

CLINICAL AND EPIDEMIOLOGIC STUDIES ON PRIMARY ATYPICAL PNEUMONIA IN THE SUBURBS OF MAIZURU-CITY

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In early summer, 1963, many patients with cough and fever were seen in the suburbs of Maizuru-city (Kasa-area). These patients were diagnosed as "primary atypical pneumonia" (PAP). The patient-number reached 60 within two-and-a-half months. This epidemic ended rapidly before August and no more patients were discovered until May, 1965. Around the end of May, 1965, a patient with pneumonia was detected again in the same area and 90 patients were found in this area during the period May through August. Most of patients were school boys and girls. Some classes of an elementary school were closed for about one month in order to isolate children from the patients. This was a great problem in this area because it disrupted school and home. If this kind of epidemic arises in a large city the damage may be much greater. Therefore, these epidemics are epidemiologically important. This paper is a report based on the experience of the epidemic.

METHOD OF STUDY

Clinical findings were those of "primary atypical pneumonia" described by Hinshaw & Garland¹⁾. Dry cough, increasing fever, marked infiltration in the lungs on X-ray, a rise in cold hemagglutinin titer ($\geq 1:32$), but no, or mild leucocytosis, no eosinophilia.

Important diseases to be considered are pulmonary tuberculosis, lobar pneumonia, influenzae pneumonia, adenovirus pneumonia, and other bacterial pneumonias. Loeffler's syndrome may also be included in a group which shows some similarity to primary atypical pneumonia. The patients were checked by clinical findings, X-ray findings and laboratory findings for diagnosis.

After diagnosis some of the patients were admitted to a hospital (Yagumo Hospital) and the others were treated in the outpatient clinic. These patients received tetracycline or chloramphenicol for 2–4 weeks, and were checked by X-ray, and cold hemagglutinin titers once a week.

July 11, 1965, a middle day in the epidemic, chest X-ray films of the inhabitants in the Okada area (a subarea of Kasa-area, where many patients were seen) were taken for detecting patients without complaint.

RESULTS

Fig. 1 shows a three-year summary of the occurrence of PAP in the Kasa-area of Maizuru-city (population about 8,000). Sixty patients were discovered in the first epidemic (May-July, 1963) and 90 patients in the second epidemic May through August, 1965. No patients with this diagnosis were seen during the period August, 1963 through April, 1965.

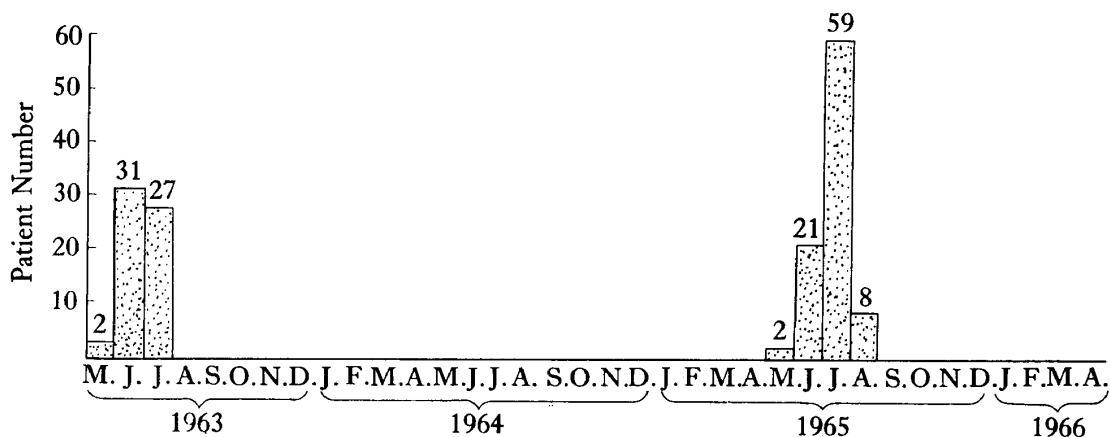


Fig. 1. Three-year summary of primary atypical pneumonia in the Kasa-area.

The pattern of this epidemic is very characteristic. It explosively appeared and quickly disappeared within two or three months. This quick disappearance may be caused by existence of immunity developed in this area.

Chest X-ray showed pneumonitis in all of patients a few days after onset of illness. In most cases pneumonitis was found in the right lower lung field. This infiltration usually vanished 2–3 weeks later. These results are shown in Table 1 and 2. and Photo. 1 and 2.

