Long term results of pars plana vitrectomy in the management of intermediate uveitis

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Rationale for vitrectomy in intermediate uveitis

Following the first observations by Diamond and Kaplan (1978) [1] the efficacy of pars plana vitrectomy in eyes with chronic and recurrent intermediate uveitis has been studied repeatedly. The instantaneous benefit from surgery is an increase in vision related to the removal of vitreal flare or to lensectomy [1, 2, 3]. Further indications to vitrectomy are the vitreous hemorrhages, PVR with retinal detachment, and persistent hypotony [2, 4]. Several previous studies have shown that vitrectomy may lead to a decreased incidence and severity of recurrences in patients not responding sufficiently to corticosteroids or cryotherapy [2, 5-7]. However, the longterm effect of vitrectomy on the course of the inflammatory disease is a matter of debate. It has been postulated that the persistent effect of vitrectomy may be caused by the removal of inflammatory components and growth factors within the vitreous, or by the removal of mechanical factors provoking macular edema, or by achieving a better penetration of antiinflammatory drugs or inhibitory factors to the site of inflammation.

Our current understanding of the immunological mechanisms in intermediate uveitis is incomplete which is related to the inaccessibility of the tissue involved. Experimental data have provided convincing evidence that the chronic posterior uveitis presenting as retinal vasculitis, focal chorioretinal infiltrates and vitritis is compassing characteristics similar to autoimmune diseases [reviewed in 8, 9]. The restricted autoreactive inflammatory cell repertoire at the site of active posterior uveitis in the early disease may be followed by a heterogeneous cell response. This is one of the reasons that previous studies of vitreal or chorioretinal specimen harvested from patients with advanced uveitis have not yielded the information neccessary to characterize the initiating disease process in great detail. A spill of migratory cells from the eye may allow to screen the disease activity by screening the peripheral blood lymphocytes [10]. However, the local cytokine environment is especially critical for the regulation of the inflammatory processes. Both, Th1 and Th2 related cytokines
were present in the inflamed tissue in experimental posterior uveitis [11]. As a consequence from the above mentioned experimental data, future treatment modalities targeting the T cell receptor/major histocompatibility complex/antigen-binding, the CD4+ T cells, and the cytokines may be a breakthrough. Furthermore, mucosal tolerance induction which has been shown to improve the clinical course of certain other autoimmune diseases is a promising novel approach [reviewed in 8, 9]. The fact that current medical treatment is nonspecific, has limited efficacy with recurrences despite treatment, and often is followed by a number of unwarranted side effects has stimulated the physicians to search for alternatives, including certain surgical approaches.

**Therapy of intermediate uveitis and indications for vitrectomy**

The therapeutic approach is dependent on the individual course of the disease. Mild disease activity may spontaneously improve and does not necessarily justify treatment. When therapy is required, a therapeutic stepladder approach has been suggested, consisting of I. antiinflammatory drugs, II. cryotherapy, III. vitrectomy, and IV. systemic immunosuppression. Since intermediate uveitis in common is limited in duration, the principal goal of treatment is to avoid vision threatening complications.

The usefulness of nonsteroidal antiinflammatory drugs for the treatment of posterior uveitis has not been convincingly supported by prospective, randomized, double blind studies. However, many uveitis experts feel that this group of medication is helpful for treating patients with moderately active intermediate uveitis.

The efficacy of corticosteroids has been repeatedly demonstrated. The results of orbital floor steroid injections to 33 eyes with various uveitic diseases were analyzed [12] with regard to the visual acuity and vitreous cellular activity. An improvement with an average duration of effect of 9 weeks was obtained in nearly 50% of injections. This is comparing favourable with the results of systemic immunosuppression. However, the response to one particular injection could not be predicted by the response to previous or to subsequent injections to the same eye indicating that repeated trials are justified. Periocular steroids may also be helpful in the treatment of cystoid macular edema (CME) [13]. Another recent study showed a 60% success rate in visual outcome at 12 year in posterior uveitis patients managed on corticosteroids alone, improving to 77% with additional other immunosuppression.
Treatment was started with 1mg/kg prednisolone and was continued in high dosages (≈40mg) for at least 5 weeks. However, side effects from steroids were noted in 50% of the patients [14], which is frightening in view of the chronic course in many of the cases with posterior uveitis. For this reason, intravitreal sustained release corticosteroid devices may be effective while preventing the harmful systemic side effects. The first experimental studies suggested that biologically effective intraocular concentrations may be released into the eye for several months. By intravitreal dexamethasone devices, experimental uveitis in New Zealand rabbits was significantly improved with regard to the clinical signs, the histological tissue damage, the aqueous protein concentration and aqueous white blood cells [15].

