MORTALITY OF ORIENTALS WITH SYSTEMIC LUPUS ERYTHEMATOSUS — A REAPPRAISAL

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SYNOPSIS

The principal causes of death of 50 patients with systemic lupus erythematosus (SLE) from 1976 to 1984 were reviewed. Infection (48%), central nervous system involvement (18%) and renal failure (14%) were the most frequent primary causes of death. Late deaths from vascular complications were infrequent.

INTRODUCTION

Previous study of mortality in systemic lupus erythematosus from Singapore in 1973 showed that neurological involvement, renal failure and infections were the three commonest causes of death (1). During the past 9 years, improvements in therapy occurrred. This report retrospectively analyses the causes of death of 50 patients with SLE during this period. Our findings showed a changed pattern amongst our patients. Infections have emerged as the leading cause of death.

MATERIALS AND METHODS

During the period 1976 to 1984, a total of 400 patients with SLE were admitted to the Medical Unit IV of Tan Tock Seng Hospital. All patients fulfilled the criteria for SLE (2). Causes of death were ascertained from reviews of hospital records. These were determined on basis of clinical data and on autopsy findings in 3 patients. When death was attributable to SLE, specific organ system activity, such as active glomerulonephritis, severe thrombocytopenia, coronary arteritis was identified when possible. The primary cause of death was defined as the immediate event responsible for the patient's demise (eg. bronchopneumonia in a patient with non-azotemic glomerulonephritis). Contributing causes of death were defined as underlying factors in the patient's demise (eg. active lupus nephritis in a patient treated with high dose steroids and died of peritonitis). When there were multiple factors involved, where no one cause predominated, the cause was listed as unknown.

RESULTS

50 patients with SLE died during the study period. 40 were Chinese, 6 Malays, 4 Indians, 3 were males. The mean age at death was 27.6 years (range 10—75 years). The mean disease duration from onset of multisystem disease to death was 46.9 months.

Causes of death

Table 1 summarizes the primary causes of death. Active SLE related specific organ involvement was the primary cause of death in 20 (40%) patients. SLE was a contributory factor in the deaths of another 16 (32%) patients.

There has been a definite shift in causes of death since 1973. Uraemia accounted for 30% of deaths in the 10 year period before 1973. It is now the primary cause of death in 7 patients (14%). Active lupus nephritis was a contributory cause of death in 18 patients. A total of 8 patients had renal biopsies. One patient underwent periotneal dialysis. None had renal transplantation. Central nervous system lupus with such diverse manifestations as seizures, focal neurological abnormalities, cerebral infarct or coma was the primary cause of death in 9 patients. Cerebral infarcts were confirmed by CT scan in 4 patients. 2 patients had refractory grand mal seizures and one, brain-stem haemorrhage.

Infection was by far the most frequent primary cause of death in 24 (48%) patients. Gram-negative bacteria, fungi, tubercle bacilli, Salmonella and cytomegalovirus were the pathogens in 13 patients (Table 2). Multiple organisms were identified in 2. Among the 24 patients whom infections were the primary cause of death, 18 had active lupus at the time of death. Active lupus nephritis was present in all patients and active lupus CNS involvement was a contributing cause in the deaths of 6 patients. One patient had haemolytic anaemia. All 24 patients who died from infection were receiving corticosteroids (a minimum of 20 mg prednisolone daily). 6 patients had in addition another immunosuppressive, either cyclophosphamide or azathioprine.

Other forms of active SLE were the primary cause of death in 4 patients, including acute gastrointestinal bleed and cerebral haemorrhage due to severe thrombocytopenia in 2 patients, myocardial infarction in a 16 year old boy and cardiomyopathy in another. One death was attributed to pulmonary embolism and 4 others of stroke.

TABLE 1: CAUSE OF DEATH IN 50 PATIENTS WITH SLE

Primary cause of death	No. of patients
Active SLE specific organ involvement	20
Renal	7
CNS	5
Haematologic	2
Cardiac	1
Infection	24
With active SLE	18
SLE inactive	6
Vascular events	1
Pulmonary embolism	1
Myocardial infarct	1
Cerebrovascular accident	4
Unrelated	1
Unknown	4

