Original article

Epidemiologic analysis of a previous outbreak of bubonic plague: The first identified outbreak with bacteriological confirmation in Kobe and Osaka, Japan

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Abstract

Objective: To characterize the case fatality and estimate the symptomatic period of bubonic plague. **Methods**: Epidemiologic analyses of a previous outbreak of plague in Osaka and Kobe, two major port cities in Japan, from 1899-1900 were performed. In addition to date of onset of symptoms, gender, age and the date of death were extracted from the historical data. The time from onset to death (symptomatic period) was fitted to gamma distribution using the maximum likelihood method. **Results**: Temporal distribution revealed suspected chains of transmission of the primary pneumonic plague at the late stage of the outbreak. The case fatality of bubonic plague without specific treatment was 83.4 %, and the mean time from onset to death was estimated as 4.7 days (95 % confidence interval: 4.0, 5.5). **Conclusion**: Case fatality of bubonic plague without specific treatment was extremely high. The symptomatic period of bubonic plague appeared to be longer than that of pneumonic plague.

Keywords: *Yersinia pestis*; Bubonic plague; epidemiology; statistical distribution; confidence interval; Japan

INTRODUCTION

Although the incidence of plague has gradually decreased worldwide, there is a serious threat of potential bioterrorist attacks using its causative agent, *Yersinia pestis*[1]. In addition to rigorous epidemiologic studies and implementation of counter measures in specific enzootic regions such as Madagascar[2,3], descriptive epidemiologic studies in other regions have also been performed, many before maturation of epidemiologic methods, possibly offering new insights into this disease. Although awareness of primary pneumonic plague perhaps has priority at present due to possible aerosolized release[4-7], bubonic plague should also be observed in the event of future attacks, and thus, the epidemiologic characteristics of this disease require further attention. In this paper, I document epidemiologic records of a first identified bubonic plague outbreak in Japan to parameterize the symptomatic period and examine the characteristic factors.

MATERIALS AND METHODS

Although there is no documentation of clarified plague outbreaks in Japan up to the mid-19th because of the country's isolated state, initiation of trade resulted in Japan's first outbreak in Osaka and Kobe, two major adjacent port cities, from 1899-1900[8]. Bubonic plague cases continuously appeared around both ports, causing the Japanese government to declare a high level of alert. Extensive

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case findings in addition to detailed active surveillance were performed by a task force group led by Dr. Shibasaburo Kitasato, Head of the National Institute of Communicable Diseases at that time. Clinical histories of those who underwent confirmed diagnosis based on the isolation of *Y. pestis* from aspiration of lymph node (bubo), blood and sputum were documented. There was no specific treatment during this outbreak.

As descriptive information, the temporal distribution of cases was obtained using the date of onset of symptoms (i.e., fever, chills or headache). Other information included gender, age and the date of death. The time from onset to death (symptomatic period) was fitted to gamma distribution using the maximum likelihood method. Those diagnosed with pneumonic plague were excluded from this estimation. The Cramer-Smirnov-von Mises test was used as a test of significance (goodness-of-fit) for the gamma distribution. Furthermore, the relationships between death or symptomatic period and the other variables (age and gender) were also investigated. Gender and death were measured as dichotomous variables while other variables were modeled as continuous. To examine the univariate associations among binary variables, between the binary and continuous variables, and correlations between continuous variables, Fisher's exact text, Wilcoxon-Mann-Whitney test, and Spearman's rank correlation were used respectively. The level of statistical significance was set at $P=0.05$. All statistical data were analyzed using statistical software JMP ver. 7.0 (SAS Institute Inc., Cary, NC).

RESULTS

Sixty-seven cases were diagnosed in total (Figure 1A); 25 cases were female (37.3 %). The mean age (and standard deviation, SD) was 27.1 (16.1). Overall case fatality was 86.6 % (n = 58), and according to the disease classification at diagnosis (bubonic, septicemic and pneumonic plague, respectively) was 83.4 (n = 35), 75.0 (n = 6) and 100 (n = 17) %. The involved lymph nodes, which allowed confirmation of diagnosis, included inguinal (n = 15; 35.7 %), femoral (n = 12; 40.0 %), cervical (n = 7; 16.7 %), axillary (n = 6; 14.3 %) and submandibular bubos (n = 5; 25.0 %). Both age (Wilcoxon-Mann-Whitney: z = −0.083, P = 0.934) and gender (Fisher: P = 0.466) showed no significant associations with death.

