Clinically Significant Macular Edema:
Argon Laser Photocoagulation Treatment in Diabetes Mellitus

ICD-9 362.07

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Abstract:
The case is a 52 year old Type 1 diabetic female that presented with blur covering the right half of her visual field in the left eye. She was treated with focal argon laser photocoagulation.

Case Report: A 52-year-old Caucasian female presented with blur of the nasal half of her left eye’s visual field that she noted on waking one week prior. She had undergone focal argon laser photocoagulation in the left eye in 2000 for clinically significant macular edema; otherwise, her ocular history was unremarkable. She had type 1 diabetes mellitus for 34 years, fibromyalgia, thyroid disease, and dermatitis herpetiformus. She was an insulin dependent type 1 diabetic, and was taking levothyroxine, diamino-diphenyl sulfone (Dapsone,) folic acid/B-12/B-6 complex (Folbic,) calcium supplements, multivitamins, and bio-identical hormone replacement therapy. The surgical history had multiple radial tunnel and shoulder repairs, and a hysterectomy. Her brother had a one-time laser treatment for macular edema;
otherwise, the family ocular history was noncontributory. Her family medical history had a brother with type 1 diabetes and other family members with multiple carcinomas and cardiovascular disease. She claimed good control of her blood glucose with a hemoglobin A1c of 5.9% from a month earlier. There were no known drug or environmental allergies. She was a pharmacy technician with only social alcohol use.

The best-corrected visual acuity was 20/25 in the right eye, and 20/50 with no improvement with pinhole in the left eye. The acuities from an exam a year prior were 20/20 in both eyes. The anterior segment examination and intraocular pressures were unremarkable. A dilated fundus exam revealed moderate non-proliferative diabetic retinopathy (NPDR) of both eyes. A focal area of retinal thickening was found temporally in the left eye. A Cirrus OCT was obtained and showed the right eye to be normal with central thickness of 284\( \mu \text{m} \), and the left eye to have a significant amount of edema with thickness of 325\( \mu \text{m} \) centrally, and 423\( \mu \text{m} \) in the temporal quadrant. CSME was diagnosed and she was referred to a retinal specialist and seen the next day. Fundus photos and a fluorescein angiography (IVFA) were obtained, confirming the focal area of macular edema of the left eye. A focal ALP of the left eye was performed a week later and she was released back to her optometrist for follow up.

At the four month follow up exam, her visual acuity improved from 20/50 in the left eye to 20/30-. Cirrus OCT revealed that the edema was still present with 310\( \mu \text{m} \) centrally, and 453\( \mu \text{m} \) in the temporal quadrant. She returned to the retinal specialist two weeks later and a second IVFA confirmed the macular edema. That day she was treated again with focal ALP and released back to her optometrist. When she returned
six months later, the visual acuity had improved to 20/25- best corrected in her left eye. The anterior segment and intraocular pressures remained unchanged. A fundus examination found mild NPDR without CSME in the right eye and moderate NPDR without CSME in the left eye. She stated that her vision was good and she was satisfied with the outcome. Differential diagnoses in her case are cystoid macular edema, central serous chorioretinopathy, epiretinal membrane, macular degeneration and hypertensive retinopathy.

**Discussion:** Diabetes affects 23.6 million people in the United States and is the leading cause of blindness in adults age 20-74, with 12,000 to 24,000 new cases every year. Treatment of diabetic eye disease with a laser reduces severe vision loss by 50-60%. Clinically significant macular edema (CSME) occurs in 38% of those with moderate to severe NPDR, to 71% of those with proliferative diabetic retinopathy (PDR). Risk increases with many factors, so control of the patient’s diabetes, blood pressure, and overall systemic health is important. Sex and obesity are not significant risk factors, although, some studies found a slightly higher risk in males. Significant risk factors are age, duration of diabetes, type 2 diabetes treated with insulin, increased HbA1c, tobacco use, high systolic and diastolic pressure, kidney pathology (microalbuminuria or proteinuria,) and dyslipidemia. For each 1% elevation of the HgbA1c level, the risk of CSME doubles.

