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Fluid misdirection syndrome associated with endothelial keratoplasty: A multicenter case series

Fluid misdirection syndrome (FMS) is a clinical condition characterised by central and peripheral shallowing of the anterior chamber (AC) in the presence of a patent iridotomy (PI) and in absence of suprachoroidal effusion or haemorrhage.[1] Grzybowski et al.[2] postulated that acute or intraoperative FMS (also known as aqueous misdirection syndrome, infusion misdirection syndrome or acute intraoperative rock-hard eye syndrome) and chronic or postoperative FMS (commonly named malignant glaucoma) are two clinical conditions that should be considered as one syndrome.[2]

FMS has been described as a complication of intraocular surgeries, especially trabeculectomy and cataract surgery.[3] Two cases related to endothelial keratoplasty (EK) have been reported previously.[4,5]

We report the first case series of eight eyes with FMS after Descemet membrane endothelial keratoplasty (DMEK) and three eyes with Descemet stripping with automated endothelial keratoplasty (DSAEK). Ethics approval for this study was obtained from the Ethical Committee of the Hospital Clinic of Barcelona (approval number HCB/2021/1197).

Acute FMS was signalled by shallowing of AC resistant to reformation and hardening of the eye. Chronic FMS was defined by progressive shallowing AC and high-intraocular pressure (IOP), over 21 mm Hg, in the presence of a PI. Other causes of angle closure were excluded.

Pathophysiologically, in acute FMS there is an accumulation of fluid in the posterior segment which causes posterior pressure, resulting in anterior displacement of the iris–lens diaphragm, AC flattening and angle closure.[1] In EK procedures, balanced salt solution (BSS) is routinely used to manipulate the graft and/or refill the AC. In our series, acute FMS developed during or before the DSAEK graft insertion, when the AC was being maintained with BSS; or during DMEK graft unfolding, which involved irrigation and manipulation of the AC.

FMS is commonly associated with lax zonular fibres, as zonular dehiscence may facilitate fluid entrapment in the posterior chamber.[1] Two of six patients with acute FMS had pseudoexfoliation, and four of six had highly hyperopic eyes. Furthermore, five of those patients developed bullous keratopathy after complicated phacoemulsification (PBK). Previous surgeries and the PI could have contributed to the creation of an anomalous communication between the AC and the vitreous cavity. Ang et al.[5] hypothesized that the possible mechanism was aqueous seepage from the AC into the anterior vitreous.

Chronic FMS can occur from hours, to months or even years following the initial surgery.[2] In our study, one case of postoperative FMS developed on the afternoon after surgery and four cases on the first postoperative day. It has been proposed that, in predisposed eyes with anteriorly rotated ciliary processes, the misdirected flow of aqueous or BSS may accumulate behind the anterior hyaloid, creating a one-way valve mechanism.[1] The posterior chamber volume then increases enough to push the lens-iris diaphragm anteriorly, closing the angle. Others suggest that choroidal expansion could play a significant role in FMS.[2]

Grzybowski et al.[2] identified similar risk factors in both acute and chronic FMS. There is an anatomical predisposition for FMS associated with small hyperopic eyes with shallow ACs. Interestingly, 81.8% of our patients ($n = 9/11$), despite being pseudophakic, had an average anterior chamber depth of 2.4 $\pm$ 0.7 mm (range 1.6–4.0 mm) (Table 1). The mean axial length (AL) in cases of FMS was 21.4 $\pm$ 0.3 mm.[3] In accordance with the literature, short AL was a common finding in our patients, with an average of 21.7 $\pm$ 0.8 mm (range 20.1–22.3 mm) ($n = 6$). However, for some patients, AL and/or intraocular lens power could not be retrieved and are missing from the dataset. FMS is more common in female patients, as they are thought to have a more anteriorly placed lens and smaller AC volume.[1] In our study, 72.7% of the patients were women.

The goal of management in FMS is to restore the normal aqueous flow into the AC. In acute FMS, we performed a pars plana decompression as recommended by Ang et al.,[5] plus we administered intravenous mannitol. In chronic FMS, a stepwise approach is recommended, beginning with medical therapy including hypotensive agents and topical cycloplegics. If medical treatment fails,

TABLE 1 Pre- and post-operative details of patients who developed fluid misdirection syndrome (FMS) after endothelial keratoplasty ($n = 11$).

