

# SALMONELLA INFECTION IN SYSTEMIC LUPUS ERYTHEMATOSUS

M L Boey  
P H Feng

## SYNOPSIS

Seven patients with systemic lupus erythematosus (SLE) complicated by Salmonellosis are described. Three patients presented with arthritis and 2 with septicaemia. All the patients had active SLE and were on steroid therapy at the onset of the infection. Salmonella was isolated from the blood, stool and pus. The common Salmonella serotype was Salmonella typhimurium. Five patients recovered from the infection. There were 2 deaths.

A high index of suspicion of Salmonella infection is needed in SLE patients with fever and arthritis. Prolonged treatment of 3-6 weeks with antibiotics is necessary to achieve adequate eradication of the infection.

## INTRODUCTION

Patients with SLE have an increased incidence of bacterial and mycotic infections (1). Salmonellosis is an unusual but not uncommon infection in patients with SLE (2). The predisposing factors include corticosteroid therapy, use of immunosuppressive drugs, renal insufficiency, haemolytic anaemia and impaired in-vitro granulocytic and monocytic phagocytosis and bacterial activity (2, 3, 4).

This paper presents 7 patients with SLE and Salmonellosis. It describes the clinical presentations, disease activity at the onset of the infection, Salmonella serotypes and outcome.

## CASE REPORTS

### Case 1

A 16 year old Indian boy with SLE first diagnosed in 1975, was admitted on February 1979 for pain in the left hip for 2 months. Clinical examination showed that he had a low-grade fever and a tender left hip joint with limited movements. Initial x-ray of the left hip was normal. His symptoms were initially considered to be a part of the lupus process or early avascular necrosis. His left hip pain persisted and 2 months later x-ray of the left hip showed extensive destruction of the head and neck of the femur with subluxation of the femur (Fig 1). A left hip arthrotomy was performed.

Department of Medicine IV  
Tan Tock Seng Hospital  
Moulmein Road  
Singapore 1130

M L Boey, MBBS, M.Med(Int.Med)  
Registrar

P H Feng, AM, MBBS, FRCPG  
Senior Physician & Head



Fig. 1 Salmonella arthritis showing extensive destruction of joint

Pus obtained grew *Salmonella typhimurium*. He was initially treated with chloramphenicol for 2 weeks but this was changed to lincomycin. He received lincomycin for a total of 6 weeks. Rehabilitation was prolonged. He died 9 months later of acute myocardial infarction.

**Case 2**

A 15 year old Malay boy was admitted to Middleton Hospital (an infectious disease hospital) in March 1980 for an unremitting fever of 3 weeks' duration and bilateral ankle and periorbital swelling. On admission he was febrile and had acneform rash on his forehead. Bilateral peri-orbital and ankle swelling were present. He had generalized lymphadenopathy and hepatosplenomegaly.

Investigations showed a haemoglobin of 10.8 gm%, total white count of 3,500, platelets 20,000. Urine microscopy: rbc 80-100, wbc 10-15 and albumin + +. S. urea was 111 mg%, S. creatinine 2.2 mg%. Widal and Weil-Felix were negative. Stool and urine cultures were negative for *Salmonella*. Blood cultures however grew *Salmonella typhimurium*. Antinuclear factor and LE cells were positive. 24 hour urinary protein excretion was 1.2 gm/24 hrs.

The diagnosis of SLE and Salmonellosis was made. He was treated with corticosteroids and ampicillin and cloxacillin. His stay in hospital was complicated by cerebral lupus. Three months later, he was discharged well.

**Case 3**

A 27 year old Chinese female with SLE diagnosed in

April 1978, presented in August 1980 with pain in the right knee and fever for 4 days. She was febrile and had a malar rash. A right knee effusion was present. X-rays of the right knee showed a nidus in the femur suggestive of sequestrum. Arthrotomy of the knee yielded 10 cc haemo-purulent fluid. This grew *Salmonella bovis-morbisicans*. She received a course of ampicillin and cloxacillin for 38 days and was discharged with minimal pains in her knee.