TABLE 2: INFECTIONS AS PRIMARY CAUSE OF DEATH

No. of patients	Organism	Involvement	Cytotoxic drugs received
3	Pseudomonas aeruginosa	Septicaemia	No
3	Cryptococcus neoformans	Meningitis	Azathioprine
2	Candida albicans	Pneumonia	No
2	Klebsiella	Septicaemia, peritonitis	No
1	Tubercle bacilli	Pneumonia	No
1	Escherichia Coli	Septicaemia	Azathioprine
1	Salmonella D	Septicaemia	No
1	β-haemolytic streptococcus	Septicaemia	Azathioprine
1	Cytomegalovirus	Viraemia	No

DISCUSSION

In this series, infection heads the list of cause of death in SLE in Chinese. It accounted for 48% of deaths. Infection has always been acknowledged as a major factor in morbidity and mortality in patients with SLE (3,4). Prior to the availability of antibiotics and corticosteroids it was a leading cause of death. Klemperer (5) observed that 40% of deaths in SLE were due to infection. Infection continues to be an outstanding cause of death in the antibiotic era. In spite of advancement of knowledge in SLE, deaths from infections were shown to be significantly associated with the peak corticosteroid dose received (6). In our study, septicaemias and pneumonias were the predominant infections, and gram-negative organisms and fungi were the most common offenders.

Death from active lupus disease was substantial (20 out of the total of 50). CNS disease was the commonest manifestation of active SLE that resulted in death. It contributed primarily to 9 (18%) deaths. This decrease compared to the previous report in 1973 (1) is striking.

Renal involvement in SLE has been extensively studied (7-9). Deaths from uraemia are substantial in a few series (10,11). However, our series shows a decline in deaths from uraemia from 30% before 1973 to 14% in this study. The availability of dialysis and transplantation undoubtedly contributed to the decreased number of deaths from renal failure in other series (12,13). In contrast, none of our patient received such forms of therapy.

The prevalence of cardiovascular events as causes of death in SLE have been reported to be on the increase (14). Vascular diseases such as myocardial infarction, pulmonary embolism, cerebrovascular accidents were encountered late in the course of SLE disease (15,16), and were responsible for death in 45% of patients in recent series (14). In this study, 5 (10%) patients died from a vascular episode. This apparent disparity in our series is due to the great number of young patients in this study. Longer follow-up and further studies may throw more light on this aspect of accelerated atherosclerosis amongst our patients.

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COMMUNITY ACQUIRED MYCOPLASMAL PNEUMONIA

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SYNOPSIS

Twelve adults with community acquired mycoplasmal pneumonia were seen over a period of two years since 1983. There were nine females and three males with a mean age of 22.2 years. Cough productive of yellowish sputum and fever were the commonest presenting symptoms and left basal pneumonia was the most frequent radiological manifestation. Prexia subsided rapidly in response to erythromycin and radiological resolution took about two weeks in the majority.

INTRODUCTION

Mycoplasmata, once referred to as Eaton's agent, are believed to be the smallest free living organisms. Several species of mycoplasmata exist as saprophytes in man; however, only mycoplasma pneumoniae is responsible for causing disease in 3 – 10% (1) of the infected persons.

Mycoplasmal pneumonia was previously thought to occur as outbreaks espeically in institutions and army barracks; however, a number of recent reports indicate it can, not infrequently, present as isolated cases.

The present study was undertaken to evaluate local presentations in relation to age, sex and racial distribution, clinical manifestations, radiological appearance and response to antibiotic treatment.

Mycoplasmal pneumonia commonly known to affect children and young adults, but older people of either sex are also susceptible. In various series mycoplasma pneumoniae was responsible for 11 – 50% of the pneumonia in patients over the age of 40. A high index of suspicion is required and diagnosis cannot be discarded merely on the basis of presenting symptoms, age or sex of the patient.

MATERIALS AND METHOD

Over a period of two years from February 1983 twelve adults with mycoplasmal pneumonia were seen in our department.

The majority of patients were Chinese and there was a marked predominance of females. Their ages ranged from 12 to 48 years with a mean age of 22.2 years (Table I).

Most of the patients had cough productive yellowish sputum and fever with chills on admission. The duration of these complaints ranged from 2 days to 2 weeks; and in about half the cases the symptoms had been present for a week or more. Three had chest pain and one had palpitation. None of the patients complained of dyspnoea (Table II).

