Candida endophthalmitis in heroin addicts

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Key words: *Candida albicans*, endophthalmitis, heroin addicts, pars plana vitrectomy

Abstract. The clinical course of endophthalmitis, presumably due to *Candida albicans*, in nine eyes of heroin addicts is described. In six of the seven eyes in which pars plana vitrectomy was performed the diagnosis was confirmed by the cultivation of *Candida albicans* from the rinsing fluid. Both purely intraocular treatment and a combination of local and systemic antimycotic therapy caused the intraocular infection to disappear. In this small group of patients the results were most favourable when treatment was started early.

Introduction

In the American literature since 1974 cases have been described of endophthalmitis in heroin addicts due to *Candida albicans*. These have been either single cases or small groups (Getnick and Rodrigues, 1974; Stone et al., 1975; Stern et al., 1977; Elliott et al., 1979; Aguilar et al., 1979; Perraut et al., 1981). In the literature there is as yet no consensus of opinion about the best treatment for this condition, which usually occurs as an isolated infection in one eye (Robertson et al., 1974; Jones, 1978; Blumenkranz and Stevens, 1980). In Western Europe so far little attention has been paid to this complication (Barthelemy et al., 1981). Between October 1980 and October 1981 nine of these patients were seen in the Ophthalmological Departments of two University Hospitals: five in Amsterdam and four in Leiden.

Patients (see Table 1)

The patients were young adults between 19 and 33 years of age with a history of 1 to 12 years of intravenous heroin administration. The complaints were indistinct vision, redness and pain in one eye and did not develop until at least a week after the last heroin injection. The visual acuity was generally markedly diminished and at the first visit varied between 1/300 and a maximum of 0.4. In five patients there was severe fibrinous iritis with marked

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Table 1. Particulars of patients

Pat Nr	Sex	Age	Time using heroin + other drugs	Duration eye complaints	Last injection	OD/OS	Visual acuity on admission	Anterior segment	Vitreous	Fundus	Systemic examination	Diagnosis at 1st consultation
1	m	28	3 years	?	?	OD	2/300	fibrinous iritis	vitreous abscess cells + flocules	not visible white exudate	lung tuberculosis recurrent gonorrhoea	tubercular eye disease uveitis cum hypopyon
2	f	28	"a long time" + cocaine	?	?	OD	1/300	fibrinous iritis + hypopyon	opacities + subhyaloid hypopyon	retinitis- focus in macula	candidiasis skin + aphthae	Beçhet's disease
3	m	33	10 years + methadon	?	8 days	OD	5/60	fibrinous iritis	white flocules	preretinal fibrosis	chron. hepatitis recurrent gonorrhoea	Candida endophthalmitis
4	m	31	6 years	4 weeks	?	OS	0.1	no abnormalities	opacities + white flocules	not visible	no abnormalities	iridocyclitis
5	m	28	12 years	≥ 7 weeks	?	OS	2/300	ext. clear cells ++	thick vitreous opacities	indistinct chorioret. central focus	hepatitis B pos.	toxoplasmic chorioretinitis
6	m	22	1 year	2 weeks	?	OD	1/60	fibrinous iritis	very thick vitreous opacities	not visible	no abnormalities	toxoplasmic chorioretinitis
7	f	19	2 years + cocaine + amphetam.	8 weeks	?	OD	1/300	ext. clear cells ++	opacities "strings of pearls"	multiple retinal foci	hepatitis B pos. alcohol abuse	Candida endophthalmitis
8	m	22	5 years + cocaine + methadon	≥ 2 weeks	?	OD	0.2	fibrinous iritis	"strings of pearls"	multiple retinal foci	hepatitis B pos. alcohol abuse	Candida endophthalmitis
9	f	22	1 year	10 days	2½ weeks	OS	0.4	ext. clear cells ++	"strings of pearls"	multiple retinal foci	hepatitis B pos.	Candida endophthalmitis

Figure 1. Arm of patient 8 showing heroin injection punctures.

pericorneal redness. In the four others the anterior segment was relatively unaffected and there was no external redness. The lens was clear in all cases. Opacities were seen in the vitreous of all the eyes, varying from so-called "strings of pearls" (white woolly opacities strung together) to a complete vitreous abscess. In three cases the fundus could not be assessed on account of very thick vitreous opacities. In four patients retinal foci were seen localised in the posterior pole.

