-transmitted amoebiasis in the western countries appear to be compatible with the definition of asymptomatic cyst

carriers by Sargeaunt⁽¹⁰⁾.

Occurrence of sexually-transmitted amoebiasis in Japan was made clear in a different manner around 1980. As amoebiasis is one of the infectious diseases which should be reported to the local health department, we could know the incidence of amoebiasis (naturally invasive, symptomatic amoebiasis) from the Statistics of communicable diseases issued by the Ministry of Health and Welfare. According to this Statistics, the incidence of amoebiasis increased from 1979. In 1978, we found less than 10 reported cases, whereas there were more than 100 in 1985 (Fig. 1). Since my laboratory was only one which could carry out the serodiagnosis of amoebiasis, we were able to collect a large number of cases with amoebic infection. The first significant observation we made through analyses of these cases was a dramatic increment in the adult male cases with confirmed symptomatic amoebiasis. Subsequently, we found that approximately 40% of our symptomatic cases were positive on Treponema pallidum hemagglutination test (TPHA), half of whom were also positive on non-treponemal antigen tests like VDRL slide test (Table 1). On the basis of these data, we proposed the occurrence of sexually-transmitted amoebiasis in Japan in 1983^(11, 12). Elucidation of hygienic conditions of biased males seemed important judging from their status in Japan. Subsequent comparison of sexually-transmitted amoebiasis between Japan and the western countries elicited some interesting differences. First of all, it seemed noteworthy that

the Japanese cases diagnosed as sexually-transmitted amoebiasis were found because they showed distinct symptoms conformed to those of amoebiasis. All of these cases were positive serologically on gel diffusion precipitin test (GDP) and indirect fluorescent antibody test (IFA). These findings indicate that the sex ratio, the prevalence of positive syphilis serology (or history) and some other epidemiological features of Japanese cases with invasive amoebiasis resemble those of the cases with sexually-transmitted amoebiasis in the western countries, virtually all of whom were asymptomatic cyst carriers. Judging from the similarity of host and environmental factors concerning oral infections between Japan and the western countries, the most reasonable explanation is that pathogenic E. histolytica is spread among biased males in Japan⁽¹³⁾. This was confirmed recently by our observation that more than 15% of biased males in some large cities of Japan were seropositive on enzyme-linked immunosorbent assay (ELISA), half of whom were also positive on GDP⁽¹⁴⁾. These data strongly suggest that Japanese biased males were frequently associated with tissue invasion of E. histolytica which may lead to development of clinical symptoms.

Serodiagnosis of sexually-transmitted amoebiasis

Concerning the serodiagnosis of invasive amoebiasis, some useful procedures like GDP and IFA have been widely employed⁽¹⁵⁾. Accordingly, there seems little problem about symptomatic sexua-

lly-transmitted amoebiasis.

As regards diagnosis of asymptomatic sexually-transmitted amoebiasis, stool examination has been the only one method to identify, because most of the carriers have been considered to lack production of anti-amoebic antibody⁽¹⁰⁾, and actually only 20 to 40% of the carriers were judged positive by the currently available serologic tests. Sargeant⁽¹⁰⁾ has even listed the absence of anti-amoebic antibody in addition to low-virulent strain type of zymodemes and the lack in the clinical symptoms to define asymptomatic cyst carriers. It is further suggested that asymptomatic cases with anti-amoebic antibody or virulent strain-type zymodemes were quite exceptional and occupy only a small part of the carriers. Moreover, GDP has been considered to be useful for selecting the carriers infected with virulent strains of E. histolytica⁽¹⁶⁾. In spite of these recent concepts on the carriers, we found that more than 85% of asymptomatic cyst carriers showed the higher absorbance of ELISA than the maximum value of the healthy controls⁽¹⁷⁾, although only 20 to 25% were positive on GDP and IFA. The absorption and blocking studies attempted to examine the specificity of this ELISA indicated that these manipulations lowered the absorbance down to the control level. Distribution of the absorbance according to the result of GDP showed that the average absorbance of the GDP-negative cyst carriers was slightly lower than that of the positive ones; however, later statistical analyses did not demonstrate any significant difference

nance between these two values.

The finding that even asymptomatic cyst carriers are often associated with production of anti-amoebic antibody was further confirmed by the Western blotting analysis⁽¹⁸⁾. This procedure indicated that the pattern of antigen recognition by the sera from GDP-negative cyst carriers and from the cases with intestinal amoebiasis were similar. The sera from the cases with amoebic liver abscess recognized the antigenic epitopes essentially in the same manner except for a high molecular antigenic epitope(s) recognized only by the sera from the cases with amoebic liver abscess. It is still not known if the antigenic epitope(s) of a high molecular weight is a specific antigen for virulent strains of E. histolytica; however, it seems interesting that the sera from the cases with amoebic liver abscess, the typical invasive amoebiasis, can recognize some peculiar antigenic epitope(s).

Conclusion

Epidemiology and serodiagnosis of a novel sexually-transmitted disease, amoebic infection in male homosexuals, were summarized in this communication. Such sexually-transmitted diseases, as judged from the route of transmission, would be increasingly important in the future particularly in relation with acquired immunodeficiency syndrome (AIDS).