Three months later, her condition was complicated by psychosis. On admission she was febrile, had a malar rash and vasculitic lesions were seen on her digits. She received 2 courses of methylprednisolone pulse therapy for 5 days (5). Her cerebral symptoms subsided. On the 24th hospital stay, an abscess on the left lateral aspect of her thigh was noticed. Cultures from the pus obtained by incision and drainage grew *Salmonella bovis-morbisicans*. Blood cultures were negative. She was treated with ampicillin and is now well.

**Case 4**

A 26 year old female Chinese nurse with SLE first diagnosed in October 1979 presented in September 1980 with arthralgia of both elbows and ankles and a cough. A low grade fever was the only significant finding. Two weeks later, she developed a left knee effusion. Aspirate from the effusion grew *Salmonella typhimurium*. Blood cultures were sterile. She was treated with ampicillin. Her right knee also developed an effusion. Cultures from the knee aspirate again grew *Salmonella typhimurium*. Altogether, ampicillin was given for 58 days. Subsequent re-aspiration of her knee joints were sterile. At present she is fully ambulant and her lupus condition is under control.

**Case 5**

A 32 year old Chinese female with SLE first diagnosed in September 1974, complained of diarrhoea in September 1980. Clinical examination was normal except for Cushingoid facies. Blood cultures were negative. Stools grew *Salmonella agona*. She was treated with ampicillin and on discharge her stools were negative for *Salmonella*. A barium enema subsequently revealed diverticulosis of the right colon. On December 1981 she was again re-admitted for fever and abdominal pain. Examination revealed a tender mass at the right iliac fossa. At laparotomy, a ruptured para-colic abscess was drained. The pus grew *Proteus mirabilis*. She died two days later following surgery of septicaemia.

**Case 6**

A 48 year old Indian woman with SLE complicated by haemolytic anaemia since 1977 was admitted in October 1981 with fever, chills and rigors and cough for 4 days. Two weeks prior to her admission, cyclophosphamide was added to her steroid therapy because of uncontrolled haemolytic process. On examination, she was febrile, toxic looking, tachypnoeic and jaundiced. Her blood pressure was 90/40 mm Hg. Lungs and bilateral basal crepitations. Liver was 12 cm. Her haemoglobin was 6.2 gm%, total white

count 27,200, platelets 110,000, reticulocyte count 1.5%. Blood urea was 181 mg% and S. creatinine 1.2 mg%. X-ray of her chest revealed a right lobar consolidation. Blood gases: pH 7.51, pCO<sub>2</sub> 26.6, pO<sub>2</sub> 62.4, bicarbonate 21.1, Std bicarbonate 23.1 and oxygen saturation was 92.8. Liver function test: total protein 5.8 gm%, albumin 3.3 gm%, bilirubin 15.5 mgm%, SAP 108 i.u., SGPT 56 units. Blood cultures grew *Salmonella bovis-morbisicans*. She died 3 days later of septicæmic shock. Consent for post-mortem was refused.

### Case 7

A 29 year old Chinese female with SLE and fibrosing alveolitis first diagnosed in July 1980 was admitted in December 1981 with fever and diarrhoea for 2 days. Clinical examination revealed a thin looking woman with jaundice and a blood pressure of 95/70 mm Hg. Lungs showed the presence of crepitations. Her liver was 3 cms and tender. Spleen was not palpable. The following day she was noted to be febrile. She threw a grand mal fit and lapsed into coma. Fundi was normal. Her haemoglobin was 11.7 gm%, total white count 5,600, platelets 100,000. Blood urea 172 mgm%, S. creatinine 4.5 mgm%. Liver function test: total protein 7.0 gm%, albumin 2.6 gm%, bilirubin 5.5 mgm%, SAP 555 i.u., SGPT 85 units. Hepatitis B antigen was negative. Blood culture grew *Salmonella enteritidis*. She died three days later. Prior to her death, she was noted to bleed easily and coagulation screen suggested mild consumption coagulopathy. Post-mortem lumbar puncture revealed an evenly blood stained CSF. The liver biopsy showed marked fatty change and hepatic tract fibrosis.