The main symptoms are shown in Fig. 2. Both cough and fever were remarkable in this clinical picture. The patients complaining of cough reached 84 cases (93%) and patients with fever ($\geq 37.5^{\circ}\text{C}$) reached 72 cases (80%). On the

Table 1. The distribution of radiological changes (150 cases).

	right	left
upper lung field	8	10* ¹
middle lung field	10	7
lower lung field	106* ^{1,2}	19* ²

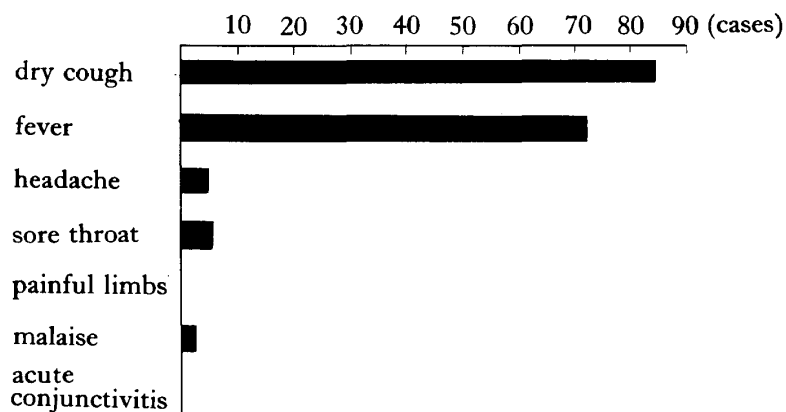
*1 Pneumonitis was seen in both left upper field and right lower field in 5 cases.

*2 Pneumonitis was seen in both left lower field and right lower field.

Table 2. The period of pneumonitis by X-ray findings (85 cases).

period (days)	<7	8~14	15~21	22~28	total
1st epidemic (1963)	4	18	6	4	32
2nd epidemic (1965)	8	24	16	5	53
total	12	42	22	9	85

other hand, sore throat, headache, painful limbs (including joint pain), malaise, and acute conjunctivitis were few or none. It is suggested that these are different from the symptoms of influenza- or adenovirus-infection. Laboratory assistance was required in order to establish the diagnosis.



6 cases were found on X-ray examination without any complaint.

Fig. 2. Clinical symptoms of patient with primary atypical pneumonia (1965).

The erythrocyte sedimentation rate was usually rapid, being over 20 mm/hr. in 70 patients and over 50 mm/hr. in 22 patients during the 2nd epidemic in 1965.

The total white blood cell count was normal or slightly elevated, and only 2 patients showed a count over 10,000/mm³. No eosinophilia was recorded.