Cryocoagulation in uveitic eyes is controversial, and may be particularly helpful in cases which are resistant to corticosteroids and develop active neovascularization of the vitreous base [16]. Since active retinal neovascularization has a high rate of secondary complications, cryocoagulation has been advocated in these conditions. The longterm effect on the inflammation and on the cystoid macular edema, however, is not clear.

**Longterm effect of vitrectomy**

The major rationale for performing pars plana vitrectomy in uveitis is the removal of significant media opacities. There is compelling evidence from various previous studies that the visual acuity may increase and remain stable after removal of vitreous infiltrations or lens opacities. Whether to do cataract extraction alone or combined with vitrectomy is still a matter of controversy. In cases with significant amounts of vitreal infiltration, combined cataract surgery and vitrectomy have been preferred. Also, intraocular lens implantation in chronic uveitis remains controversial. The longterm results after lens implantation may only be favourable when inflammation is abolished by appropriate immunosuppression. Otherwise, the course may be complicated by severe uveitic episodes, recurrent capsular opacifications, severe iridocyclitic membranes, hypotony, profound PVR and hemorrhages in the anterior chamber or vitreous.

The longterm results after vitrectomy in uveitis patients and reattachment of simultaneously detached retina or removal of epiretinal membranes generally were satisfactory by anatomical means. However, the improvement in vision was restricted by the unfortunate primary damage to the retina in various cases. In addition, the surgical removal of cyclitic
membranes causing ciliary traction has been repeatedly suggested as being beneficial for a long-term stabilization of persistent hypotony.

The influence of vitrectomy in uveitis patients on the course of the underlying disease process is not well defined. Recent experimental data are suggesting that the persistence of the vitreous is associated with the reactivation of a secondary immune response. Consequently, the removal of the vitreous may have a favourable influence on the subsequent uveitis course. Also, the timing of surgery is discussed controversially. Some authors have recommended to do vitrectomy immediately when topical or systemic corticosteroids failed [17]. A decrease in both the recurrence of disease and the need for immunosuppressive medication after pars plana vitrectomy has been noted recently [18]. This is in agreement with previous observations that vitrectomy may reduce the inflammatory activity postoperatively, and may allow to taper the immunosuppressive medication in certain cases. Correspondingly, these authors are suggesting to perform vitrectomy if loss of vision is progressive or prolonged corticosteroid therapy fails. Surgery, in conclusion, may be warranted to prevent the development of irreversible anatomical damages to the retina.

However, others are advocating to delay surgery. These authors are referring to the possible complications of vitrectomy which have in some cases been substantial and have to be considered in every single case. The most common complication was cataract formation. Others were vitreous hemorrhages, tractional retinal detachment, rhegmatogenous retinal detachment, proliferative vitreoretinopathy, and glaucoma. Altogether, these were occasionally requiring additional surgery.

Regardless of the timing of vitrectomy in uveitis, the preoperative control of intraocular inflammation is vital in all patients. It is important in this regard that postoperative disease recurrence has been observed especially in patients not being on perioperative immunosuppression or having active inflammation at the time of surgery. Furthermore, active uveitis is a risk factor for the development of severe postoperative PVR [19]. The angiogenetic activity of inflamed vitreous is supported by the observation that vitreous extract obtained from rabbit eyes with endotoxin-induced uveitis may induce severe neovascularization. This harmful effect has been attributed to the prostaglandin E2 and leukotriene B4 [20].

Cystoid macular edema accounts for visual impairment in a majority of patients with chronic uveitis. CME may resolve with posterior subtenon injections of depot corticosteroid
injections when given before irreversible macular degeneration develops or before vision decreases below 20/60 [13]. It has been recently shown that vitrectomy may have a beneficial effect on cystoid macular edema in uveitis patients not responding to steroid treatment. While 64% of the cases improved by vitrectomy, 18% worsened in this preliminary study [21], which is in correspondence to the findings of others. The individual response to vitrectomy has not been reliably predictable by any preoperative test. Unfortunately, no general recommendation can be drawn from the recent studies with regard to the role of vitrectomy in treating CME or in inducing CME in each individual case.