## RESULTS

### PRESENTING SIGNS AND SYMPTOMS (TABLE 1)

Fever was the common finding in all 7 patients. The presenting symptoms was diarrhoea in 2, arthritis in 3 and septicaemia in 2. All patients were on corticosteroids at the onset of their symptoms and 2 others were on cyclophosphamide as well. All were regarded to be in an active stage of their disease.

### THERAPY AND COURSE

Oral ampicillin, cloxacillin and chloramphenicol were the drugs used. They were administered from between 3 to 6 weeks to eradicate the infection. Those with *Salmonella* arthritis received antibiotics for 6 weeks. Therapy less than this in *Salmonella* arthritis and bacteremia result in unsatisfactory responses and relapses (6, 7).

Five patients survived the *Salmonella* infection and the 3 who had the infection localized to the joint showed favourable and satisfactory improvement. In 2, the infection was fatal. Two patients (case 1 and 5) died later of causes unrelated to the infection.

### LABORATORY DATA

The laboratory values concurrent with *Salmonellosis* are shown in Table 2. Four patients had raised serum creatinine values. Of the 4 whose anti-DNA titer were measured, all had raised values. *Salmonella typhimurium* was the serotype in 3 patients (43%). This strain is responsible for a high incidence of enteric fevers in children in Singapore (8). Other non-typhoidal serotypes of *Salmonella* were also isolated in our

Table 1 Clinical data of patients

Case No.	Age (yr)	Medication	Signs and symptoms	Lupus activity	Localization of infection	Antibiotic	Duration	Outcome
1	16	M Prednisolone 15 mgm/day	Left hip pain	Fever Arthritis Rash	Hip	Chloramphenicol Lincomycin	14 days 42 days	Died of AMI
2	15	M Prednisolone 45 mgm/day	Ankle swelling	Fever Renal Lymphadenopathy Hepato-splenomegaly	Blood	Ampicillin Cloxacillin	28 days	Well
3	27	F Prednisolone 15 mgm/day	Right knee pain	Fever Arthritis	Knee	Ampicillin Cloxacillin	38 days	Well
(second adm)		Prednisolone 30 mgm/day	Disturbed behaviour	Fever Vasculitis Psychosis Rash	Muscle	Ampicillin	32 days	Well
4	26	F Prednisolone 30 mgm/day Cyclophosphamide 100 mgm/day	Cough Knee pain	Fever Arthritis Depression	Knee	Ampicillin Cloxacillin	58 days	Well
5	32	F Prednisolone 30 mgm/day	Diarrhoea	Fever alopecia	Gut	Ampicillin	21 days	Died of intra-abdominal sepsis
6	48	F Prednisolone 20 mgm/day Cyclophosphamide 100 mgm/day	Cough chills rigors shock	Fever Jaundice Haemolysis Arthritis	Blood	Ampicillin Cloxacillin	3 days	Died
7	29	F Prednisolone 30 mgm/day	Diarrhoea	Fever Fibrosing alveolitis Hepatitis	Blood	Ampicillin Cloxacillin	3 days	Died

**Table 2 Laboratory data of patients**

Case	Salmonella serotype	Site of culture	Hb	TW	Urea	Creatinine	Anti-DNA
1	Sal typhimurium	Knee aspirate	10.7 gm	16500	33 mgm	1.0 mgm	59
2	Sal typhimurium	Blood	10.8	3500	111	2.2	106
3	Sal bovis-morbisicans	Knee aspirate Muscle abscess	6.7	3000	26	-	114
4	Sal typhimurium	Knee aspirate	7.8	5200	86	1.6	37
5	Sal agona	Stools	8.6	3700	188	2.8	-
6	Sal bovis-morbisicans	Blood	6.2	27000	181	1.2	-
7	Sal enteritidis	Blood	11.7	5600	172	4.5	-

patients and the sources of isolation were stools, blood and pus.

