

Sudden Reversible Vitritis After Keratoprosthesis

An Immune Phenomenon?

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Purpose: To report our experience with late vitritis associated with keratoprosthesis (KPro).

Methods: Between 1990 and 2003, 218 patients underwent an all-polymethylmethacrylate, collar button-shaped KPro surgery. Eight patients developed a total of 12 episodes of sudden, massive vitritis. Five of these patients had an Ahmed shunt implant, 3 had anterior vitrectomy during surgery, and 4 had a soft contact lens in place. Preoperative diagnoses were multiple graft failures, chemical burn, Stevens-Johnson syndrome, or ocular cicatricial pemphigoid. All patients were maintained on prophylactic topical ofloxacin 0.3% or polymyxin-B/trimethoprim, as well as prednisolone acetate 1% (in 2 cases, medroxyprogesterone 1%), at least twice daily. Vancomycin (14 mg/mL) was also given twice daily in 2 patients.

Results: Vitritis occurred in 8 patients (12 episodes), 2 to 23 months postoperatively. All patients presented with sudden, very marked decrease in vision, with little or no pain, tenderness, conjunctival redness, or discharge. Eight of the 12 events were subjected to vitreous tap and injection of antibiotics and steroids on the day of presentation. Cultures grew *Staphylococcus epidermidis*, only in liquid (broth) media, in 3 cases; the other 5 showed no growth. The vitritis episodes resolved after 2 to 9 weeks. Full recovery to pre-episode status of a quiet eye with clear vitreous was seen in all patients. Visual acuity recovered almost completely or completely (mental debilitation in one patient made accurate assessment uncertain).

Conclusions: This phenomenon of sudden vitritis after KPro, with few other symptoms and with complete recovery, would be uncharacteristic of a bacterial endophthalmitis. It may represent a uveitic immune phenomenon.

Key Words: keratoprosthesis, sterile vitritis

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We have previously reported on the incidence and characteristics of bacterial endophthalmitis after the Boston (Dohlman-Doane) collar-button keratoprosthesis (KPro). These events occurred almost exclusively in presumed autoimmune diseases, such as in Stevens-Johnson syndrome (SJS) and ocular cicatricial pemphigoid (OCP). They were characterized by a sudden decrease in vision accompanied by severe pain, redness, and discharge, with resultant complete loss of vision in all but 3 cases, who had some recovery of vision.¹

In addition, we observed the phenomenon of sudden vitritis without the other signs and symptoms of bacterial endophthalmitis, with rapid and full recovery of vision. These events happened without any warning, and no obvious precipitating factor was identified.

Vitritis after KPro has only been vaguely alluded to in the literature. However, Rao et al² and Aquavella et al³ more specifically described “aseptic vitritis” 3 to 12 months postoperatively, which was treated with steroids only, “without concomitant use of antibiotics.”

Here we report our experience of 12 episodes of sudden vitritis in 8 patients, with a discussion of etiology and treatment.

MATERIALS AND METHODS

Two hundred eighteen patients had a KPro implanted in Boston between 1990 and 2003, all operated on by the same surgeon (C.H.D.) with similar techniques. The devices were made of polymethylmethacrylate (PMMA) and were of collar-button design (Boston KPro).⁴ Device manufacturer and device-related factors were similar in all cases. All devices were made by the machine shop (JG Machine, Woburn, MA) from medical grade PMMA. They were cleaned by the same technician using the same cleaning procedure. All devices were placed in the Ster-Vac 5XL-3M ethylene oxide sterilizer for 12 hours at the Massachusetts Eye and Ear Infirmary surgical instrument room. Samples of the devices were subjected to bacterial culture in the bacteriology laboratory, which yielded no growth. All devices were supplied sterile before each use.

There was a total of 210 cases employing the same devices, which did not result in late inflammatory reaction. One hundred fifty-five type I and 63 type II KPro's were used. In our series of 8 vitritis, 6 had type I and 2 had type II.

