Medical Memorandum

Subacute Bacterial Endocarditis Due to *Salmonella typhi-murium*

In view of the rarity of subacute bacterial endocarditis due to *Salmonella typhi-murium*, the following case may be considered worthy of publication.

CASE REPORT

A single girl, aged 19, a bottler in a mineral-water factory, was admitted to hospital on June 1. There was no previous history of illness of any kind apart from some fits in infancy. The present illness had started seven weeks before with general weakness, occasional rigors, and epistaxis, and during the week preceding admission there had been unproductive cough and bouts of diarrhoea.

On examination there were marked pallor, furred tongue, sordes on the teeth, prostration, and mental depression; temperature 103° F. (39.4° C.), pulse 112, respirations 40; throat clear; pupils and fundi normal; no neck rigidity or Kernig's sign; abdominal reflexes absent, but all deep reflexes present. A few scattered rhonchi were heard in the lungs. Examination showed no enlargement of the heart clinically, but there was a marked gallop rhythm and a blowing apical systolic murmur not conducted into the axilla and not accompanied by a thrill. The abdomen was slightly distended and tumid on palpation, but the liver and spleen were not felt. B.P. 120/80. A chest radiograph on admission was clear. Her white cells numbered 13,800 (80% polymorphs) and red cells 4,510,000 per c.mm.; Hb 81%. Blood was sent for culture and agglutination, and specimens of stool and urine for culture.

Her condition remained serious and her temperature continued without intermission as in the accompanying Chart; penicillin, 100,000 units three-hourly, was started on June 3 and

increased next day to 150,000 units three-hourly without any effect. On June 3 it was reported that there were no agglutinations to *Salm. typhi* O, *Salm. typhi* H, *Salm. paratyphi* B O, *Salm. paratyphi* B H, non-specific *Salmonella* H, or *Brucella abortus*, but on June 6 *Salm. typhi-murium* had been cultured from the Widal clot. In the meantime petechiae had appeared on the upper arms and at the root of the neck, and her general condition had deteriorated still further. The diagnosis was now apparently septicaemia due to *Salm. typhi-murium* (? subacute bacterial endocarditis), and it was decided to try to obtain a supply of chloramphenicol ("chloromycetin") from Parke, Davis and Co. in view of the results obtained in other *Salmonella* infections. Pending the arrival of the drug (over the Whitsun holidays), and in view of the patient's desperate condition, streptomycin was given six-hourly in 1-g. doses. The chloramphenicol arrived after a total of 8 g. of streptomycin had been given, and by then the patient's general condition was decidedly better, with fewer fresh petechiae and

improvement in the gallop rhythm, but no marked fall in temperature. Sensitivity of the organism was demonstrated to chloramphenicol and to a greater degree to streptomycin.

Chloramphenicol 4 g. (16 capsules of 0.25 g.) was given at 10 a.m. on June 8 and was continued in 1.5-g. doses twice daily; by 10 p.m. her temperature was normal. The next day the improvement in her toxæmia was quite marked, but she developed sudden pain and swelling in the right knee with severe limitation of movement. Fundus examination showed severe toxic changes in the right macular region, and a small subhyaloid haemorrhage in the left macular region. Her diarrhoea rapidly improved and was replaced by complete constipation; but fresh petechiae continued to appear, and in view of a slight rise in temperature on June 12 and 13 it was decided to double the dose of chloramphenicol by giving 1.5 g. six-hourly. From then on her temperature did not rise above normal until she died. She continued to be extremely irritable and prostrated, however, and fresh petechiae appeared, though fewer in number; the blood pressure fell progressively to 66/50; the apical systolic murmur changed suddenly to a high-pitched musical murmur, and in spite of increasing the dosage again to 1.5 g. three-hourly she developed acute pulmonary oedema and died on June 22. At no time were specific agglutinins demonstrated against this strain of *Salm. typhi-murium*, and all specimens of stools and urine were negative on culture for that organism throughout.

Post-mortem examination showed no abnormality in the nervous system or in the abdomen, and in particular there were no lesions in the intestines, but two small white infarcts were found in the spleen. The lungs were very oedematous and there were a few small subpleural infarcts. The heart was normal in size but extremely flabby, and the myocardium was very toxic in appearance and necrotic in parts. There were two vegetations on the mitral valve, one small and one moderate in size, and apparently still active but sterile on culture. Microscopy of the vegetations showed only polymorphs present in the fibrin, and no bacteria were seen.

COMMENT

Systemic invasion with *Salm. typhi-murium* appears to be comparatively rare. Seligmann and Hertz (1944) report a case of cholecystitis and two cases of salpingitis; Angrist and Mollov (1946) quote Seligmann's post-mortem findings of infected dissecting aneurysm of the aorta and a case of mitral endocarditis. In general, mortality appears very high when *Salmonella* infections become invasive, and the chief help from chemotherapy is likely to be the prevention of systemic invasion by early control of the primary infection. In the present case of established endocarditis the continuing occurrence of petechiae in spite of a normal temperature, and the sudden change in quality of the cardiac murmur at the end of 12 days' intensive treatment, suggest that a much higher maintenance dosage is required at the onset of treatment than is employed in typhoid (i.e., 1.5 g. of chloramphenicol three-hourly instead of twelve-hourly), and this would possibly have to be continued for at least 28 days, on the analogy of penicillin therapy for subacute bacterial endocarditis. Fortunately the drug appears to be completely non-toxic even in such large doses.

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