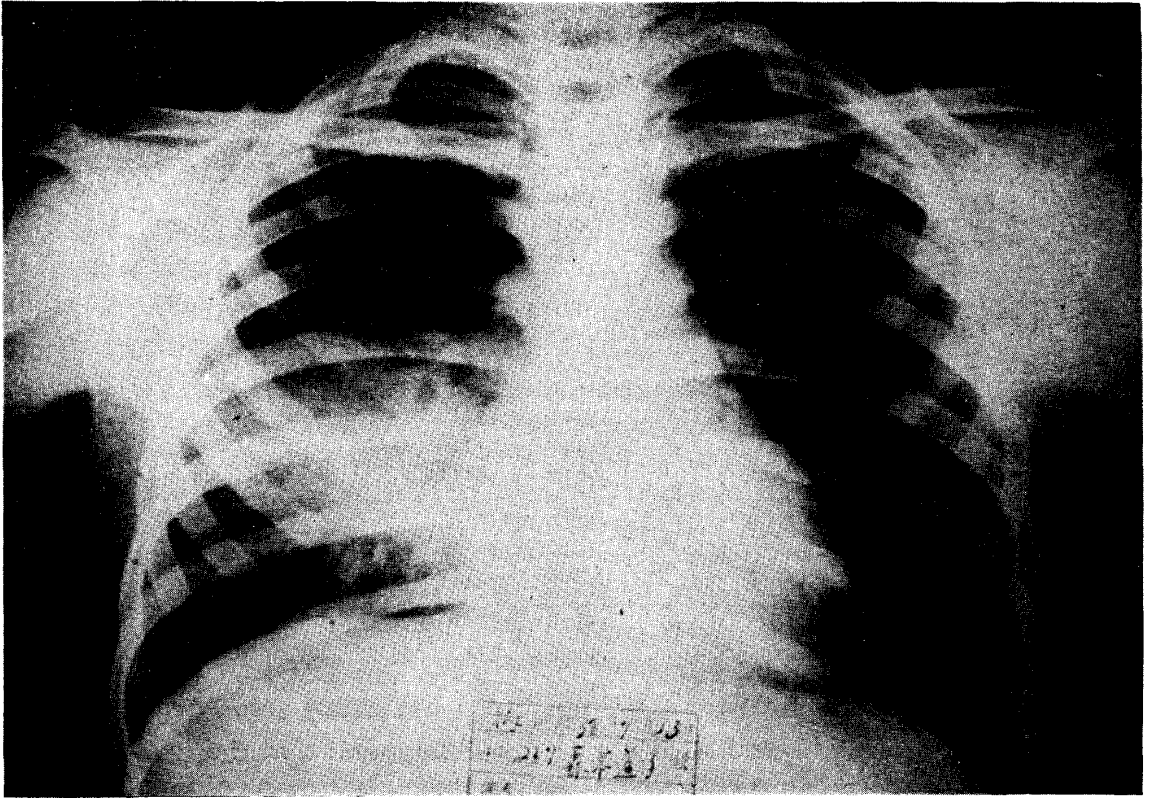


Photo. 1. M. M., ♀, 9 years old

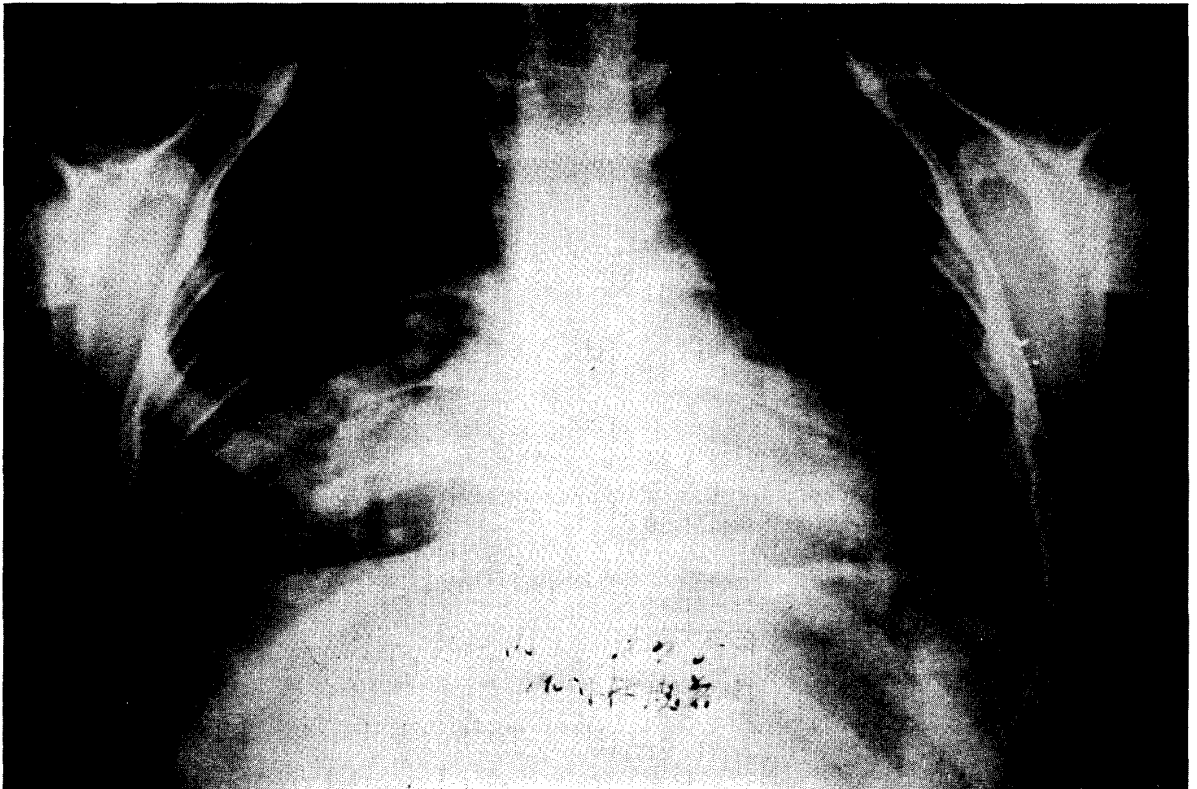


Photo. 2. T. N., ♂, 7 years old

Cold hemagglutinin tests were performed on patient-sera. The results are shown in Table 3. In the first epidemic, 1963, 49 of 60 (81%) patients were regarded as "cold-agglutinin-positive", and showed titers ≥ 32 . In the second epidemic, 1965, 67 of 77 (87%) patients showed positive results. This is an evidence of "primary atypical pneumonia". Then we tried to isolate the pathogen on a plate from throat rinse following methods described by Chanock et al.²⁾ However, it was not successful.

Table 3. Cold hemagglutinin titers of patients with primary atypical pneumonia (137 cases).