There were 54 out of the 218 cases without holes in the back plate. The rest had holes. No titanium ring was present in any of the cases at that time. The holes and the front and back plates all had smooth surfaces, because the buffing process during the manufacturing leaves no sharp edges. Of the

8 patients with vitritis, 3 had no holes in the back plate; the rest had holes. Approximately 142 cases had glaucoma shunt tube devices implanted. Of the 8 patients who developed vitritis, 5 had also received an Ahmed shunt (S-2) implant during the initial surgery.⁵ Of the 8 patients who developed vitritis, the numbers of intraocular surgical procedures before the KPro surgery were as follows: patients 1 and 5 had none, patient 2 had 2, patients 3 and 6 had 1, patients 4 and 8 had 3, and patient 7 had 4.

Three patients had anterior vitrectomy. Five eyes were aphakic, and 3 were pseudophakic. The specifications of the intraocular lens are not known because they had been in place for a long time.

Four of the 6 patients with the type I device had a soft contact lens on the eye on presentation.

The preoperative diagnoses were multiple failed grafts in nonautoimmune, nonburn cases (5 patients), chemical burns (1), SJS (1), and OCP (1). The OCP and SJS patients had a through-the-lid (type II) KPro; the others had the standard (type I) device.⁴ The initial cohort of patients with SJS included a total of 24 cases; only the 1 included in the study had significant late vitritis.

All patients were maintained on prophylactic medication consisting of topical ofloxacin 0.3% or polymyxin-B/trimethoprim, in addition to prednisolone acetate 1% (in 2 cases, medroxyprogesterone 1% was substituted for the prednisolone), at least twice daily. Vancomycin (14 mg/mL) eye drops were also given twice daily in 2 patients.⁶ Similar management was used in all 218 cases in terms of choice of antibiotic, steroids, and systemic antibiotics perioperatively.

In eight of the 12 episodes, intraocular tap, or vitrectomy, and injection of antibiotics and steroids were performed at the time of presentation with vitritis.

One case report will serve as an example. The patient was a 54-year-old man who had an acid burn in both eyes in 1990. He had undergone 3 prior penetrating keratoplasties in the right eye and was pseudophakic. He underwent type I KPro surgery in his right eye in 2001, including removal of intro-ocular lens (IOL). One month after surgery, his corrected vision was 20/60, and after 20 months, it was 20/50+ uncorrected. He was using ofloxacin 0.3% and prednisolone acetate 1% 4 times daily as chronic prophylaxis. Twenty months after surgery, he presented with history of intermittent discomfort in the right eye and decreasing vision. He was pain free on the day of presentation but was found to have hand movement—only vision. Examination was significant for a quiet conjunctiva, fibrin in the anterior chamber seen through a perfectly positioned KPro with soft contact lens in position, and normal intraocular pressure. Immediate anterior chamber aspirate for culture and antibiotic injection of vancomycin (1 mg) and amikacin (400 µg), as well as dexamethasone (400 µg) into the anterior chamber, were performed. He was admitted to the hospital for intravenous antibiotics (vancomycin 1 g every 12 hours and ceftazidime 1 g every 8 hours) and topical vancomycin and ofloxacin 0.3% eye drops. The following day, he still had fibrin in the aqueous and therefore 40 mg of triamcinolone as peribulbar injection was given. On post-vitritis day 2, the fibrin had cleared, and he was discharged from the hospital on vancomycin (14 mg/mL),

ofloxacin 0.3%, and prednisolone acetate 1% drops (all 4 times daily). Cultures were negative.

Follow-up examination 1 month later revealed visual acuity of 20/60 with correction and no cells in the anterior chamber. Six weeks after the vitritis event, his vision with correction was 20/40+2. His last examination in February 2003 revealed stability with maintained vision, normal intraocular pressure, an uninflamed eye, and perfectly positioned KPro. He was using levofloxacin 0.5% and prednisolone acetate 1% eye drops twice daily.

RESULTS

Eight patients had a total of 12 episodes of sudden severe vitritis from 2 to 23 months after surgery. Significant past medical histories for each patient were reviewed, and there was no common predisposing factor identified. The patients were from different categories as described above.

