PS. PYOCYANEUS EYE INFECTION*

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Few cases of corneal ulceration, proved to be of *Ps. pyocyaneus* origin, have been described. The case described below is similar to two reported by Ainslie and Smith (1952), and to ten reported by Bignell (1951), all of which were seen in London. The clinical history and appearance of the ulcer were so typical, and the response to Polymyxin B was so prompt that this case is considered worthy of record.

Case Report

A Bantu male aged 40 attended on June 18, 1952, complaining of soreness in the right eye of 9 days' duration. He presented a note from another hospital saying that a corneal foreign body had been removed there on June 9, since which date he had had daily 10 per cent. sulphacetamide eye irrigations without any improvement.

Examination.—A large corneal ulcer of the right eye extended from below the pupillary margin at 7 o'clock upwards and medially to cover the entire pupillary area. The upper margin of this ulcer had a dead-white sloughing overhanging crescent. The main base of the ulcer was whitish and translucent. There was no pannus and little pain. A 2 mm. hypopyon was present.

Culture and smears were taken immediately and the patient was admitted to hospital.

Therapy.—Atropine 1 per cent., sulphacetamide 10 per cent., hot steamings all to the right eye three times a day; ascorbic acid tablets 1,000 mg. three times a day. The patient was strictly isolated.

On June 20 the temperature was 99-4° F., but subsided promptly after a course of oral sulphadiazine.

On June 21 the condition of the eye remained unchanged. There was good mydriasis, and absence of pain, and the patient's general condition was satisfactory. A subconjunctival injection of 200,000 units penicillin in 4 minims distilled water was given.

On June 22 there was still no change in the eye condition. The original culture + smear report was as follows:

Microscopic examination showed pus cells and Gram-negative bacilli. Culture yielded a growth of *B. pyocyaneus*. Subculture for sensitivity showed resistance to penicillin, streptomycin, chloramphenicol, aureomycin, and terramycin.

It was decided to obtain Polymyxin B sulphate, and meanwhile, to counter any secondary infection, a further subconjunctival injection of 200,000 units penicillin was given, and the ulcer was carbolized.

On June 26 the condition of the eye remained unchanged except that the hypopyon was slightly smaller. 500,000 units Polymyxin B sulphate were diluted with 10 ml. sterile water. 0.5 ml. of this dilution of polymyxin was injected subconjunctivally after an

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initial subconjunctival dose of 4 minims procaine hydrochloride 4 per cent. There was no immediate or delayed pain whatsoever. The remainder of the polymyxin was given as hourly drops.

On July 1 the hypopyon had completely disappeared. There was almost complete disappearance of the crescentic white fold at the upper edge of the original ulcer. The eye remained injected. Swabs and cultures were repeated.

On July 6 the cultures and swabs were reported negative for all bacteria. The eye was now slightly injected.

On July 9 the polymyxin drops were stopped, as the ulcer appeared inactive. Slit-lamp microscopy showed a remarkably thinned cornea over the whole extent of the ulcer, the cornea here being only one-third of its usual thickness (this finding was also noted by both Bignell and Ainslie). There was complete absence of vascularization. The cornea was remarkably clear except that its superficial layers showed scattered white opacities. Visual acuity was counting fingers at 4 m. The patient was discharged from hospital with instructions to use sulphacetamide 10 per cent. and atropine drops 1 per cent., both three times daily, together with Multivite tablets twice a day.

On July 15 he was seen in the out-patient department and the eye was almost white.

On August 11 the eye was white, and the previously ulcerated area of the cornea was now quite flat and completely epithelialized. There were a few flecks of intracorneal pigment at 7 o'clock, but no sign of pannus. Instillation of fluorescein showed no staining, but the original corneal defect still showed as a marked declivity. Visual acuity was now 6/60.

Discussion

Brownlee and Bushby (1948) reported an antibiotic substance with remarkable activity against Gram-negative bacteria. This was "Aerosporin"* (Polymyxin A)—a polypeptide produced by the soil organism B. aerosporus (identical with B. polymyxa). The latter produces a number of polypeptides with similar antibiotic properties but differing from each other both in their amino acid content and in their toxicity to animals.

(1) Polymyxin A ("Aerosporin") was found to be five to fifty times more active against certain Gram-negative bacteria than streptomycin. It is bacteriocidal rather than bacteriostatic and susceptible organisms did not readily develop resistance to its action. Clinical trials showed a good response against Gram-negative infections. It did not contain the amino acid d-serine believed to be nephrotoxic (Jawetz and Coleman, 1949).

