Pyrrolidinomethyl tetracycline in cavernous sinus thrombosis

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Before the advent of antibiotics, cavernous sinus thrombosis of septic origin was invariably fatal (Grove, 1936). After the introduction of sulphonamides and antibiotics, Shaw (1952) collected from the literature sixty cases of cavernous sinus thrombosis in which these drugs were used, and observed that the mortality rate had come down to 11.7 per cent., but that 77 per cent. of those who survived showed residual abnormalities. Clune (1963) reported a survival rate of 72 per cent. with a 50 per cent. morbidity rate in those who recovered. In an attempt to reduce the high morbidity rate in survivors, newer antibiotics and anti-inflammatory and anti-thrombotic agents have been tried in various combinations. The present study reports our experience of treating seven cases of septic cavernous sinus thrombosis with pyrrolidinomethyl tetracycline (Reverin).

This is a pyrrolidinomethyl derivative of tetracycline with the molecular formula $C_{27}H_{33}O_8N_3$. It is a water-soluble compound which can be administered intravenously or intramuscularly; it quickly attains high and reliable blood concentrations and the normal intestinal flora are not much affected. After the intravenous injection of 275 mg. Reverin the initial serum concentrations are almost ten times as high as after the oral administration of 250 mg. tetracycline hydrochloride (Strauch and Koch, 1958); 8 hours later the former is still almost twice as high as the latter, and even after 24 hours therapeutic blood levels of Reverin can still be demonstrated (Finland, Purcell, Wright, Del Love, Mou, and Kass, 1954). Dimmling, Huner, Lutzeyer, and Simon (1958) have shown that the potency and bacteriostatic range of Reverin is similar to that of tetracycline hydrochloride, but with a much lower general and local toxicity.

Because of these advantages, it has been extensively used in fulminating infections with encouraging results, and it is therefore surprising that only one previous report of its use in a case of cavernous sinus thrombosis has been found (Khare, 1967).

The usual organisms encountered in cases of cavernous sinus thrombosis are the *Streptococcus*, *Staphylococcus*, *B. proteus*, *B. pyocyaneus*, *Pneumococcus*, and *Meningococcus* (Walsh, 1957). Tempea and Gorun (1959) stated that the first two organisms were most commonly encountered, and Clune (1963) found *Staphylococcus aureus* (coagulase-positive) to be the most frequent.

Reverin is effective against all these organisms (Finland and others, 1954), but sulphonamides and antibiotics, including broad-spectrum tetracycline and chloramphenicol, have not proved to be very effective (Table III, p. 115).

Material and methods

Seven cases of septic cavernous sinus thrombosis were treated with intravenous pyrrolidinomethyl

tetracycline (Reverin) 275 mg. 8-hrly. Other supportive therapy, including anti-coagulants and Diamox, was added when necessary.

All the patients presented in a semiconscious or unconscious state, with high fever and neck rigidity. The clinical particulars are given in Table I.

Table I *Clinical particulars of seven cases of cavernous sinus thrombosis treated with intravenous Reverin*

Case no.	Age (yrs)	Sex	Precipitating cause	Latent period (days)	General examination					Duration of treatment (days)	Outcome
					Appearance	Blood pressure	Temperature (°F.)	Leucocyte count (per cu. mm.)	Erythrocyte sedimentation rate (mm./1st hr)		
1	40	M	Boil on nose	8	Dehydrated and toxic	112/70	103°	22,000	80	7	Died
2	35	F	Septic abortion	4	Unconscious	100/60	102°	10,000	60	15	Cured
3	20	F	Furuncle on nose	5	Semiconscious	100/70	102°	10,500	101	30	Cured
4	40	F	Acute exacerbation of chronic suppurative otitis media	8	Semiconscious	150/70	103°	19,200	80	20	Cured
5	30	F	Septic abortion	9	Unconscious Flexor plantar reflexes	140/95	104°	20,000	100	5	Died
6	20	F	Abscess on right temple	7	Semiconscious	140/80	104°	12,000	100	24	Cured
7	12	M	Not known	Not known	Semiconscious	110/80	103°	15,400	104	16	Cured

The results of the ophthalmological examination are shown in Table II (opposite). All the patients showed lid oedema and conjunctival chemosis.

Observations

Of the seven patients treated, five (71·4 per cent.) recovered without any residual effects, and two died with cardiorespiratory failure during the acute phase of the illness. The duration of treatment required in the survivors ranged from 15 to 30 days.

Unfortunately the blood cultures taken in our Cases 2, 3, and 4 were sterile. In one case *Staphylococcus saprophyticus* was grown.

Comment

The most significant feature noted in the present series was that there was no evidence of residual damage in the five patients who recovered, whereas previous reports have shown morbidity rates of from 50 to 77 per cent. (Table III, opposite).

We therefore feel that pyrrolidinomethyl tetracycline is the drug of choice in the management of septic cavernous sinus thrombosis, and that it should be administered from the start, without first trying less potent agents.

Table II *Ophthalmological findings in seven patients*

Case no.	Eye involved	Fundus	Other observations
1	Both (left more than right)	Hyperaemic disc Dilated vessels	Proptosis Limitation of movement Mastoid oedema
2	Right	Hyperaemic disc Blurred margins Dilated vessels	Axial proptosis Mastoid and facial oedema Pupils semidilated with sluggish reaction
3	Both (left more than right)	Not visible	Axial proptosis Exposure keratitis Mastoid oedema
4	Both (left more than right)	Normal	Proptosis Limitation of movement Mastoid oedema
5	Right	Hyperaemic disc	Proptosis Limitation of movement Mastoid oedema Pupils semidilated with sluggish reaction
6	Right	Dilated vessels	Proptosis Limitation of movement
7	Left	Hyperaemic disc Retinal oedema Dilated vessels	Proptosis Limitation of movement

Table III *Mortality and morbidity rates in cases reported by other workers compared with the seven cases here reported*

Author	Year	Total cases	Mortality (per cent.)	Morbidity (per cent.)
Shaw	1954	60	11.7	77.0
Yarington	1961	878	80.0	75.0
Clune	1963	36	28.0	50.0
		5	60.0	50.0
Present series	1969	7	28.6	Nil

Summary

Pyrrolidinomethyl tetracycline (Reverin) was given intravenously in seven cases of septic cavernous sinus thrombosis, and was found to be useful in eliminating residual morbidity in the five patients who recovered.

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