Presentation of the vitritis was acute in onset, with 1 to 2 days of marked decrease in visual acuity but with minimal (if any) ocular discomfort or redness. All episodes occurred while patients were on topical antibiotics and steroids (or medroxyprogesterone in 2 cases of type II KPro) as noted in Table 1. Slit lamp examination in all patients was significant for a minimally inflamed conjunctiva (in type I), with anterior chamber inflammation, cellular reaction, and flare, but no hypopyon. There was a massive, almost “snowflake” vitritis that obscured the view of the fundus (Fig. 1).

Eight of the 12 episodes were treated like bacterial endophthalmitis. These patients underwent intraocular tap and injection of vancomycin (1.0 mg), amikacin (0.4 mg), and dexamethasone (0.4 mg). Intravenous antibiotics were started on 4 patients, and the frequency of topical antibiotic eye drops was increased in all patients.

The summary of the gram stain and cultures is listed in Table 1. There were no organisms isolated on solid culture media. Three patients' anterior chamber tap cultures revealed *Staphylococcus epidermidis* from meat broth only. One patient (1) did not have a tap on 3 episodes and was treated with triamcinolone peribulbar injection only. Another patient (6) was initially seen elsewhere, and no intraocular tap or antibiotic injection was done.

The recovery of vision to the pre-episode level was seen in all 7 patients who could be assessed (mental debilitation precluded assessment in one patient). The severe vitritis cleared in all cases within a few days. Visual rehabilitation was complete in 2 to 9 weeks.

No immediate relapse or recurrence of inflammation on steroid taper was seen in any of the patients. However, there were 2 patients who later had multiple, yet similar, inflammatory episodes. The patient with SJS, patient (1), had 3 such vitritis episodes, with a sudden decrease in vision while on prophylactic antibiotic regimen (Table 1). The keratoconus patient (8) had 3 brief vitritis episodes while on vancomycin, ofloxacin, and prednisolone drops (Table 1). The patients have been regularly followed over periods between 3 months and 4 years.⁷

DISCUSSION

We report our experience with this phenomenon of sudden, severe intraocular inflammation resulting in massive

TABLE 1. Summary of Cases

Patient No.	Diagnosis	Shunt	Pre-episode Topical Medications	VA Before Episode	VA at Episode	Occurrence Months After Surgery	Tap/Result	Treatment Beyond Eye Drops	Weeks to Clear Vitritis	Best Post Episode VA
1	SJS	Yes	Erythromycin ung Ciprofloxacin Ciprofloxacin Ofloxacin po	20/40	HM	3	No	Triamcinolone IV Abx	Rapid	Good
				“Good”	HM	8	No	IV Abx Terso over KPro	7	20/80
			Polymixin-trimeth. Cephalexin po	20/80	HM	11	No	Triamcinolone IV Abx	6	20/100
2	Graft failure	Yes	Medroxyprogest Ofloxacin	20/30	HM	23	Yes, negative	Re-KPro Vitrectomy Vitreous vanco	2	20/100
3	Graft fail	No	Medroxyprogest Ofloxacin	20/25	HM	6	Yes, negative	Vitrectomy Abx/Inj	?	20/40
4	Chemical bum	Yes	Ofloxacin Prednisolone acet	20/50	HM	9	Yes, negative	AC Inj Vanco, amik Dexameth. IV Abx Ceftaz	3	20/40
5	Edema uveitis	No	Prednisolone acet Polymixin-trimeth.	20/70	HM	7	Yes, Staph Epl (broth)	AC Inject Ceftaz Vanco, dexta	2–4	CF (somnolent)
6	OCP	Yes	Vanco, medroxyprog Ofloxacin	20/100	CF @ 1'	4	No	IV Abx Vanco, oflox	3	20/30
7	Trauma graft fail	No	Prednisolone acet Polymixin-trimeth.	20/50	HM	2	Yes, Staph Epi (broth)	AC Inj Vanco, amik	9	20/50
8	Keratocon graft fail	Yes	Prednisolone acet Ofloxacin	20/30	HM	2	Yes, Staph Epi (broth)	AC Inj Vanco, tobra, dexta	2	20/30
			Prednisolone acet Ofloxacin Vancomycin	20/200	HM	13	Yes, negative	AC Inj Vanco, amikacin, dexta	2	20/60
			Prednisolone acet Ofloxacin Vancomycin	20/60	20/125	16	Yes, negative	AC Inj Vanco, amikacin, dexta	2	20/30