TABLE I
RACE, AGE AND SEX DISTRIBUTION

TOTAL NO OF MYCOPLASMAL PNEUMONIA 12	
RACE	
Chinese	9 (75%)
Malays	3
AGE	
10 — 19 Years	5
20 — 29 Years	6 (50%)
30 — 39 Years	0
40 — 49 Years	1
SEX	
Male	9 (75%)
Female	3

TABLE II

TOTAL NO OF MYCOPLASMAL PNEUMONIA 12	
SYMPTOMS	
Cough	11
Sputum	10
Fever	12
Chest Pain	3
Sore Throat	1
Palpitation	1
Dyspnoea	0
Headache	2
Arthralgia/Arthritis	0
Skin Rash	0

All patients had a complete medical examination and routine investigations included haemoglobin concentration, total white count, sputum cultures and chest x-rays. Blood cultures for pyogenic organisms and ECG were carried out in six.

The diagnosis of mycoplasmal pneumonia was confirmed only in the presence of significant cold agglutinins (titre of 1/64 or more) and or mycoplasmal antibodies (a four fold rise in titre or a single titre of 1/128 or more).

Table III shows that none of the patients had anemia and leucocytosis was present in only three. Though purulent sputum was observed in eleven, none grew pyogenic organisms on culture. Cold agglutinins were detected in nine cases, but it was significant in only four. (Case no. 6, 7, 10 & 11) Serology revealed mycoplasmal antibodies in all ten patients in whom the test was performed.

All twelve patients had radiological evidence of segmental pneumonia. (Fig. 1 & 2) It can be seen from Table IV, the left lower lobe was most frequently in-

TABLE III
INVESTIGATIONS

Case No Sex & Age	Haemoglobin GM%	Total White Count	Sputum Culture	Blood Culture	Cold Agglutinin	Mycoplasma Antibody
1 (F/48)	13.4	10,000	Negative	Negative	Negative	Positive
2 (M/19)	13.9	6,100	Negative	Negative	Negative	Postive
3 (F/12)	12.1	5,300	Negative	Not Done	Present	Positive
4 (F/24)	13.7	19,700	Negative	Not Done	Not Done	Positive
5 (F/21)	14.6	6,600	Negative	Negative	Present	Positive
6 (F/12)	12.4	5,000	Negative	Not Done	Present	Not Done
7 (F/22)	11.7	15,300	Negative	Not Done	Present	Positive
8 (F/18)	12.4	7,000	Negative	Negative	Present	Positive
9 (F/29)	12.7	7,800	Negative	Negative	Present	Positive
10 (F/22)	12.8	7,900	Negative	Negative	Present	Positive
11 (F/16)	13.9	9,300	Not Done	Not Done	Present	Not Done
12 (M/23)	14.3	10.300	Negative	Negative	Present	Positive

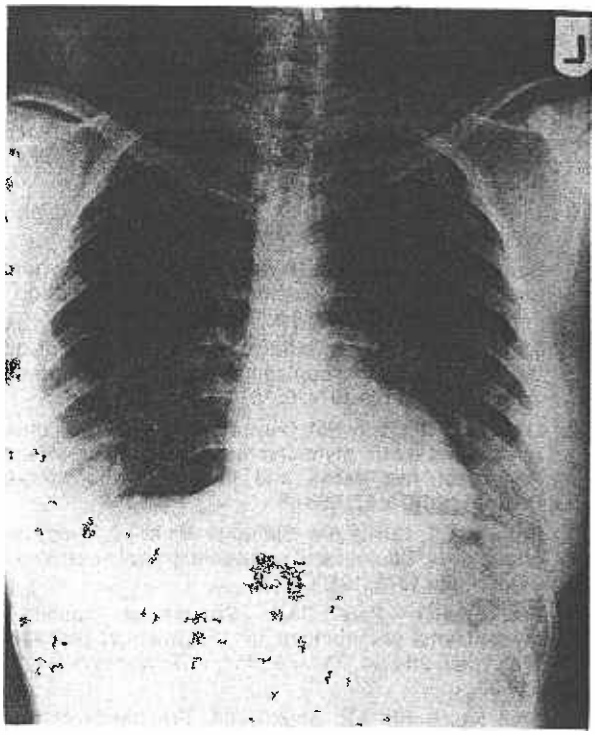

Fig 1: Bilateral patchy basal pneumonia (Bronchopneumonia)

