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Case Report

Inherent Challenges in Managing Long Standing Refractory Diabetic Macular Edema

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Abstract

Introduction: Diabetic macular edema (DME) poses a significant management dilemma for visual impairment. We present a challenging case with terrible centre-involved maculopathy, unsuitable for ranibizumab and heading toward steroid implant relatively soon. To date, no similar reports have been published.

Case Presentation: A 54-year-old man presented with poor visual acuity (VA) [right count fingers, left 20/100], bilateral proliferative diabetic retinopathy (PDR) and DME. He was hypertensive, anaemic, had poor renal function and diabetic control. Optical coherence tomography (OCT) and fundus fluorescein angiography (FFA) confirmed mixed maculopathy, worse in right.

Management and Outcome: Diabetic parameters were examined and optimized. In the 20 months following urgent laser treatment, he was followed up every three months with serial VA, stereoscopic biomicroscopy and OCT. Despite further laser therapy, his DME persisted, and VA remained poor. A recent stroke precluded ranibizumab use. A flucinolone implant was considered to save his vision.

Discussion: Flucinolone implant has recently been approved in Scotland for pseudophakic chronic DME cases unresponsive to other options; effects last 3 years, with promising visual recovery. We plan to perform cataract surgery at the time of flucinolone implantation and monitor intraocular pressure (IOP) and other potential side effects post-operatively. In the manuscript, we provide an integrated treatment approach to help physicians treating chronic DME.

Conclusion: Flucinolone has a place as an implantable drug delivery device that offers benefits in chronic DME therapy, adding to a new range of treatment options to suit specific lines and to recover vision in patients previously unresponsive to treatment.

Keywords: *Diabetic Macular Edema; Flucinolone; Visual acuity; Proliferative Diabetic Retinopathy; Optical Coherence Tomography; Fundus Fluorescein Angiography*

Introduction

We present a challenging case of persistent, bilateral maculopathy. The patient's diabetic parameters were poor, and laser photocoagulation had failed. A recent stroke precluded ranibizumab use. A flucinolone implant was considered to save his vision. No similar reports have to date been published.

Case Presentation

A 54-year-old schizophrenic man presented with bilateral PDR and DME. He noticed gradual, painless blurring of vision for several months, with recent profound loss of vision in his right eye. Three years earlier, he had been diagnosed with type 2 diabetes mellitus. Following a period of erratic control, aggravated by poor compliance, he recently tightened his control. His medications included gliclazide, lisinopril, and sulpiride.

His Snellen VA was right count fingers and left 20/100. Slit lamp examination revealed mild cataracts and aggressive PDR and DME (Figure 1). Other causes of poor vision were excluded.

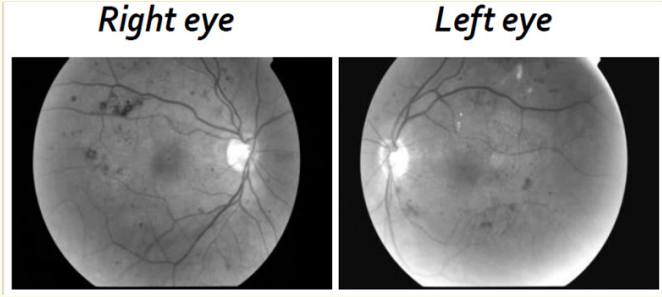

Figure 1: *Red free photos showing evidence of PDR and DME in both eyes.*

Management and Outcome

OCT confirmed right diffuse DME and left focal edema (Figure 2). FFA identified mixed maculopathy (Figure 3). The patient had elevated blood pressure (185/87) with HbA1c 70 mmol/mol, and an acute decline in renal function with significant albuminuria and normochromic normocytic anaemia.

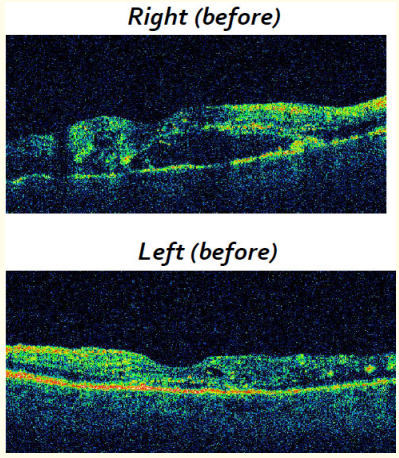

Figure 2: *Spectral-domain OCT showing diffuse edema in the right eye and focal edema in the left eye.*

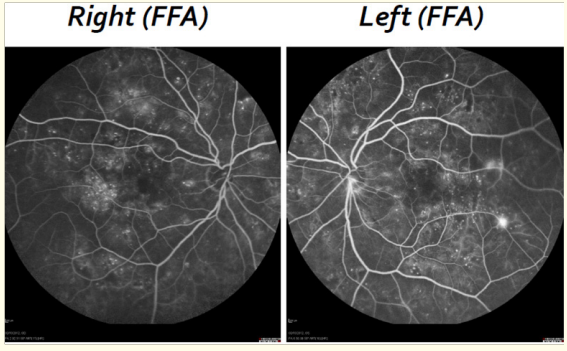

Figure 3: *FFA with mixed exudative-ischemic maculopathy and foveal avascular zone enlargement.*

He had urgent bilateral PRP and concurrent macular laser with Pascal system. Over the next 20 months, he received 4 PRP and 4 macular lasers (3 grid, 1 focal) to his right and left eyes (2 grid, 2 focal).

