At 34 weeks the mother was hypothyroid and L-thyroxine 100 μg/day was started and the carbimazole was reduced. Ultrasound measurement of the fetal biparietal diameters at 32 and 36 weeks indicated a normal growth rate. At 37 weeks she delivered spontaneously a boy of 2·60 kg (10th-25th centile for the period of gestational age). At birth the baby was clinically thyrotoxic with a pulse rate of 169/min. His FTI was 29·8. Oral carbimazole 500 μg six-hourly, Lugol's iodine 1/15 ml eight-hourly, and phenobarbitone 7·5 mg eight-hourly were started. By six weeks he was euthyroid and having no treatment.

Comment

A maternal history of thyrotoxicosis (particularly if recurrent after thyroidectomy), the presence of pretibial myxoedema, or a history of an affected thyrotoxic neonate are usually associated with raised serum LATS and LATSP concentrations and indicate a high probability of fetal thyrotoxicosis in subsequent pregnancies.

If there is the possibility of fetal thyrotoxicosis the fetal heart rate should be counted at each antenatal visit. A rate persistently above 160 beats/min should be considered diagnostic of this condition. The treatment of fetal thyrotoxicosis should be oral carbimazole (10 mg eight-hourly initially) to the mother. Carbimazole crosses the placenta and will reduce the fetal production of thyroid hormone. The dose of carbimazole should be adjusted to keep the fetal heart rate between 120 and 160/min. Thyroxine may be added to keep the mother euthyroid if necessary. Thyroxine does not readily cross the placental barrier.

Premature labour and low birth weight for gestational age are associated with fetal thyrotoxicosis. Fetal growth rate as judged by ultrasound may be regarded as an additional criterion of the fetal thyroid state.

In this case fetal growth rate was normal. The pregnancy continued until 37 weeks (four weeks longer than the first pregnancy) and the baby was clinically and biochemically less toxic than the first child.

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[1] Ramsay, I, *British Medical Journal*, 1976, **2**, 1110.
[2] Maisey, N M, and Stimmler, L, *Clinical Endocrinology*, 1972, **1**, 81.
[3] Petersen, S, and Serup, J, *Acta Paediatrica Scandinavica*, 1977, **66**, 639.
[4] Dirmikis, S M, and Munro, D S, *British Medical Journal*, 1975, **2**, 665.

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Paratyphoid A fever diagnosed from bone marrow culture after indiscriminate antibiotic treatment

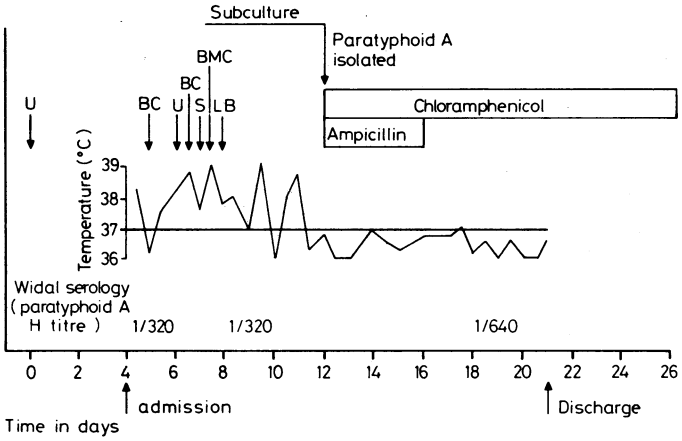
Enteric fevers are common among immigrants and travellers returning from endemic areas.[1 2] Blood cultures are normally diagnostic, but among patients with typhoid fever, many of whom had treated themselves with antibiotics, blood culture proved negative in 60% of cases.[3] The diagnosis was confirmed in these cases by bone marrow culture. Bone marrow culture is not, however, performed routinely when typhoid fever is suspected[4] and experience of this diagnostic method in patients with paratyphoid infections is limited.[5] We report here a case of paratyphoid A fever partially treated with antibiotics in which bone marrow subculture finally established the diagnosis.

Case report

A 32-year-old Pakistani woman was admitted with a three-week history of general malaise, poor appetite, weight loss, intermittent fever, abdominal pain, and diarrhoea. One week before her illness she had returned from a three-month visit to Pakistan, during which her 3-year-old son had developed a suspected Salmonella infection. She had received smallpox and cholera vaccination two weeks before travelling abroad but no TAB vaccine or prophylactic antimalarial agents. Before admission she had been treated with separate four-day courses of cephalexin, amoxycillin, and chloroquine, with no clinical improvement. She denied respiratory and joint symptoms and had not noticed a rash.

She appeared unwell with temperature 38°C, pulse rate of 90 beats/min, and tender hepatosplenomegaly. There was no rash and the chest was clear. Investigations showed haemoglobin 14·0 g/dl; white cell count 5·5 × 10^9/l, neutrophils 50%, lymphocytes 40%, monocytes 10%; erythrocyte sedimentation rate 31 mm in first hour. The sickle cell test was negative, as were three blood smears for malarial parasites. Two cultures each of blood and urine and single stool and liver biopsy cultures were negative. Sternal bone marrow aspirated on the third day of admission was negative on direct culture but grew paratyphoid A phage type 1 five days later after subculture from 0·1% glucose broth. The organism was sensitive to ampicillin, chloramphenicol, co-trimoxazole, tetracycline, and cephalosporins. Widal serology showed an O antigen titre of 1/30 and an H titre of 1/320 on admission (O titres for Salmonella typhi and paratyphi B were less than 1/20 and H titres were, respectively, 1/80 and 1/20). Two weeks later, shortly before discharge, the O titres for all three organisms were unchanged, the H titres being 1/640 for paratyphi A, 1/80 for Salmonella typhi, and 1/20 for paratyphi B. Liver function tests showed a raised alkaline phosphatase concentration of 48 U/l (normal range 5-35 U/l) and aspartate transaminase concentration of 62 U/l (normal range 5-40 U/l). The liver biopsy specimen showed non-specific reactive hepatitis. Bone marrow microscopy and chest radiography showed nothing abnormal.

The patient was treated with chloramphenicol 500 mg four times a day for two weeks with ampicillin 250 mg four times a day for the first four days only. Her fever resolved within 24 hours of starting treatment, and her symptoms rapidly settled (see figure).



Course of disease showing changes in temperature, times of cultures, Widal serology, and response to treatment. U = Urine culture. BC = Blood culture. S = Stool culture. BMC = Bone marrow culture. LB = Liver biopsy culture.

Comment

This case clearly illustrates the hazards of indiscriminate antibiotic treatment in patients returning with symptoms from areas where enteric fever is endemic. Without bone marrow subculture we might not have been able to confirm the diagnosis of paratyphoid A fever in this patient. We suggest that bone marrow culture should become routine in all patients with suspected typhoid or paratyphoid fever who have had antibiotic treatment or when blood, urine, and stool culture results prove negative. The factors permitting survival of the organism in bone marrow remain undetermined and deserve further study.

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[1] *British Medical Journal*, 1978, **1**, 377.
[2] *British Medical Journal*, 1978, **2**, 63.
[3] Gilman, R H, *et al*, *Lancet*, 1975, **1**, 1211.
[4] Nye, F J, and Bell, D R, *Medicine* (3rd series), 1978, May, p 234.
[5] Wahab, M F A, *et al*, *Annals of Internal Medicine*, 1969, **70**, 913.

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