**DISCUSSION**

Infection should always be considered as a possible cause in a patient presenting with arthritis. Even when a definite diagnosis of a specific chronic polyarthritis has been made the physician must continue to be on guard against complicating infectious arthritis. Infectious arthritis has been reported as a complication of gout and pseudogout (9), the arthritis of sickle cell disease (10) and rheumatoid arthritis (11). Salmonella and other bacterial infection has also been found to be associated with ulcerative colitis (12), uraemia (3) and in the debilitated (13). With regard to SLE, the recognition of Salmonellosis maybe delayed as in patient 1 partly because of their similar manifestations (Table 3).

**Table 3 Similarities in clinical involvement between salmonellosis and SLE**

SALMONELLOSIS (14, 15, 16)	SLE (17, 18)
Rose spots, drug eruption	Rash
Pleural effusion, empyema, pneumonitis	Pleuritis, effusion atelectasis
Endocarditis	Libman-Sacks endocarditis
Proteinuria, pyelonephritis, glomerulonephritis	Glomerulonephritis
Anaemia, leukopenia, thrombocytopenia	Anaemia, lymphocytopenia, autoimmune thrombocytopenia
Osteomyelitis, septic arthritis, arthralgia	Synovitis, arthralgia
Meningitis	Cerebral involvement

The use of steroids, immunosuppressive drugs, haemolysis and azotaemia are factors increasing the risk of the number and severity of infections in SLE (19). All our patients were on steroids at the onset of infection. Two in addition received cyclophosphamide. Five of our patients had raised blood urea. Another important risk factor is the impaired mononuclear phagocytic system in SLE patients (20). This system is required for effective handling and eradication of Salmonella which is an intracellular parasite.

The local serotypes of Salmonella (typhoidal and non-typhoidal) are generally susceptible to most of the antibiotics routinely tested such as chloramphenicol, ampicillin, trimethoprim-sulphamethoxazole and tetracycline (8). However because of the possibi-

lity of neutropenia with chloramphenicol the latter is not frequently used in our patients as most of whom already exhibit some abnormality in their blood counts. For bone infections a prolonged period of 6 weeks of oral therapy is necessary. Other regimes reported include a period of intravenous ampicillin or chloramphenicol followed by oral therapy with 1-2 gm of ampicillin for several weeks (6). Young has indicated that prolonged treatment with trimethoprim-sulfamethoxazole is a viable alternative for Salmonella arthritis (21). In our patients therapy of joint infection was successful but there was considerable residual damage radiologically in two of our patients (Fig. 2 and 3). Cloxacillin was the other common anti-



Fig. 2 Residual joint damage following salmonella arthritis in Case No. 3



Fig. 3 Residual joint damage following salmonella arthritis in Case No. 4

biotic used since most of the patients were thought to have a septic process before definitive bacteriological cultures were available.

Finally no attempt was made to identify the source of the infection in our patients. Lockyes et al (3) in a study of an outbreak of *Salmonella* enteritis and septicaemia in a population of uraemic patients traced the source of the outbreak to the refrigerator and sink in the nephrological unit. However since typhoid and paratyphoid infections are endemic in Singapore the presumptive conclusion is that the infection is acquired outside hospital except possibly in patient 2 who was initially admitted to an infectious disease hospital. Our study suggests that *Salmonella* infection should be considered as a possible cause of arthritis and fever in SLE patients. Besides a high index of suspicion the infection should be treated vigorously since two of our septicaemic patients died within a few days of admission.

