Unusual Complications of Typhoid Fever

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SUMMARY

Typhoid fever is endemic in most of tropical Africa. The common complications encountered include perforation, haemorrhage, acute renal failure, cholecystitis, pyelonephritis and pneumonia. Typhoid meningitis and endocarditis are quite rare. We report here a case of proven meningitis and a case of endocarditis.

CASE REPORTS

Case 1. V.S. a 31 year-old female, was admitted to Harare Central Hospital with a three-day history of headache, vomiting and confusion. Prior to this she had noticed generalized abdominal pains for four days.

Physical examination revealed that she was pyrexial (39.8°C), pale but not icteric. The pulse rate was 138/min, with a BP of 130/70 mmHg. The heart was normal. The abdomen was diffusely tender without any organ enlargement. Her conscious level was graded as 3/5 on the Glasgow scale, and there was mild nuchal rigidity. There was no cranial nerve palsy. The clinical impression was that of acute pyogenic meningitis.

Relevant tests included: haemoglobin of 9.5 g/dl; white blood count of 6.3 x 10^9/L (normal differential); platelet count of 633 x 10^9/L; ESR of 66 mm first hour (Westergren); urea and Correspondence to: Dr I.C. Chikanza
Electrolytes, as well as chest X-rays, were normal. A blood slide for malaria was negative. The cerebrospinal fluid (CSF) was clear and colourless with a pressure of 120 mm CSF; cells were 15/mm³ mainly mononuclear cells, Gram stain revealed no organisms; protein 0.8 g/L; glucose 6.2 mmol/L; culture grew no organisms. Blood culture was positive for Salmonella typhi, but the urine and stool cultures were negative. The Widal test showed a titre of 1:320 for H antigen and was negative for O antigen.

The patient was treated with oral chloramphenicol 2 g/day. Her temperature did not settle, and she became more confused and obtunded. Her repeat Widal test showed a H antigen titre of 1:640 and an O antigen titre of 1:320. Repeat spinal tap on the twelfth hospital day revealed turbid CSF; cells 200/mm³ mainly polymorphs; Gram stain showed Gram negative rods, protein 2.2 g/L, glucose 0.3 mmol/L (concurrent blood sugar 4.0 mmol/L), and culture grew Salmonella typhi. Her treatment was changed to intravenous chloramphenicol and intravenous ampicillin 2 g/day each for 14 days. Her temperature settled and she improved clinically except for residual weakness of both legs.

Seventy-two hours after cessation of antibiotics she spiked a fever and a repeat lumbar puncture was positive for Salmonella typhi on culture. She was treated with chloramphenicol 2 g/day for a further 21 days, and made an uneventful recovery. Repeat LP was completely normal.

Case 2. H.M., a 40 year-old male, was transferred to Harare Central Hospital from a district hospital because of intractable heart failure and progressive anaemia.

On arrival he gave a history of dyspnoea, palpitations and orthopnoea; in addition he had episodes of abdominal pain and diarrhoea, punctuated by periods of constipation, two weeks prior to hospitalization. Physical examination revealed he was pale but not icteric. He was febrile (37.5°C) and he had pedal and sacral oedema. There was no digital clubbing, no splinter haemorrhages and no Osler's nodes. The jugular venous pressure (JVP) was elevated to 8 cm, with a pulse rate of 70/min which was collapsing in nature with a BP of 130/50 mmHg. The apex was in the 6th left intercostal space along the anterior axillary line and was left ventricular in character. There was an early diastolic murmur grade 3/6, best heard at the left sternal edge. The liver was 5 cm palpably enlarged and there was a 2 cm soft splenomegaly. There were bilateral pulmonary basal crepitations. A working diagnosis of aortic regurgitation consequent upon infective endocarditis was entertained.

The relevant investigations showed:

- Hb, 9.0 g/dl; WBC, 7.2 x 10⁹/L; ESR, 105 mm in first hour (Westergren). Initial urea, electrolytes and liver function tests were normal. Salmonella typhi was cultured in two separate blood culture bottles, and Salmonella heidelberg in a third. Urine and stool cultures were negative. Widal reactions were initially negative but on repeating two weeks later the titre was 1:640 for both O and H antigens. The chest X-ray confirmed cardiomegaly and bilateral basal congestion. Echocardiography revealed dilatation of both ventricles with vegetations on the aortic valve. The mitral valve was normal. The VDRL and FTA as well as a latex test for rheumatoid factor were negative.

