

## Paratyphoid fever in Thai children: an eleven-year experience S6-3

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### Abstrak

Telah dipelajari demam paratifoid pada anak-anak di RS Chulalongkorn, Bangkok, Thailand sebanyak 22 kasus kultur positif *Salmonella paratyphi A* terdiri dari 13 kasus wabah tahun 1986-1995 dan 9 kasus wabah tahun 1996. Anak laki-laki lebih sering terkena, dan pada umur sekitar 6 bulan-14 tahun. Gejala yang utama termasuk: demam dengan rata-rata 9,6 hari, gangguan gastrointestinal, terutama hepatomegali, muntah, anoreksia, nyeri abdomen, perut kembung, dan diare. Hampir semua pasien menunjukkan nilai hematokrit normal, hitung jenis leukosit 5000-9000 sel/mm<sup>3</sup> dan persentase neutrofil 33-88. Empat pasien mengalami komplikasi, dua di antaranya mengalami kelainan jantung: perikarditis dan endokarditis. Semua isolat kuman sensitif terhadap kotrimoksazol, ampisilin, kloramfenikol dan seftriakson yang diukur dengan menggunakan metode difusi cakram. Antibiotika diberikan sampai 20 hari, dan panas turun setelah 2-8 hari pengobatan. Tidak terjadi kematian pada kasus-kasus tersebut.

### Abstract

To study children with paratyphoid fever at Chulalongkorn Hospital, Bangkok, Thailand, twenty-two cases of hemoculture-proved *Salmonella paratyphi A* were studied: 13 cases during 1986-1995 and 9 cases during the outbreak in 1996. Boys were affected more commonly and the age range was between 6 months and 14 years. Major presentations included fever with the average duration of 9.6 days, and gastrointestinal manifestations, mainly hepatomegaly, vomiting, anorexia, abdominal pain, abdominal distension and diarrhea. Most patients had normal hematocrit value, white blood cell count of 5,000-9,000 cells/mm<sup>3</sup> and percent neutrophils of 33-88. Four patients had complications, with two rarely reported cardiac involvement including pericarditis and endocarditis. All tested isolates were sensitive to cotrimoxazole, ampicillin, chloramphenicol and ceftriaxone by disk-diffusion method. Different antibiotic regimes were used for up to twenty days with subsidence of fever within 2-11 days after treatment. There was no mortality.

## INTRODUCTION

Enteric fever remains a serious health problem in many regions of the world. The etiologic agents are *Salmonella typhi*, causing typhoid fever and *Salmonella paratyphi A, B and C*, causing paratyphoid fever. The latter disease was relatively uncommon in Thailand. However, in 1996 there was an outbreak of *Salmonella paratyphi A* infections in Bangkok. This study was conducted to determine the natural history of paratyphoid fever in Thai children during a 10-year period and in 1996 during the outbreak.

## PATIENTS AND METHODS

The medical records of all children treated at Chulalongkorn Hospital between 1986 and 1996 who were diagnosed as having enteric fever and a positive blood culture of *Salmonella paratyphi* were reviewed. We studied demographic data, clinical manifestations, laboratory findings, treatment and outcome.

## RESULTS

### Demographic data

Of 22 children with positive blood culture of *Salmonella paratyphi*, there were 13 boys and 9 girls, with age range between 6 months and 14 years and the average age of 8.3 years. Seventy-five percent of study patients were five years of age or older.

### Clinical Manifestations

Symptoms included fever (100%) with average duration of 9.6 days, gastrointestinal symptoms (87.5%) comprising of vomiting (62.5%) anorexia (50%) diarrhea (31.3%), abdominal pain (31.3%) constipation (6.3%), cough (37.5%), drowsiness (18.8%), chills (18.8%) and sore throat (18.8%). Signs included hepatomegaly (75%), splenomegaly (18.8%), abdominal distension (12.5%), "toxic looking" appearance (6.3%) and rales (6.3%).

### Complications

Four patients developed complications including pneumonitis (2), endocarditis (1) and pericarditis (1). Details of the last two patients are described below.

### Laboratory Findings

The majority of patients had normal hematocrit level, white blood cell count of 5,000-9,000 cells/mm<sup>3</sup> with the range of neutrophils from 33 to 88 percent.

All isolated strains were *Salmonella paratyphi A*. Susceptibility test using disk diffusion method revealed 100 percent sensitivity to all six drugs commonly used: cotrimoxazole, ampicillin, chloramphenicol, ceftriaxone, ciprofloxacin and imipenem.

### Treatment and outcome

Different antibiotic regimes were used for up to twenty days. Common drugs used included ampicillin and cotrimoxazole. The response of fever declination was 2-11 days after treatment. Three patients did not receive antibiotics. There was no mortality.

#### Patient 1

An eight-year-old boy, underlying Tetralogy of Fallot (toF), presented with ten days of fever, headache and vomiting. Physical examination revealed high fever, cyanosis, heart murmur and clubbing of fingers. High hematocrit with normal white blood cell and platelet counts were observed. Echocardiogram was compatible with TOF and revealed 0.7x0.7 centimeters vegetation. Hemoculture showed *Salmonella paratyphi A* in three out of four specimens. Ampicillin was used and was eventually changed to cefotaxime after the appearance of rash, indicating ampicillin allergy.

