FAILURE OF ANTIBIOTICS IN A CASE OF STAPHYLOCOCCAL BACTERIAEMIA

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Penicillin-resistant staphylococci are now so frequently encountered in hospital practice that reliance often has to be placed on the newer antibiotics in treating infections due to these organisms. The following case history is of particular interest in that aureomycin and chloramphenicol failed to cure penicillin-resistant staphylococcal bacteriaemia in spite of (1) being effective against the organisms *in vitro*, and (2) the absence of a demonstrable focus of infection. Nichols and Needham (1949) mention a somewhat similar case, but with a much shorter illness.

Case Record

A West African nurse aged 26 was admitted to North Middlesex Hospital, under the care of Dr. Norman Whittaker, with a fever (102° F.—38.9° C.) and a four-days history of pains in the back of the neck following upon the healing of a small furuncle in the nose. She gave a past history of malaria and of appendicectomy.

No abnormal physical signs were discovered. The urine and C.S.F. were normal, blood films revealed no malaria parasites, and leucocytes totalled 8,900 per c.mm., with 80% polymorphs. The fever persisted despite penicillin, and two blood cultures grew *Staphylococcus aureus* sensitive to aureomycin and chloramphenicol, relatively resistant to streptomycin, and resistant to penicillin. A 10-days course of aureomycin (0.5 g. six-hourly) was given in place of penicillin. Fever subsided in 48 hours, but recurred two days after the end of the course and blood culture again grew *Staph. aureus*. This story was repeated after a second and a third course of aureomycin lasting 31 days and 48 days respectively. On her fourth course of treatment, lasting 34 days, *Staph. aureus* was grown from the blood while she was afebrile and still taking aureomycin. Fever recurred during the latter part of this course, with yet another positive blood culture, and the patient was transferred to the care of Sir Neil Hamilton Fairley at the Hospital for Tropical Diseases.

During her stay in the North Middlesex Hospital all attempts to find a focus of infection failed, and white-cell counts varied between 6,200 and 9,600 per c.mm. Full radiological investigations of the teeth, sinuses, chest, and skeleton proved negative. Intravenous and retrograde pyelography showed the kidneys to be horse-shoe in type and functioning normally.

On admission to the Hospital for Tropical Diseases a blood culture yielded a heavy growth of coagulase-positive *Staph. aureus* sensitive to aureomycin and chloramphenicol, and a fifth course of aureomycin was given for 14 days. Temperatures became normal after nine days but rose again the day after stopping treatment, and blood culture now grew *Staph. aureus* sensitive only to chloramphenicol while moderately sensitive to aureomycin, streptomycin, and oxytetracycline (terramycin). The organism was sensitive to 5 μg. of chloramphenicol per ml. A course of this antibiotic was given until the patient died 57 days later, the dosage being 0.5 g. six-hourly for the first week and 1 to 1.5 g. six-hourly thereafter. On the lower dosage a blood level of 20 μg. per ml. was obtained in a sample of venous blood collected six hours after a dose. In spite of this the organism was repeatedly recovered on blood cultures, even with the high dosage. Complete E.N.T. and gynaecological examinations revealed no septic focus, and urinary deposit was consistently normal. The leucocyte count remained below 10,000 per c.mm., with about 75% polymorphs, until the final stage, when it rose to 13,200. The haemoglobin dropped steadily, and repeated blood transfusions were given with little avail. Bronchopneumonia closed the scene after an illness lasting 226 days.

A detailed post-portem examination was carried out by Dr. D. S. Ridley. The lungs were oedematous and there was a patch of bronchopneumonia at the left base. The heart and its valves and arteries were normal. The spleen was rather enlarged but not soft or septic. The kidneys were horse-shoe but otherwise normal. No evidence of sepsis or other abnormality was found in the liver, intestines, gall-bladder, pancreas, suprarenals, ovaries, uterus, bladder, brain, mastoids, maxillary and frontal sinuses, and spine. No enlarged glands and no infarcts were found. Histological examination revealed nothing further.

Discussion

It may be argued that antibiotics failed owing to a localized infection somewhere in the body. No such focus was found in spite of comprehensive clinical, laboratory, radiological, and post-mortem examinations.

The development of staphylococcal resistance to aureomycin and chloramphenicol may be postulated. It was not until the fifth month of her illness, however, that some resistance to aureomycin occurred, after a total dosage of 178 g. Treatment was then changed to chloramphenicol, and no resistance of this particular strain to chloramphenicol was found on repeated *in vitro* tests.

The dosage of antibiotics may be considered. Aureomycin was given in five courses of 1 to 2.5 g. daily over a total period of 137 days. With chloramphenicol the blood level was estimated. The Oxford staphylococcus used as a standard is sensitive to 5 μg. of chloramphenicol per ml. This staphylococcus was equally sensitive. A blood level four times the *in vitro* level is recommended in treatment (Pharmaceutical Society, 1952) and was achieved here on a dosage of 0.5 g. six-hourly, but pyrexia and positive blood cultures persisted even when the dosage was raised.

Aureomycin and chloramphenicol act on bacteria by inhibiting growth rather than by direct bactericidal action, and radical cure of an infection is ultimately dependent on the defensive mechanism of the body itself. This patient may have had a defective cellulo-humoral response, for throughout her illness the total neutrophils were lower than would normally be expected in staphylococcal bacteriaemia.

Summary

A young African woman developed staphylococcal bacteriaemia following a small furuncle in the nose, the organism being sensitive only to aureomycin and chloramphenicol. In spite of five courses of the former (total 178 g.) and one course of the latter (252 g.) the organism persisted in the blood without any focus of infection being found. A blood concentration of at least 20 μg. of chloramphenicol per ml. failed, although *in vitro* tests showed the staphylococcus to be sensitive to 5 μg. per ml.

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References

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