The maximum likelihood estimate of the mean time from onset to death was 4.7 days [95% confidence interval (CI): 4.0, 5.5]. Figure 1B shows the fitted gamma distribution, yielding estimates of scale and shape parameters of 4.13 and 1.14 respectively. A Cramer-Smirnov-von Mises goodness-of-fit test revealed no significant deviation between the observed and expected distributions (W^2 = 0.104, P = 0.250). Gender (Wilcoxon-Mann-Whitney: z = -1.263, P = 0.207) and age (Spearman's P = 0.192, P = 0.150) revealed no association or correlation with the symptomatic period respectively.

DISCUSSION

Case fatality (CF) of bubonic plague without specific treatment appears to be extremely high. Although it is likely that the case histories, which were limited to those with confirmed diagnosis, might cause slight overestimations of CF due to sampling bias, the obtained estimates were compatible with earlier suggestions[1]. It is notable that the outbreak terminated with subsequent occurrence of pneumonic plague cases within a few households. Ishigami and Kitasato demonstrated that a total of 7 family members in addition to a medical doctor and a nurse who took care of earlier cases showed probable contact and presented without bubo, and were suspected of having primary pneumonic plague[8]. Thus, the estimate of symptomatic period was obtained excluding pneumonic plague. The estimate was longer than that of pneumonic plague previously documented[1], suggesting that the disease progressed from a bubonic form. The lack of an association between age/gender and two outcomes (death and the symptomatic period) was consistent with previous studies[2,3].

In conclusion, temporal distribution of a plague outbreak was investigated, distinguishing the clinical types of plague at diagnosis. The maximum likeli-

hood estimate of time from onset to death, which appeared to be longer than that of pneumonic plague, was reasonably obtained.

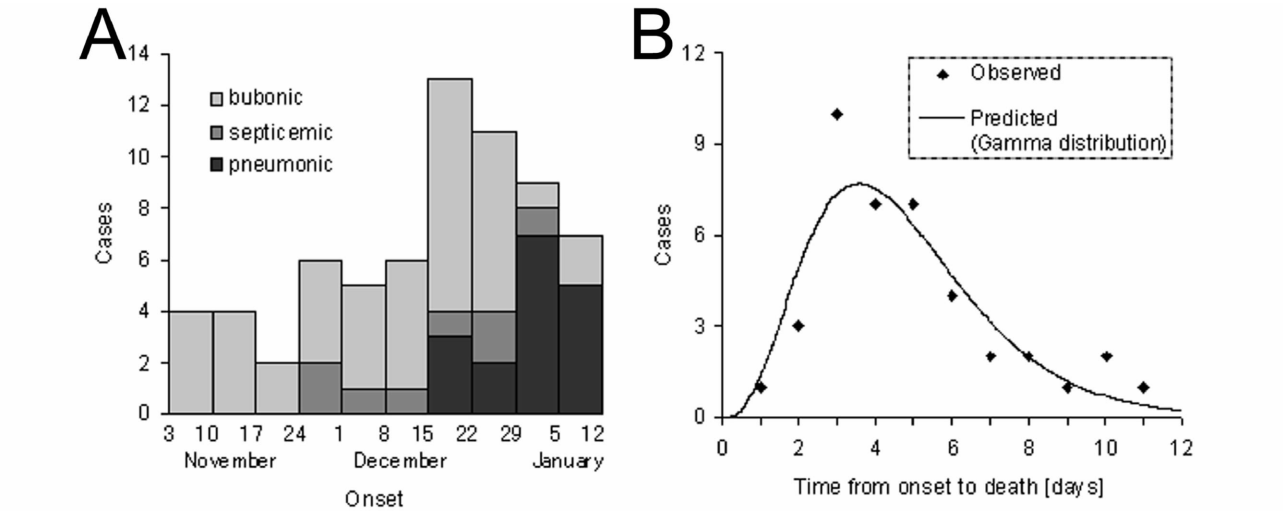

Fig. 1 Epidemiologic description of the plague outbreak in Kobe and Osaka, Japan, from 1899-1900.

A. Temporal distribution of the cases ($n = 67$) by date of onset and clinical classification at the time of diagnosis. B. Frequency distribution of the time from onset to death among the bubonic plague cases ($n = 40$) based on a maximum likelihood estimation assuming gamma distribution (solid line). The observed frequency is shown as dots.

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