Patients with CSME can be asymptomatic with no changes in visual acuity or can present with blurred vision and metamorphopsia once the fovea itself is involved. The
Early Treatment of Diabetic Retinopathy Study (ETDRS) definition of CSME is retinal thickening or exudates with thickening within 500\(\text{m}\) of the fovea, or there is a zone of edema larger than one disc diameter within one disc diameter of the fovea seen biomicroscopically or with stereo photography.\(^4\) Increasingly, OCT is utilized to monitor pre and post laser surgical outcomes. OCT allows for rapid detection, and provides a quantified measure of thickness. It was found that post surgically, for every 100\(\text{m}\) decrease in thickness, there was an improvement of acuity by approximately 4.4 letters.\(^5\)

The pathogenesis of CSME is not fully understood. The loss of pericytes and endothelial cells of the vascular wall that help regulate transport and vascular permeability are the main factors in leakage.\(^6,7\) Fluids, proteins and lipids leak into the retina and are visible as thickening and as exudates. Increased protein kinase C (PKC) activity and glycosylation of proteins form advanced glycation end products (AGE). It is proposed that AGE mediates most of the changes involved in the vasculature in diabetes. These cause inflammatory changes, and vasoconstriction.\(^6\) This inflammation causes leukostasis of macrophages. Stasis of leukocytes induce endothelial cell death, causing vascular obstruction and leakage and the formation of acellular capillaries.\(^7\) Vascular endothelial growth factor (VEGF) levels also rise as PKC activation increases and is 50,000 times more potent than histamine in causing vascular permeability. As endothelial integrity is disrupted, the amount of ischemia increases and the levels of VEGF increase.\(^7\) The inflammatory response is the target of intravitreal steroids and VEGF inhibitors target the increased VEGF levels that lead to neovascularization.\(^6\)
Diabetic macular edema can present as focal or diffuse areas of thickening. Focal ALP treats only the thickened areas and the individual microaneurysms in focal CSME. For diffuse CSME, a grid pattern is used with 1 burn width intervals. Laser photocoagulation uses blue green light (488nm) to green-yellow (532nm), which targets melanin and hemoglobin. Therapeutic effects come from the absorption of the laser energy by the retinal pigment epithelium and the photocoagulation of leaking microaneurysms. Laser power can vary but there needs to be enough power to cause a light color change of the tissue. Properly treated microaneurysms will turn white or dark red. A small spot size of 50-200μm is generally used for focal ALP. The type of contact laser lens used needs to be taken into account as depending on the type of lens as to how much magnification of the spot size there is. Also, post treatment, the spot size will expand by 7-12% per year. Treating in the foveal avascular zone and using confluent burns are generally avoided, as there is a risk of central scotomata. Side effects of treatment can be pain during treatment, moderate vision loss, and visual field losses. Long term effects include glare, retinal detachment, ciliochoroidal effusion, IOP increases, and epiretinal membrane formation. In cases where pan-retinal photocoagulation (PRP) is necessary in addition to treatment for CSME, the CSME is treated first as PRP can exacerbate the edema.

Patients should be evaluated every 3 months to determine if further treatment is needed. Up to 63% of treated patients will not need further treatment and continue to improve. When HbA1c, demographics, diabetes types, duration, OCT measurements, prior laser treatments, and other factors were taken into account, the only correlation in
improvement in visual acuity were those with poor starting acuity of 20/32 or worse.\textsuperscript{10} Fifteen percent of patients will have acuity improvement, 61\% will stabilize, and 24\% will worsen.\textsuperscript{11}

Intravitreal steroid injections or inserts have been used off label to target inflammation and to down regulate VEGF expression. It was found that although initial results were promising, after three years, no long term benefit was gained over laser treatments. In addition, depending on the steroid and delivery system, 83-95\% of patients had to have cataract surgery and up to 35\% had uncontrolled IOP.\textsuperscript{12}

The VEGF inhibitors ranibizumab (Lucentis), bevacizumab (Avastin), and pegaptanib (Macugen), are showing promise with significantly better visual outcome than laser, but long term data is lacking. Study groups are small and the uses of these drugs are off label. Both steroids and VEGF inhibitors show promise in diffuse CSME that is refractory to laser treatment or where it is contraindicated.\textsuperscript{11,13}

**Conclusion:** Treating CSME with laser photocoagulation remains the gold standard and can reduce vision loss by up to 95\%.\textsuperscript{8} Medical treatments show promise but are not FDA approved and long term results are not available. We should remain aware of what is on the horizon, but for now, timely treatment of CSME by ALP serves our patients best.
Clinical Pearls:

• Educate your patients!
  
  - Some don’t realize that just because it is part of the disease, doesn’t mean we can’t do something about it. She had gone a week without seeing a doctor and wasn’t going to until her son, an O.D. insisted that she be seen immediately. She thought that it was just routine symptom in diabetes.

• Have a good relationship with your retinal specialist.
  
  - Her specialist did the treatment and fluorescein angiography and her O.D. did all the follow ups.

• Stay on top of treatment studies.
  
  - This field changes greatly and quickly.
References:


### CODES AND FEES

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