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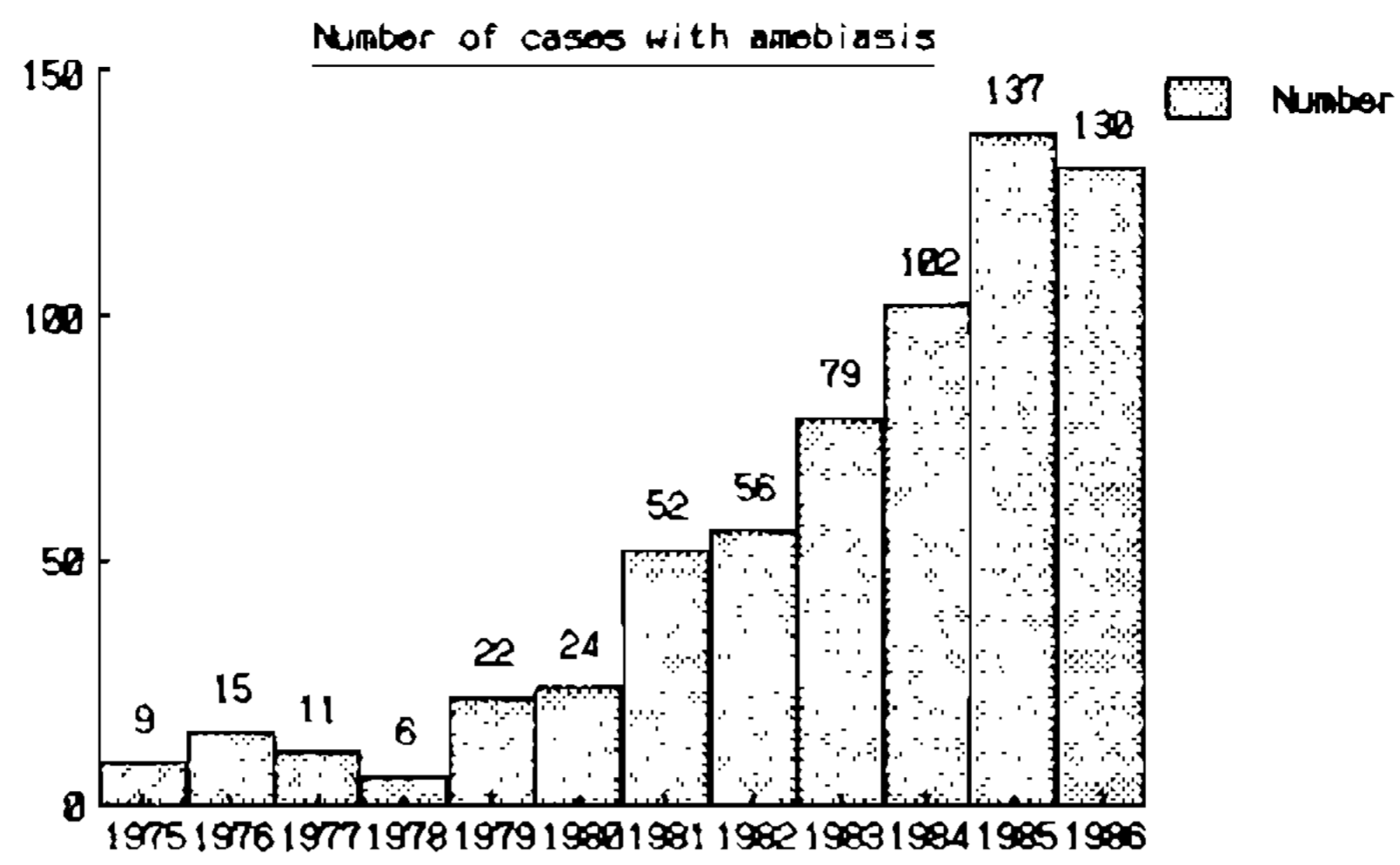


Figure 1 Number of cases with confirmed symptomatic amoebiasis reported to the Ministry of Health and Welfare, the Japanese Government (Data from the Statistics of Communicable Diseases issued by the Ministry)

Table 1 Correlation of positive syphilis serology with gel diffusion precipitin test (GDP) for amoebiasis

| | Japanese | | Indo-Chinese refugees | |
|-------------|----------|---------|-----------------------|---------|
| | GDP*(+) | GDP (-) | GDP (+) | GDP (-) |
| TPHA** (+) | 25 | 0 | 2 | 31 |
| TPHA (-) | 30 | 109 | 35 | 633 |
| NTAS*** (+) | 12 | 0 | 3 | 22 |
| NTAS (-) | 43 | 109 | 34 | 642 |

Indo-Chinese refugees were examined as a reference group of the amoebic infection outside Japan.

GDP*: GDP is one of the most reliable serological tests for the diagnosis of invasive amoebiasis.

TPHA**: Treponema pallidum hemagglutination test. One of the best tests for the serodiagnosis of syphilis

NTAS***: Non-treponemal antigen tests like VDRL slide test, RPR card test and Ogata's test.