The patient was treated with intravenous ampicillin and chloramphenicol as well as with digoxin and diuretics. He showed an initial improvement with a return of the temperature to normal, and was thought to be out of cardiac failure. However, 12 days after initiation of therapy he suddenly changed for the worse. He developed signs of cardiac failure. The urea concentration, which was normal initially, was noted to be 37.5 mmol/L, with a serum creatinine of 365 µmol/L and a potassium of 7.7 mmol/L. This hyperkalaemia was temporarily controlled with an insulin/dextrose infusion while arrangements were being made for dialysis. His ECG showed features of myocarditis with low voltage and generalized T wave inversion. He deteriorated rapidly and died the following day. Unfortunately permission for autopsy was refused.

**DISCUSSION**

Typhoid fever still poses a major health problem in the Third World. The manifestations of this condition are manifold and have been well documented for at least three decades. It is difficult to define what constitutes an uncomplicated attack, as typhoid is a septicaemic illness with toxaemia, so that the manifestations of both these features might be classed as 'unusual features of the disease. It has, however, been customary to separate usual from unusual presentations and the deviations from the usual can be arbitrarily divided into different aetiological groups:

1. Due to the typhoid organisms, eg. relapse, meningo, endocarditis, osteomyelitis, pyelitis and cystitis.
2. Due to toxaemia: the typhoid state, myocarditis, hyperpyrexia, hepatitis and bone marrow suppression.

3. Due to local lesions in the gut: haemorrhage, perforation and paralytic ileus.

4. Due to severe illness: parotitis, bronchitis, bed sores and pneumonia.

5. Due to treatment: marrow damage and hypersensitivity.


The cases presented in this paper would fall into the Categories 1 and 2.

In so far as typhoid meningitis is concerned in the Zimbabwean experience, true typhoid meningitis is rare except in young children and to date there have been only two case reports of this complication in the medical literature from Zimbabwe, both of whom were young children. A retrospective study by Todd and Thomas on the complications of typhoid at Harare Hospital in 1982 reveal no cases of typhoid meningitis in 218 cases of typhoid fever reviewed. On a global basis there have been a number of sporadic reports, mainly from the Third World. It would seem, therefore, that since 1966 our case is the third report of this complication from Zimbabwe. Previously reported cases were diagnosed by spinal tap and CSF culture with the main indication for this investigative procedure being an alteration in the mental state and nuchal rigidity in a febrile patient. The cases we have come across in the literature have been said not to have shown a clinical relapse, but this has not been substantiated by normal CSF biochemistry, microscopy and culture. Previously reported cases were all treated with chloramphenicol for five days. The organisms grown in our case were sensitive to chloramphenicol, ampicillin and co-trimoxazole. Our case demonstrates that it is necessary to treat typhoid meningitis for longer than 14 days until the CSF is completely clear. We strongly feel that treatment should be continued for 21 days, and that any patient with proven or suspected typhoid fever whose mental state is abnormal must have a lumbar puncture. The presence of nuchal rigidity should alert the clinician to the possibility of meningitis in these cases. To date we have found no documentation in the literature of neurological deficit after treatment. The case reported in this paper recovered completely once the CSF had become clear.

In Zimbabwe there have been no previous reports of Salmonella typhi endocarditis in the literature. On a global basis, Rowland reported a case of presumed S. typhi endocarditis in a 10 year-old girl with no valvular lesion in 1961, who subsequently succumbed to the illness. In 1962 the Mayo Clinic published a case of Salmonella endocarditis and was successfully treated with kanamycin. Since then there has been a paucity of documented reports on this complication. The latest report to date of Salmonella typhi endocarditis concerned a 24 year-old Egyptian woman with aortic incompetence and mitral stenosis, who was successfully treated with chloramphenicol and ampicillin. The authors claim that in so far as they could ascertain, their case was the first ever to be reported on this complication in the medical literature. We reported a case of aortic incompetence in whom Salmonella typhi and Salmonella heidelberg were grown. Vegetations on the aortic valve were demonstrated at echocardiography.

This case differs from previous reports in that it is rather unusual for two serotypes of Salmonella to cause endocarditis in the same patient. In so far as we could search the medical literature on this complication, this is the first case to be reported. Our patient developed myocarditis which is a rather rare complication in adults with typhoid fever in Zimbabwe, and if it does occur, is frequently associated with a poor prognosis. The patient went on to develop acute renal failure, a not infrequent complication of typhoid fever in Zimbabwe and tropical Africa.

Typhoid myocarditis manifests itself clinically as undue tachycardia, feeble pulse and muffled heart sounds, and is sometimes associated with hypotension. Eventually cardiac failure ensues. The electrocardiographic changes are those of low voltage complexes, changes in the PR interval, QTc interval, ST segment displacement and non-specific T wave changes in many of the leads.

CONCLUSION

Two cases with unusual complications of typhoid fever have been presented. The usual aspects of these cases have been reviewed. A review of the medical literature on typhoid meningitis and endocarditis has also been given.

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