#### ACKNOWLEDGEMENT

We wish to thank Assoc Prof R Pho, University Department of Orthopaedic Surgery, Singapore General Hospital and Dr Tong G Ong, Head, Department of Orthopaedic Surgery, Tan Tock Seng Hospital for

managing some of the patients.

#### REFERENCES

1. Staples PJ, Gerding DN, Decker JL, Gordon RS Jr: Incidence of infection in SLE. *Arthritis and Rheumatism* 1974; 17: 1-9.
2. Lovy MR, Ryan PFJ, Hughes GRV: Concurrent SLE and Salmonellosis. *Journal of Rheumatology* 1981; 8: 605-11.
3. Lockyer WA, Feinfeld DA, Cherubin CE, Carvounis G, Iancu M, Avram MM: Outbreak of *Salmonella* enteritis and septicaemia in a population of uraemic patients. *Arch. Intern Med* 1980; 140: 943-5.
4. Svennison BO: Serum factors causing impaired macrophage function in SLE. *Scand J Immunol* 1975; 4: 145-50.
5. Eyanson S, Passo MH, Aldo-Benson MA, Benson MD: Methylprednisolone pulse therapy for nonrenal lupus erythematosus. *Annals of Rheumatic Diseases* 1980; 39: 377-80.
6. Ortiz-Neu C, Marr JS, Cherubin CE, Neu HC: Bone and joint infections due to *Salmonella*. *Journal of Infectious Diseases* 1978; 138: 820-8.
7. Warren CPW: Arthritis associated with *Salmonella* infections. *Ann Rheum Dis* 1970; 29: 483-7.
8. Lam S, Tan SE: *Salmonella* infections in Singapore. *Annals Academy of Medicine* 1981; 10: 34-9.
9. McConville JH, Polotsky RS, Calia FM et al: Septic and crystalline joint disease. A simultaneous recurrence. *JAMA* 1975; 231: 841.
10. Palmer DW, Ellman MH: Septic arthritis and Reiter's syndrome in sickle cell disorders: case reports and implications for management. *South Med J* 1976; 69: 902-6.
11. Kellgren JH, Ball H, Fairbrother RW et al: Suppurative arthritis complicating rheumatoid arthritis. *Br Med J* 1958; 1: 1193-200.
12. Lindeman KJ, Weinstein L, Lévitár R et al: Ulcerative colitis and intestinal salmonellosis. *Am J Med Sci* 1967; 254: 855-61.
13. Willkens RF, Healey LA, Decker JL: Acute infectious arthritis in the aged, chronically ill. *Arch. Int Med* 1960; 106: 354-64.
14. Hook EW: *Salmonella* infections other than typhoid fever in Cecil Textbook of Medicine, 15th Ed, edited by Beesen PB, McDermott W, Wyngaarden JB, Philadelphia, WB Saunders, 1979, p 449-52.
15. Saphra I, Winter JW: Clinical manifestations of *Salmonellosis* in man. An evaluation of 7779 human infections identified at the New York *Salmonella* Center. *N Eng J Med* 1957; 256: 1128-34.
16. Cohen ML, Ganarosa EJ: Nontyphoid salmonellosis. *South Med J* 1978; 171: 1540-5.
17. Harvey AM, Shulman LE, Tumulty PA et al: Systemic lupus erythematosus. A review of the literature and clinical analysis of 138 cases. *Medicine* 1954; 33: 291-437.
18. Dubois EL: Clinical picture of systemic lupus erythematosus, in *Lupus Erythematosus*, edited by Dubois EL, Los Angeles, University of Southern California Press, 1974, p 232-379.
19. Ginzler E, Diamond H, Kaplan D, Weiner M, Schlesinger M, Seleznik M: Computer analysis of factors influencing frequency of infection in systemic lupus erythematosus. *Arthritis Rheum* 1978; 21: 37-44.
20. Svensson B, Hedberg H: Impaired Phagocytosis by macrophages in SLE. *Scand J Rheum* 1973; 2: 78-80.
21. Young LS: Personal communication.