vitritis several months postoperatively in 8 patients. They presented with externally quiet eyes and minor ocular complaints but a sudden decrease in vision caused by flocculent “snowflake” vitritis. This is markedly different from the slower and usually milder uveitis sometimes experienced after other types of eye surgery. Aside from the fact that these eyes had undergone previous eye surgeries in the past, the patients were generally healthy at the time of presentation, with the exception of 1 patient reporting flu-like illness a few days before the vitritis episode. The vitritis was a one-time event with full recovery of vision and without immediate recurrence on tapering of steroids, with the exception of 2 patients who had additional milder episodes at later dates while on prophylactic antibiotic (and in one case, steroid) regimens.

There do not seem to be any device-related factors contributing to this phenomenon, because similar material and techniques were used in all 218 cases. Different designs, such as presence or absence of holes in the back plate, do not seem contributory.

The devices were not tested for endotoxin levels.⁸ Regression analysis would be limited because of the small

number of cases. In addition, because there are very few variables to be included in the analysis, the power to detect any factor as being contributory would be very limited. These would make the conclusions regarding null findings very speculative, at best.

Studies have been noted in the literature, for the development of intraocular lenses, in terms of the choice of the biomaterial as well as the presence of sharp edges and the intraocular response to inflammation. It has been noted that with certain designs (ie, sharp vs. smooth edges), there are different types of reactions in terms of posterior capsular opacification.^{9,10} Memory lens has also been cited in the literature to be associated with postoperative sterile endophthalmitis.¹¹

There is a serious question of whether bacteria may have played a role in these cases. Although *S. epidermidis* was isolated in 3 cases, it only grew from the meat broth, and the primary plates were negative. These culture results would have been considered “equivocal” rather than positive in the Endophthalmitis Vitrectomy Study.¹² They could have been the result of contamination during the tap.

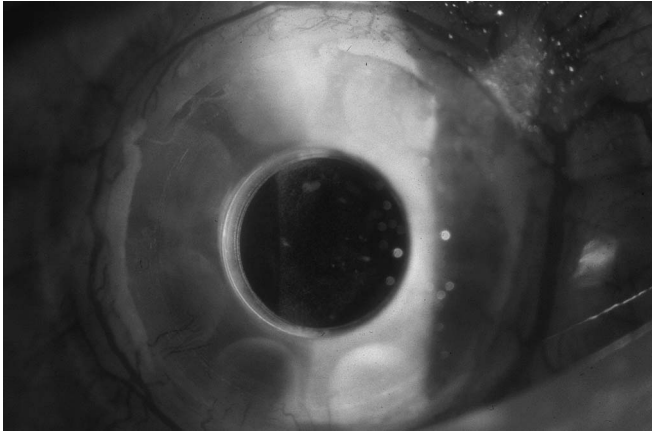


FIGURE 1. Sudden decrease in visual acuity in patient 8 (type I KPro) with “snowflake” appearance of the vitreous seen through a slit lamp on presentation. Even gross vitritis is difficult to photograph. This illustration shows the flocculent appearance and heavy flare. Vision was hand movements (preceding day vision was 20/60).