CHA titer	1st epidemic (1963)	2nd epidemic (1965)	total
≤ 4	4	5	9
8	3	1	4
16	4	4	8
32	10	2	12
64	18	14	32
128	7	23	30
256	12	13	25
512	2	14	16
1024	0	1	1
total	60	77	137

The age-distribution of all of the patients in this study is shown in Table 4. Many patients are seen in the range of 4-11 years old. On the contrary, few adult patients may be another proof of acquired immunity or subclinical infection in adults.

Table 4. Distribution of patients by age.

age	1~3	4~11	12~17	18~49	≥ 50	total
1st epidemic (1963)	11	34	12	0	3	60
2nd epidemic (1965)	4	55	27	3	1	90
total	15	89	39	3	4	150

A screening X-ray examination was performed in the Okada-area for the purpose of discovering asymptomatic patients on 11 July, 1965. The day was located in the middle of an epidemic. Seven hundred sixty four of the inhabitants were checked for X-ray findings. Pneumonitis was found in the lungs of twelve persons. They were examined by both clinical and laboratory means. Nine were

primary atypical pneumonia and the other three were tuberculosis. Five in nine were 4–11 years old and none was 17–49 years old. The result shows that there are few adult patients.

DISCUSSION

“Primary atypical pneumonia” (PAP) is a disease named by the Commission of Acute Respiratory Diseases at Fort Bragg, NC in 1943. However, the pathogen was unknown for many years though many investigators tried to isolate it.

In 1944, Eaton et al.³⁾ reported that a virus-like agent isolated from the patient could cause the pneumonia in cotton rats or hamsters.

This agent lost its activity after neutralization with convalescent-patient serum. This agent was called “Eaton Agent”.

Liu⁴⁾ also isolated the pathogen from patients and identified the “Eaton Agent” immunologically using the fluorescent antibody technique.

Marmion et al.⁵⁾ reported that this agent was a kind of mycoplasma because growth was inhibited in the culture-media by adding organic gold salt.

Chanock et al.²⁾ succeeded in culturing the agent with cell-free media and identified the agent with mycoplasma using both fluorescent antibody technique and complement fixation technique. The agent has been called “mycoplasma pneumoniae”.

It is well known that mycoplasma pneumoniae is the cause of an epidemic. Chanock et al.²⁾ reported an epidemic in the marine camp on Parris Island in 1959. Jansson et al.⁶⁾ reported an epidemic in Helsinki, 1962–1963 and Grayston et al.⁷⁾ reported another epidemic in Seattle, 1962–1963. In Japan, Niizu et al.⁸⁾ and Kitamoto et al.⁹⁾ reported epidemics. However, the scale of those epidemics was not so large and occurred just once in each place except Parris Island. The epidemic described in this report is one of the largest scale of epidemics in the world. Fortunately, the epidemic did not cause much damage because the infectious area had a limited population, but if it had happened in a large city, the results could be miserable. So, I hope that this report will be an alarm bell for public health services.

Two characteristic points were found in the epidemic as follows;

- 1) The epidemic was found in early summer only and no patient was seen in winter.
- 2) Most of patients were of school-age and few patients were more than 18 years old.

Jansson et al.,¹⁰⁾ and Kitamoto et al.⁹⁾ reported that epidemics of PAP are usually seen in winter and very few in summer. On the contrary, Chanock et al.²⁾

reported an epidemic during the period July through December, 1959. It is possible to find an epidemic of PAP even in the summer as we report.

The second point; the patients were quite young. Most of patients were children in elementary school. It is generally believed that PAP can be found in all ages as shown by the reports of Jansson et al.,⁶⁾ Graystone et al.,⁷⁾ Kitamoto et al.⁹⁾ and Niizu et al.⁸⁾ However, in their data they also realized that young persons were apt to catch PAP. In our report, this tendency is very clear, probably caused by the acquired immunity to the pathogen in adults. This area is closed and immigration from other places is very limited. So all adults who have lived in this area for many years, might have experienced PAP already and acquired immunity. Then only children might not have immunity in this epidemic. These facts may suggest that a strong immunity exists in PAP. Actually, we did not find any person who caught PAP twice during these three years (May, 1963–April 1966). In addition, the end of the epidemics came so quickly that acquired immunity seemed the only explanation for this phenomenon. Several years ago, this disease was not given attention as an important disease because of the good prognosis. Some people believed that it was just catching cold in summer. But, there is a problem when the disease makes an epidemic which can disrupt school and home. I believe that it is possible to prevent an epidemic of the disease by vaccination which gives us acquired immunity to PAP.

SUMMARY

Epidemics of primary atypical pneumonia were observed for three years (1963–1966) in Kasa-area in the suburbs of Maizuru-city, Japan. Two epidemics were seen in this area in early summer (1963 & 1965). Most of the patients were children of elementary school age. The total number of the patients reached 60 in 1963, 90 in 1965. It is suggested by the investigation that acquired immunity to this disease exists.

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