In spite of intensive screening in no case were other foci of *Candida albicans* infection found, in particular there were no indications of endocarditis. At least four patients had had a hepatitis B infection.

A pars plana vitrectomy was performed on 7 patients and 5 μ g amphotericine B was introduced into the vitreous cavity (see Table 2). In 6 cases *Candida albicans* could be cultivated from the rinsing fluid from the operated eye; in case 3 the *Candida* culture was negative although the clinical picture was typical for the condition. Patients 3, 4 and 5 were treated with intra-

Figure 2. Patient 4: Candida endophthalmitis with white woolly opacities in the vitreous.

Figure 3. Patient 4, 3 months after vitrectomy + 5 µg gram amphotericine B intra-vitreally.

Pat. Nr	Pars plana vitrectomy	Culture rinsing fluid	5 µgram amphotericine B intravitreally	systemic antimycotic therapy	Complications	Visual acuity 1st consult.	Visual acuity last consult.	Follow-up
1	—	n.a.	—	—	atrophia bulbi	2/300	0	1 month
2	(paracentesis anterior chamber)	(negative)	—	—	strab. divergens + cataract	1/300	3/300	7 months
3	+	negative	+	—	—	5/60	2/60	1½ months
4	+	Candida albicans +	+	—	—	0.1	0.1	6 months
5	+	Candida albicans +	+	—	retinal detachment + mpp	2/300	1/∞	1½ months
6	+	Candida albicans +	+	400 mg miconazol i.v. for 2 weeks 2 dd 200 mg ketokonazol for 2 months 60 mg prednison for 1 week	—	1/60	4/60	4 months
7	+	Candida albicans +	+	amphotericine B i.v. for 2 weeks 5-fluorocytosine + ketokonazol per os for 6 weeks amphotericine B i.v. up to 50 mg/day in comb. with 12 gr 5-fluorocytosine/day for 6 weeks 2 x 400 mg ketokonazol/day for 6 weeks	retinal detachment + mpp	1/300	0	3 months
8	+	Candida albicans +	+	amphotericine B i.v. up to 50 mg/day in comb. with 12 gr 5-fluorocytosine/day for 6 weeks 2 x 400 mg ketokonazol/day for 6 weeks	—	0.2	1.0	1½ months
9	+	Candida albicans +	+	amphotericine B i.v. up to 50 mg/day in comb. with 5-fluorocytosine 9 gr/day for 6 weeks	transient cystoid macular oedema	0.4	1.0	8 months

mpp = massive panretinal proliferation

ocular antimycotics only. Patients 6, 7, 8 and 9 were given both intraocular and systemic antimycotics. In the seven patients who received treatment the inflammatory symptoms disappeared. In 2 eyes, however, (patients 5 and 7) retinal detachment developed about a week after the pars plana vitrectomy, which was resistant to treatment. Three eyes healed leaving a visual acuity of from 0.1 to 2/60, as the result of a central glial scar. Two eyes (patients 8 and 9) got back a visual acuity of 1.0, almost free of residual side-effects; both these patients came for treatment at a relatively early stage. In patients 1 and 2 the diagnosis was made retrospectively on the grounds of the clinical picture and the case history. These patients were not treated with antimycotics; both eyes became atrophic.

In this small group of 9 patients the results of treatment appeared to depend largely on the visual acuity and the severity of the endophthalmitis at the start of therapy (Graph 1).

Graph 1.

Discussion

Candida endophthalmitis was originally only seen in patients with reduced vital resistance and/or after serious operations, in association with parenteral feeding, indwelling catheters and infusions, and particularly with prolonged use of broad-spectrum antibiotics, corticosteroids and other immunosuppressants (Griffin et al., 1973; Henderson et al., 1981). In these forms of *Candida* endophthalmitis both eyes are affected in about half of the patients (Clarkson and Green, 1981). In addition autopsy on patients who had suffered from *Candida* endophthalmitis revealed in at least 78% of cases other *Candida* foci, especially in the heart and the kidneys (Edwards et al., 1974).