Because of concern for possible bacterial endophthalmitis, 8 of the 12 episodes were treated with injection of antibiotics (amikacin and vancomycin). These measures would have been helpful if the etiology was indeed infectious. It is unlikely, however, that, in the event of a bacterial infection, complete recovery would have been seen so rapidly. We have previously reported our experience with surveillance cultures and bacterial endophthalmitis in patients with KPro.¹ The clinical presentation in these cases was vastly different, with a very inflamed conjunctiva, discharge, and pain. The bacteria isolated were all due to gram-positive cocci. All these patients had been sustained on topical antibiotics consisting of either a fluoroquinolone or polymyxin B/trimethoprim sulfate (but no vancomycin), which could have left gaps in coverage against these bacteria. All of these endophthalmitis cases resulted in complete loss of vision in all but 3 cases, who had some visual recovery.¹ In contrast, our vitritis cases ran a much more benign clinical course. They presented with exceptional suddenness and massive vitritis, but they recovered completely in 4 to 9 weeks. It would be very uncharacteristic for a true bacterial endophthalmitis to result in such an outcome.

Additional aspects speak against a bacterial etiology in the vitritis cases described here. Thus, 3 episodes occurred while the patient received prophylactic vancomycin drops. Such a regimen has completely prevented the development of severe bacterial endophthalmitis in our KPro cases during the last 4 years, even in susceptible autoimmune diseases. Also, the fact that 4 of the 12 episodes were successfully treated without injection of antibiotics into the eye (only with systemic antibiotics and peribulbar steroids) makes a bacterial cause less likely. The previously reported cases by Rao et al² and Aquavella et al,³ which were successfully treated with steroids only, support a nonbacterial etiology.

If a bacterial cause is unlikely, could this represent some kind of an immune phenomenon in the uvea, perhaps similar in nature to corneal graft rejection? In favor of this possibility is the sudden appearance of inflammation without the ocular

symptoms of pain, redness, or discharge and the rapid clearing without immediate recurrence. This is in contrast to the more gradual and less dramatic uveitis seen late after other types of eye surgery (eg, keratoplasty after herpes simplex keratitis). It is possible that proteins that are not normally recognized by the intraocular structures may be released by the corneal tissue around the KPro (ie, through holes in the back plate), leading to the development of the sudden inflammation with outpouring of plasma elements into the vitreous. An additional factor may be predisposition of some patients from an immunologic stand point. The keratoconus and SJS patients who had 3 such episodes may have some immunologic factor contributing to more severe reactions to such proteins while these patients were maintained on prophylactic antibiotics. There did not seem to be an association with any chronic comorbid condition.

An observation that also may have some connection to our findings has been reported by Ching et al.¹³ They encountered episodes of violent vitritis after implantation of glaucoma tube devices in 4 patients: 2 with Ahmed and 2 with Baerveldt implants. Two cases were treated as bacterial endophthalmitis with injection of antibiotics, and 2 received no treatment. All 4 cases resolved. Glaucoma shunts cannot be fully blamed in our series, however, because 3 of our 8 patients had no shunt.

Thus, we have not been able to identify the cause(s) of our vitritis events with certainty, although an immune mechanism is most probably a contributing factor.

An interesting aspect was the occurrence of 6 episodes while patients were maintained on prophylactic doses of topical prednisolone acetate 1% 2 to 3 times daily. Thus these reactions had broken through the prophylactic regimen. This also raises the question of treatment. Because of the uncertainty of etiology in the individual cases, we still recommend KPro patients who present with sudden vitritis to be treated for possible bacterial endophthalmitis. In these cases, we recommend an immediate anterior chamber or vitreous tap for gram stain and culture, followed by injection of the standard combination of 1.0 mg vancomycin, 0.4 mg amikacin, and 0.4 mg dexamethasone, as well as systemic antibiotics. In externally relatively quiet eyes, without pain, we advise only peribulbar injection of 40 mg triamcinolone followed by topical vancomycin (14 mg/mL), a fluoroquinolone and prednisolone acetate, at least 4 times daily.

Patients should be warned of possible sudden adverse events and should be told to report them immediately at the first notice of change in visual acuity. Patients may be assured that, based on the clinical appearance or culture results, visual acuity will most likely be recovered. However, these vitritis episodes cannot be dismissed as completely harmless and nonthreatening. More must be learned about their prevention.

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