(2) Polymyxin B has a pH of 7·2 to 7·4. It is readily soluble in water and has a remarkable stability in the frozen state. Very dilute solutions deteriorate slowly at room temperatures, but in a concentration of 4 mg./ml. its activity was significantly diminished only after 62 days at 4°C. (37°F.). The dry preparation is stable for over 5 months at 22°C. Changes in hydrogen ion concentration do not influence its potency. The action of Polymyxin B appears to be bacteriocidal. The growth of resistant strains in its presence does not destroy its activity and its potency remains unchanged. No bacteria dependent on it for growth have been observed to date (Jawetz and Coleman, 1949).

Used parenterally and without a local anaesthetic, it is painful for a few hours. Any systemic side-effects are avoided by the small subconjunctival dose of 25,000 units daily.

* Aerosporin—Chas. Pfizer & Co. Inc., U.S.A.
According to Pulaski and others (1949), drug resistance does not develop in any cultures. Severe granulating wounds infected with *Ps. aeruginosae* have been treated with topical Polymyxin B (in saline or in carbowax base) with the eradication of all organisms in every case excepting when devitalized tissue was present. No toxicity follows its oral or topical administration. Many strains of *Pseudomonas* and *B. proteus* are fairly resistant but this resistance is inherent and not acquired (Jawetz and Coleman, 1949).

(3) Polymyxin C was reported in 1951, but its use was restricted by the damage it produces to the renal convoluted tubules.

(4) Polymyxin D was reported in 1949 and shown to be nephrotoxic to animals (Swift and Bushby, 1951). Its clinical use was therefore abandoned.

(5) Polymyxin E, which appears to have a less toxic effect, was used by Ainslie and Smith (1952). Its toxicity is similar in effect to that of Polymyxin B, but the results are less marked, and irritation is not produced at the site of injection. A dosage of 10,000 units kg. body weight has been given 4-hourly to patients for 2 weeks continuously without any apparent untoward effects. Ainslie and Smith (1952), after reporting their experiments with *pyocyaneus* infections in rabbits, mention that Polymyxin E would probably be at least equally effective against infections due to other Gram-negative organisms. They remark that eye infections with Gram-negative bacilli are uncommon, but may be very severe. Recently there have been some encouraging responses with streptomycin. These authors use local Polymyxin E, and say it is unsuitable for systemic administration against intra-ocular infections owing to its large molecular structure which prevents its passage through the blood-aqueous barrier. It does, however, penetrate intra-ocularly, when given by the subconjunctival route, and local reaction of the ocular tissues is clinically minimal. In rabbits, Polymyxin E given subconjunctivally took 45 minutes to enter the anterior chamber, and remained in detectable concentration for about 24 hours. It was also found to enter the vitreous to similar levels, and the corneal tissue itself showed a high concentration. When they inoculated the cornea of rabbits with *Ps. pyocyaneus* and then treated them with Polymyxin E, they noted one case of a hypopyon developing on the 4th day, and another in which the cornea became thin in the centre. Their dosage to patients was 200,000 units daily by the subconjunctival route, and they reported varying degrees of itching which began after 30 minutes and lasted for three-quarters of an hour.

Bignell (1951) states:

Practically the only severe corneal ulcers occurring at the Moorfields, Westminster and Central Eye Hospital, London, during a year were due to *B. pyocyaneus*. A typical history included abrasion of the cornea or removal of a foreign body from the cornea. Loss of the eye or loss of useful vision occurred in nineteen out of twenty-three cases recorded since 1922.

Bignell also mentions thinning and vascularization of the cornea and emphasizes the importance of early clinical recognition. This can be achieved by noting the characteristic dead-white area in the cornea with central superficial necrosis, and the later formation of a white ring with a semi-transparent centre. His cases were treated with subconjunctival strepto-
mycin 0.5 g. daily together with streptomycin drops hourly until no dead-white infiltration remained. Premature cessation of therapy, that is, before the infiltration had disappeared, resulted in two cases of severe recrudescence which did not show until 2 to 3 days after the drug was stopped. Sorsby, Ungar, and Bailey (1952) describe these ulcers as:

an infection of the cornea running a rapidly destructive course, for the corneal reaction is essentially a proteolytic phenomenon consistent with the proteolytic properties of these organisms.

It is likely that what went under the name ‘corneal abscess’ included the group of infections of the cornea by Gram-negative bacilli.

Summary

A case is described of *Ps. pyocyaneus* ulceration of the cornea in a Bantu patient. It is compared with cases previously published and found to be clinically similar. The condition responded promptly to Polymyxin B given subconjunctivally and topically. The literature on the various polymyxins (A, B, C, D, and E) is reviewed, with special reference to their use in ophthalmology.

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