SALMONELLA INFECTION IN SYSTEMIC LUPUS ERYTHEMATOSUS

SYNOPSIS

Seven patients with systemic lupus erythematosus (SLE) complicated by Salmonellosis are described. Three patients presented with arthritis and 2 with septicemia. 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.
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. ura 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 nodule in the femur suggestive of sequestrum. Arthroscopy of the knee yielded 10 cc haemo-purulent fluid. This grew Salmonella bovis-morbiicsans. 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-morbiicsans. 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, pCO₂ 26.6, pO₂ 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-mor lascis. She died 3 days later of septicaemic 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 enteriditis. 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 (6). Other non-typhoidal serotypes of Salmonella were also isolated in our

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yr)</th>
<th>Medication</th>
<th>Signs and symptoms</th>
<th>Lupus activity</th>
<th>Localization of infection</th>
<th>Antibiotic</th>
<th>Duration</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16 M</td>
<td>Prednisolone 15 mgmiday</td>
<td>Left hip pain</td>
<td>Fever</td>
<td>Hip</td>
<td>Chloramphenicol</td>
<td>14 days</td>
<td>Died of AMI</td>
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<tr>
<td>2</td>
<td>15 M</td>
<td>Prednisolone 45 mgmiday</td>
<td>Ankle swelling</td>
<td>Fever</td>
<td>Blood</td>
<td>Ampicillin</td>
<td>28 days</td>
<td>Well</td>
</tr>
<tr>
<td>3</td>
<td>27 F</td>
<td>Prednisolone 15 mgmiday</td>
<td>Right knee pain</td>
<td>Fever</td>
<td>Knee</td>
<td>Cloxacillin</td>
<td>38 days</td>
<td>Well</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Prednisolone 30 mgmiday</td>
<td>Disturbed behaviour</td>
<td>Fever</td>
<td>Muscle</td>
<td>Ampicillin</td>
<td>32 days</td>
<td>Well</td>
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<tr>
<td>4</td>
<td>26 F</td>
<td>Prednisolone 30 mgmiday</td>
<td>Cough</td>
<td>Fever</td>
<td>Knee</td>
<td>Ampicillin</td>
<td>58 days</td>
<td>Well</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cyclophosphamide 100 mgmiday</td>
<td>Knee pain</td>
<td>Arthritis</td>
<td>Cloxacillin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>32 F</td>
<td>Prednisolone 30 mgmiday</td>
<td>Diarrhoea</td>
<td>Fever</td>
<td>Gut</td>
<td>Ampicillin</td>
<td>21 days</td>
<td>Died of intra-abdominal sepsis</td>
</tr>
<tr>
<td>6</td>
<td>48 F</td>
<td>Prednisolone 20 mgmiday</td>
<td>Cough, chills, rigors, shock</td>
<td>Fever</td>
<td>Blood</td>
<td>Ampicillin</td>
<td>3 days</td>
<td>Died</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cyclophosphamide 100 mgmiday</td>
<td></td>
<td>Jaundice</td>
<td>Cloxacillin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>29 F</td>
<td>Prednisolone 30 mgmiday</td>
<td>Diarrhoea</td>
<td>Fever</td>
<td>Blood</td>
<td>Ampicillin</td>
<td>3 days</td>
<td>Died</td>
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<td></td>
<td></td>
<td>Fibrosing alveolitis</td>
<td></td>
<td>Cloxacillin</td>
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</tbody>
</table>
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

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

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 possibility 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-M. Five of our patients had raised blood urea.

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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

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