Serial VA, fundoscopy, and OCT were monitored at three-month intervals. Nearly 2 years after his presentation, his right VA remained poor (count fingers) but his left VA improved to 20/80. OCT confirmed the persisting DME (Figure 4).

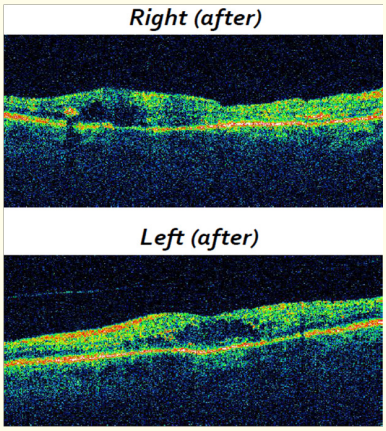

Figure 4: *Spectral-domain OCT confirming persisting DME, which is more marked in the right eye.*

A recent stroke precluded anti-VEGF use. Scotland recently approved flucinolone implants, and we await local use. Continued holistic, multidisciplinary care with diabetologists should optimize his prognosis.

Discussion

Detecting DME requires careful examination with high magnification, stereoscopic biomicroscopy (e.g., 78D lens) [1]. VA is best measured with the ETDRS chart, but the Snellen is widely used [2]. OCT provides information on retinal swelling, central retinal thickness, morphology (e.g., cystoid) and vitreo-macular traction [3]. FFA identifies leakage, extent, and macular ischemia [3].

Figure 5 shows our recommended treatment approach: we suggest two - to four-month reviews to assess VA, fundoscopy, and OCT +/- FFA. Patients with severe DR warrant earlier intervention. FFA should be repeated if ischemia is suspected of limiting the treatment response. Patients with poor response show mixed maculopathy, extensive macular ischemia, severe retinopathy, diffuse disease, uncontrolled hypertension, renal disease, and increased Hba1c levels [1].

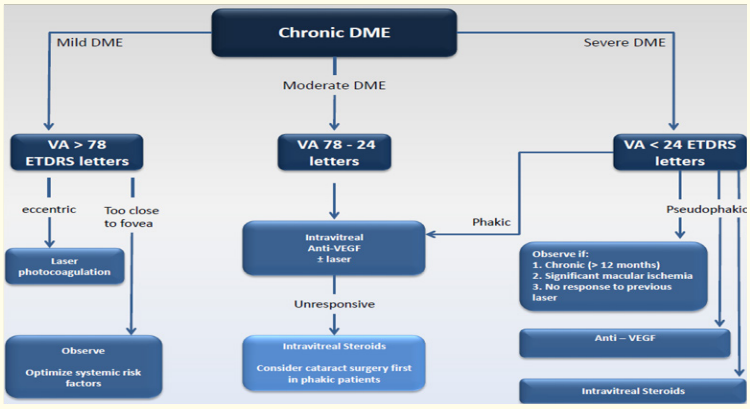

Figure 5: *An integrated treatment algorithm based on current evidence (2014) and consensus of opinion that may help a physician's treating DME. Includes criteria generated of those insufficiently responsive to current therapies.*

Lasers remain the mainstay of therapy, but do not routinely restore lost vision. Some eyes appear refractory to treatment [4]. Potential complications include transient increased edema, scars and foveal non-perfusion after repeated treatments.

Microalbuminuria and anaemia are risk factors for DR severity and progression, increasing cardiovascular and stroke risks [5]. Aim for Hba1c < 6.5%, and BP 130/80 with co-existing nephropathy [6]. Fenofibrates should be considered [7].

Ranibizumab improves and restores vision and slows DR progression [8,9]. Multiple injections are required, and there is a small risk of stroke [10,11]. According to drug manufacturers' information, ranibizumab use is contraindicated following stroke.

Intravitreal triamcinolone is associated with significant adverse events, including elevated IOP and cataracts [12]. Long-term effects, even at 2 years, show no significant benefit [13].

Fluocinolone acetonide (Illuvien®) has recently been licensed in Scotland for pseudophakic chronic DME cases unresponsive to other options. This non-biodegradable intravitreal inset is designed to release lower sustained doses (0.59 µg/day) of flucinolone for up to 36 months.[14] In the FAME study, 40% gained ≥ 3 VA lines [14].

We plan to perform cataract surgery during his flucinolone implantation. Concurrent bilateral implantation is not recommended, although an additional implant might be administered after 12 months of worsening DME. Ophthalmologists should practice on a model eye to get a feel for the preloaded applicator. Sterile techniques should be used to place the implant inferior to the optic disc and posterior to the equator. Successful placement after insertion should be verified with indirect ophthalmoscopy. Optic nerve perfusion and IOP must be immediately checked and repeated, 2 to 7 days' post-implant. IOP, lens clarity, and complications (e.g., endophthalmitis, retinal detachment) should be monitored at least every 3 months [15]. To assess potential for steroid response, we will perform a pre-operative trial with topical dexamethasone qds for one month. Patients who sustain IOP elevation might require glaucoma drops or surgery.

Conclusions

We presented a challenging case with terrible maculopathy in both eyes that was unsuitable for ranibizumab and heading toward steroid implant relatively soon. Flucinolone's place in chronic DME therapy, adds to a new range of treatment options for recovering vision in previously hard-to-treat patients.

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