Characteristic	Acute FMS 54.5% ($n = 6$)	Chronic FMS 45.5% ($n = 5$)
Sex		
Male	0	40.0% (2/5)
Female	100.0% (6/6)	60.0% (3/5)
Surgical indication		
Bullous keratopathy	66.7% (4/6)	60.0% (3/5)
Fuchs endothelial dystrophy	33.3% (2/6)	40.0% (2/5)
Surgical procedure		
DMEK	66.7% (4/6)	80.0% (4/5)
UT-DSAEK	33.3% (2/6)	20.0% (1/5)
Previous PCB	0.0% (0/6)	20.0% (1/5)
Inferior PLI	100.0% (6/6)	100.0% (5/5)
Pre-existing glaucoma/ocular hypertension	33.3% (2/6)	40.0% (2/5)
IOP preoperative (mmHg)	17.7 ± 2.9 ($n = 6$) (range 12–20)	17.3 ± 2.2 ($n = 5$) (range 14–19)
AL (mm)	21.5 ± 0.9 ($n = 4$) (range 20.1–22.1)	22.2 ± 0.1 ($n = 2$) (range 22.2–22.3)
ACD (mm)	1.9 ± 0.2 ($n = 5$) (range 1.6–2.2)	2.9 ± 0.9 ($n = 4$) (range 2.3–4.0)
IOL diopter power (D)	27.6 ± 1.7 ($n = 4$) (range 25.5–30.0)	27.8 ± 1.0 ($n = 3$) (range 26.5–30.0)
Treatments		
Medical	16.6% (1/6)	40.0% (2/5)
Surgical	66.6% (4/6)	20.0% (1/5)
Medical and surgical	16.6% (1/6)	40.0% (2/5)
Final IOP (mmHg)	17 ± 2.5 ($n = 6$) (range 14–20)	20.2 ± 4.8 ($n = 5$) (range 14–27)
Post-operative anti-glaucoma drugs	33.3% (2/6)	80.0% (4/5)

Abbreviations: AL, axial length; ACD, anterior chamber depth; DMEK, Descemet membrane endothelial keratoplasty; IOP, intraocular pressure; IOL, intraocular lens; PCB, posterior capsule break; PLI, peripheral laser iridotomy; UT-DSAEK, ultrathin Descemet stripping automated endothelial keratoplasty.

laser YAG iridotomy with anterior hyaloidotomy and posterior capsulotomy might stabilise IOP. However, the effect may be short-term, with a high-recurrence rate of 75%.[2] Two cases were treated with laser YAG, but the IOP continued to be high, and surgical treatment was offered. Preferred surgical treatment is a total pars plana vitrectomy combined with zonulectomy, iridectomy and capsulectomy.[1,3] Two of five cases of chronic FMS could be managed with medical therapy and the other three required surgical treatment.

A deepening of the central AC, with an IOP of 21 mmHg or less, was achieved in 9 of the 11 cases (81.8%).

Our observations indicate that FMS in EK may be more frequent in elderly women with preoperative shallow AC and a short AL. In our series, five cases had previously undergone complicated cataract surgery, developing PBK, and we believe that prior complicated surgeries could have contributed to the creation of an abnormal communication between anterior and posterior chamber that caused entrapment of fluid.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Survey of intravitreal injection outcomes amongst ophthalmologists using pre-filled aflibercept syringes

Prefilled syringes (PFS) of aflibercept, an anti-vascular endothelial growth factor (anti-VEGF) agent, have several theoretical advantages, including reduced total preparation and injection time, improved precision in the volume and dose administered and increased ease of use.[1] Retina specialists within our institutions reported an increased incidence of transient vision loss associated with aflibercept PFS injections.[2] Similar observations have been reported in Europe.[3] Thus, we collected intravitreal injection experiences from ophthalmologists to better understand vision and intraocular pressure (IOP) outcomes following aflibercept PFS use.

This study followed the tenets of the Declaration of Helsinki. Institutional review board approval was obtained at Oregon Health & Science University (Protocol #00022596) prior to study initiation. Qualtrics software (Qualtrics, Provo) was used to create a 22-question cross-sectional anonymous online survey to query residency-trained ophthalmologists practicing within the United States. Informed consent was obtained prior to the start of the survey.

There were 118 total survey respondents. Vitreoretinal surgeons were the most common sub-group, consisting of 41.7% of respondents ($N = 48$), followed by comprehensive ophthalmologists ($N = 32$, 27.8%), and medical retina specialists ($N = 29$, 25.2%). Most respondents were attending ophthalmologists ($N = 103$). The survey ended early if participants had never used aflibercept PFS. Seventy-eight participants (66.1%) met the screening criteria, with 68/78 respondents (87.2%) completing all 22 questions. Respondents reported performing a monthly average of 126 intravitreal anti-VEGF injections (95% CI 103–149), including an average of 68 monthly vial or PFS aflibercept injections (95% CI 55–81). Participants estimated that 84% of their aflibercept injections were performed using aflibercept PFS. Of those using aflibercept PFS, the majority reported improved efficiency of use (73/78, 94%), safer delivery (38/78, 49%), and ease of use (40/78, 51%) with the aflibercept PFS compared with the vial preparation.

Though the perception towards PFS was favourable in our study, approximately one-third of PFS users (24/77, 31%) noted a perceived increase in the frequency of IOP spikes with aflibercept PFS compared to other drugs and/or preparations (Figure 1A). Only one respondent noted a perceived decrease in frequency of IOP spikes with PFS. Fifty-one out of 76 respondents (67%) had experienced at least one episode of an acute IOP spike after aflibercept PFS use compared to 36% (27/76) after using the vial preparation (Figure 2; $p < 0.0001$). Of these respondents, 11 ophthalmologists noted having at least six patients experience significant transient vision loss following aflibercept PFS use fivefold more than traditional vial preparation. Although the vision loss after aflibercept PFS often resolved without intervention, 32% of PFS users (25/78) reported performing an anterior chamber paracentesis to normalise IOP and/or to return vision following aflibercept PFS injection.

Many ophthalmologists believed that syringe design played a contributing factor to the IOP spikes observed after aflibercept PFS use. Commonly cited comments