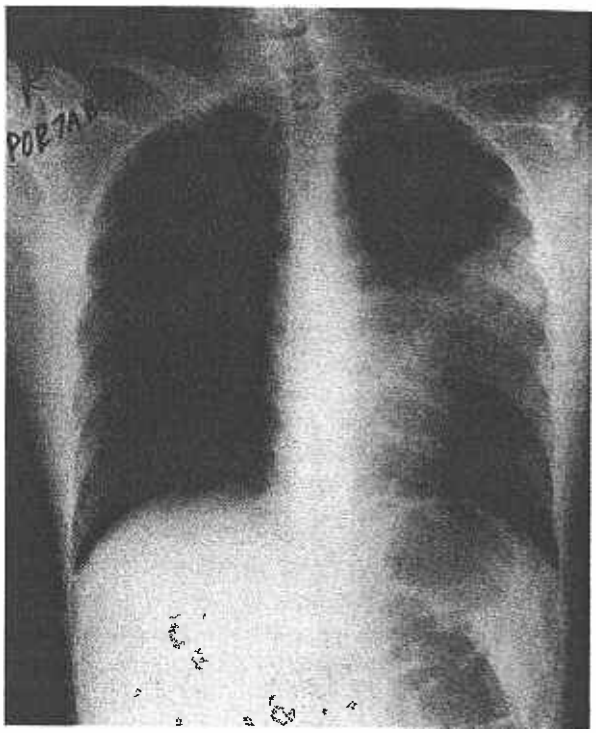

Fig 2: Homogeneous opacity in left mid zone (Segmental consolidation)

vovled. Bilateral basal pneumonia was seen in one patient. A consolidation was seen in four patients, bronchopneumonic pattern in seven and reticular appearance in one.

The ten patients in whom mycoplasma pneumonia was thought to be likely at the time of admission were commenced on erythromycin 500 mg 6 hourly and continued for a period of two weeks. In all these patients the temperature, which ranged from 38°C to 39.5°C on admission, settled in 48 hours. The two patients, a 48 year old female and a 19 year old male, in whom bacterial pneumonia was suspected, were treated with ampicillin, and crystalline penicillin and gentamycin respectively. In the female patient the fever took 5 days to subside and in the young male it took 12 days to settle. In eight out of the ten who received erythromycin radiological resolution occurred in two weeks. None of the patients had a relapse.

TABLE IV
CHEST X-RAY

Site	No of Cases
Right Upper Lobe	0
Left Upper Lobe	2
Right Middle Lobe	1
Right Lower Lobe	2
Left Lower Lobe	8

DISCUSSION

Eaton, Meiklejohn and Von Herick isolated a filtrable agent in 1944 (2) which was later identified as mycoplasma pneumoniae. Mycoplasmal pneumonia is worldwide in distribution. Though epidemics (3) are known to occur every 2 to 6 years, it is also endemic throughout the year. School aged children are most frequently infected, many such infections are mild and may be radiologically clear. Pneumonias, however, occur predominantly in between the ages of 10 and 30 yeHrs (4). In our department where patients aged 12 years and above are admitted the age distribution of mycoplasma pneumonia is similar.

Cough and fever were present in almost all the patients, whereas Dean (5) in his collection of 42 cases found fever in only 20. Surprisingly purulent sputum was seen in ten of the patients, and none of the sputa grew pyogenic organisms on culture. Murray et al (6) have noted a marked predominance of polymorphonuclear leucocytes on gram staining of sputa and subsequent culture revealed only a normal flora. A similar observation was made by Collier (7), who in addition also reported on the purulent character of sputum.

Extrapulmonary manifestations such as cutaneous exanthems (8,9,10) gastrointestinal (5,11), and neurological complications (12) were not seen in any of the patients. One patient (48 year old female) and inverted T-waves in the anterior chest leads, and another patient who complained of palpitations was found to have paroxysmal atrial tachycardia on ECG. Pericarditis, myocarditis and heart block have been mentioned in previous reports, but PAT has not been noted in the past.

There is marked female preponderance in the present series, and a similar finding was also seen in Dean's collection of forty two patients. Patnam (13) on the other hand and equal number of male and female patients in his study of 100 patients.

Bronchopneumonia and consolidation were the main roentgenographic features, and only one patient had suggestion of reticular appearance. Fraser (14) thinks the different radiological features merely represent various phases of mycoplasmal pneumonia. Pleural effusion has been reported to occur in up to 20 percent (15) of the patients, was not observed in any.

Though M. pneumoniae can be cultured, the procedure is tedious and expensive; and diagnosis is based on serological methods using complement fixation tests. Indirect immunofluorescence titre is claimed to be a rapid and sensitive test according to Smith (16).

In all ten patients who were commenced on erythromycin the temperature settled within 48 hours, and radiological resolution occurred in most in two weeks. Erythromycin was administered for a period of at least two weeks, as a shorter course has been associated with clinical relapse (17). Tetracycline is an alternative effective drug.

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