#### Patient 2

An eleven-year-old boy, underlying atrial septal defect, patent ductus arteriosus and tricuspid insufficiency, presented with prolonged fever and vomiting for three weeks. One week prior to admission, he was dyspneic. Physical examination showed heart murmurs, pericardial rub and hepatomegaly, without evidence of embolic phenomenon. Mild leukocytosis without left shifting was noticed. Chest x-ray suggested pulmonary congestion and enlargement of cardiac shadow. Echocardiogram disclosed pericardial effusion without vegetation. Inotropic drugs, diuretic and erythromycin were given. Hemoculture revealed *Salmonella paratyphi A*, sensitive to ampicillin and cotrimoxazole in four out of five specimens. Paratyphoid fever with pericarditis was diagnosed. Intravenous ampicillin was used with successful outcome.

### DISCUSSION

Thisyakorn U, Mansuwan P and Taylor DN in 1987<sup>1</sup> reviewed 29 children with paratyphoid fever in Children's Hospital, Bangkok, Thailand between 1977 and 1984. Most children studied and in our study presented with prolonged fever and gastrointestinal manifestations. Cough was found approximately 40 percent in both studies. The susceptibilities to cotrimoxazole and ampicillin were 99 and 82 percent respectively whereas all tested strains in our study were sensitive to ampicillin, chloramphenicol, cotrimoxazole, ceftriaxone, ciprofloxacin and imipenem. Therefore, any out of the first four mentioned antibiotics can be selected.

There was an outbreak of *Salmonella paratyphi A* infections in Bangkok in 1996. Most patients were middle to upper class adolescents and young adults, with significant history of fast food consumptions. There was, however, a limited number of infected children.

In our study, two patients had relatively rare cardiac complications including one patient with endocarditis and the other with pericarditis.

*Salmonella* endocarditis was not common. Saphra I and Winter JW in 1957<sup>2</sup> reported 20 cases of endocarditis among 7,779 cases of salmonella infections and none of these was caused by *Salmonella paratyphi*. Previous literature reports and reviews<sup>2-9</sup> showed that there were only four cases of endocarditis caused by *Salmonella paratyphi*. Of these, only one was a pediatric case aged 11 months.

*Salmonella* pericarditis was also an uncommon entity. Haggman DL, Rehm SJ, Moodie DS and Mackenzie AH in 1986<sup>10</sup> reviewed 23 cases of nontyphoidal salmonella pericarditis between 1936-1986 and four of these were caused by *Salmonella paratyphi*. In 1990 there was a reported case of salmonella pericarditis caused by *Salmonella paratyphi A* in a 23-year-old female with underlying Systemic Lupus Erythematosus (SLE)<sup>11</sup>.

Paratyphoid fever was relatively uncommon in Thai children between 1986 and 1995 until the outbreak in Bangkok in 1996. Most cases presented with fever and gastrointestinal manifestations. All tested isolates were sensitive to cotrimoxazole, ampicillin, chloramphenicol and ceftriaxone. Two children with rare cardiac complications were reported during this outbreak.

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with significant history of fat food consumption. There was, however, a limited number of infected children.

In our study, two patients had relatively rare cardiac complications including one patient with endocarditis and the other with pericarditis.

*Salmonella enteritidis* was the commonest *Salmonella* species among 1,779 cases of salmonella infections and none of these was caused by *Salmonella paratyphi A*. Previous literature reports and reviews<sup>1,2,3,4,5,6,7,8,9,10,11,12,13,14,15,16,17,18,19,20,21,22,23,24,25,26,27,28,29,30,31,32,33,34,35,36,37,38,39,40,41,42,43,44,45,46,47,48,49,50,51,52,53,54,55,56,57,58,59,60,61,62,63,64,65,66,67,68,69,70,71,72,73,74,75,76,77,78,79,80,81,82,83,84,85,86,87,88,89,90,91,92,93,94,95,96,97,98,99,100</sup> have shown that *Salmonella paratyphi A* is a common cause of salmonella infections in children.

*Salmonella paratyphi A* was also an uncommon enteric pathogen in 1980s reviewed 22 cases of nontyphoidal salmonella pericarditis between 1936-1986 and four of these were caused by *Salmonella paratyphi A*. In 1990 there was a reported case of salmonella pericarditis caused by *Salmonella paratyphi A* in a 22-year-old female with underlying systemic lupus erythematosus (SLE).<sup>11</sup>

Paratyphoid fever was relatively uncommon in Thai children between 1980 and 1995 until the outbreak in Bangkok in 1996. Most cases presented with fever and gastrointestinal symptoms. All tested isolates were sensitive to chloramphenicol, tetracycline, cotrimoxazole, rifampicin and ceftriaxone. Two children with one cardiac complication were reported during the out-

Patient 1

An eight-year-old boy, underlying pathology of fever (not present with any signs of fever, headache and vomiting). Physical examination revealed high fever, tachycardia, heart murmur and clubbing of fingers. Right hemipelvis with normal white blood cell and platelet counts were observed. Bacteriostatic was commenced with TMP and revealed 0.7 x 10<sup>7</sup> c.f.u./ml. *Salmonella enteritidis* was cultured from blood. Ampicillin was used in three out of four specimens. Ampicillin was used and was eventually changed to ceftriaxone after the appearance of rash indicating hypersensitivity.

Patient 2

An eleven-year-old boy, underlying renal cystic disease, presented with prolonged fever and vomiting for three weeks. One week prior to admission, he was febrile. Physical examination showed heart rate 120/min, tachycardia and tachypnoea. Mild tachypnoea, without left shifting was noted. Chest x-ray showed bilateral pulmonary congestion and enlargement of cardiac shadow. Echocardiogram showed pericardial effusion without vegetation. Isotopic drug, thallate and thallomycin were given. Hemocultures revealed *Salmonella paratyphi A*, sensitive to ampicillin and cotrimoxazole in four out of five specimens. Paratyphoid fever with pericarditis was diagnosed. Intravenous ampicillin was used with successful outcome.