The probable sources of infection by intravenous heroin administration are the impure heroin itself, insufficient disinfection of the skin, the unsterile way of dissolving, filtering and injecting the heroin, and the use of dirty syringes and needles (Tuazon et al., 1974, 1975). Patients 7, 8 and 9 obtained their heroin, independently of each other, via the same dealer, and all developed a *Candida* endophthalmitis at about the same time, so that contaminated heroin appears likely in these three patients. Vastine et al. (1976) describe a similar small explosion in Chicago.

In the recent literature two methods of treatment have been described:

1) After making the diagnosis on the grounds of the history and the clinical picture, and in some cases with the help of a vitreous biopsy to establish the diagnosis of *Candida* endophthalmitis, antimycotics are administered systemically only: intravenous amphotericine B in increasing doses up to a maximum of 10 mg/kg body weight, in combination with the synergically working 5-fluorocytosine per os (150 mg/kg body weight/day) for 2 to 6 weeks, then continuation of the 5-fluorocytosine, sometimes supplemented with the new preparation ketokonazol per os (Stone et al., 1975; Snip and Michels, 1976; Jones, 1978; Aguilar et al., 1979; Elliott et al., 1979; Barthelemy et al., 1981; Clarkson and Green, 1981; Jones et al., 1981). Heroin addicts, however, tend to withdraw from the lengthy treatment before it is completed. The possible toxicity of antimycotics in the vitreous and the chance of complications after extensive vitreous surgery are avoided by this method of treatment. The side-effects of the systemic administration of amphotericine B, however, should not be underestimated (see Table 3). The drug may only be administered when a strict check is held on the kidney function, electrolytes, blood picture and liver function.

Table 3. Side effects of amphotericine B

nephrotoxicity
hypokalaemia
anaemia
nausea and vomiting
hyperthermia and shivering
headache

2) On account of the toxicity of systemic antimycotics, if no other foci can be demonstrated clinically, a diagnostic and therapeutic vitrectomy is performed with the introduction of 5 μ g amphotericine into the vitreous space. The reasons for this are that the culture medium for the fungus is removed, material is obtained for a definite diagnosis by means of stained specimens and culture, and antimycotics are administered directly to the affected site. From animal experiments (Axelrod et al., 1973; Huang et al., 1979) and several case histories (Stern et al., 1977; Perraut et al., 1981) it appears that the above dosage is not toxic for the retina if it is introduced into the centre of the vitreous space. Souri & Green (1974), on the other hand, saw local retinal necrosis in rabbits following an intravitreal injection of only 1 μ g of amphotericine B. Patients 3, 4 and 5 were treated exclusively with intraocular amphotericine B. Their inflammatory symptoms disappeared. Patients 5 and 7 developed a postoperative retinal detachment. In the case of patient 5 pars planitis with a white pars plana encircling the eye was visible at operation. A few weeks after the detachment operation new large round defects developed in several quadrants. Patient 7 also showed, some time after detachment surgery, a very large defect arising from the periphery. We do not know whether this was caused by retinal necrosis due to the infection itself (Axelrod and Peyman, 1973) or to the amphotericine B, as demonstrated in animal experiments (Axelrod et al., 1973; Souri and Green, 1974). Patients 6, 7, 9 and 9, on the advice of the Department of Infectious Diseases of the Academisch Ziekenhuis in Leiden, were treated with a combination of systemic and local antimycotics, on the theoretical basis that *Candida albicans* spreads to the internal eye via the blood stream. In this way the single intraocular antimycotic treatment was backed up and, at the same time, other possible foci which were not yet clinically demonstrable were treated. In these eyes too all signs of infection soon disappeared. In patient 7 severe hypokalaemia occurred as a complication of the intravenous amphotericine B therapy, which was then stopped.

Conclusion

Candida endophthalmitis associated with intravenous heroin administration can be treated by intraocular antimycotics alone, by systemic antimycotics alone, or by a combination of the two. A clear preference cannot yet be given. The two eyes which were treated shortly after the onset of the symptoms retained the best visual acuity.

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