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Role of Corticosteroid Treatment for Diabetic Macular Oedema in Pregnancy

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Abstract: Diabetic macular oedema (DME) is the leading cause of reversible blindness in diabetes mellitus. Intravitreal steroids have been proven to be effective for treatment of DME. Diabetic patients who become pregnant carry higher risks of development and further progression of diabetic retinopathy and DME. We report a case of a pregnant diabetic who was treated with intravitreal dexamethasone bilaterally and responded satisfactorily with resolution of the DME and recovery of vision.
Keywords: Diabetic retinopathy, diabetic macular oedema, pregnancy, intravitreal, corticosteroid.

INTRODUCTION

Diabetic retinopathy (DR) is a leading cause of blindness among the working-class population. Pregnancy is a major risk factor for the development and further progression of DR[1]. Although pregnancy does not have any long-standing effects on DR, progression occurs in 50-70% of pregnant diabetics. Factors associated with progression include severity of retinopathy at conception, poor hyperglycaemic and hypertension control, and anaemia. Good control of diabetes and hypertension is essential to prevent progression and vision loss.

Treatment options for diabetic retinopathy during pregnancy are limited. DME and DR both usually regress after delivery but may persist in some patients, causing significant visual impairment [1, 2]. We report a case of intravitreal 0.7mg dexamethasone implantation (Ozurdex®; Allergan) in bilateral eyes resulting in substantial resolution of DME during pregnancy.

CASE REPORT

A 31-year-old pregnant lady presented in her 1st trimester (13 weeks of gestation) for diabetic retinopathy staging. She was an inpatient at the time for uncontrolled diabetes mellitus (DM) in pregnancy. She was a known case of type 2 DM for 7 years with a BMI of 37.33 and an initial HbA1c of 11.9%. She had a history of 2 miscarriages. There was no history of oral contraceptive use and she had not undergone eye screening before. This patient was monitored regularly with slit-lamp examination, Goldmann tonometry, fundus photography and SD Optical Coherence Tomography (OCT).

On initial presentation, she was asymptomatic with good visual acuity (VA) of 6/9 in her right eye (RE) and 6/6 in the left eye (LE). Both eyes' anterior segments were unremarkable and fundus examination revealed moderate non-proliferative diabetic retinopathy (NPDR) with clinically significant macula oedema in both eyes. Baseline intraocular pressures were 12mmHg (RE) and 14 mmHg (LE). SD-OCT revealed centre-involving macula oedema in both eyes (Figure 1). Her ophthalmic findings were reported to the feto-maternal unit, and the decision was to optimise her blood pressure and sugar control.

A week later, she complained of reduced vision bilaterally (VA 6/60 in both eyes). Fundus examination revealed worsening of DR with increasing macula oedema. Treatment options were discussed with the patient, which included a trial of orbital floor triamcinolone (OFTA), or Dexamethasone implant. However, she elected for observation. Her insulin dosage had been adjusted by feto-maternal unit following which her HbA1c improved to 10.2%.

At her subsequent follow-up at 16 weeks of gestation, her right eye vision remained at 6/60, while the left eye improved to 6/18 although with new complains of bilateral metamorphosis. There was worsening of DME in both eyes (Figure 2). Due to limited resources, the patient agreed to have RE OFTA

injection while waiting for financial approval for a Dexamethasone implant. Following the OFTA injection, her RE VA improved to 6/18 with minimal reduction of intrarenal fluid. However, fundus examination revealed progression of diabetic retinopathy to severe NPDR, thus scatter laser photocoagulation had to be performed.

This patient finally agreed to have a RE Dexamethasone implant at her 19th week of gestation. One-month post procedure, her RE VA improved to 6/9 with resolution of macula oedema (Figure 3A). Subsequently, her LE DME also deteriorated and OCT showed increasing intrarenal fluid (CRT of 676 µm). We proceeded with LE Dexamethasone implant at her 25th week of gestation. After a month, VA in both eyes improved to 6/6 with preservation of foveal contours (Figure 3B) although she developed moderate raised intraocular pressure of (RE) 27mmHg and (LE) 23mmHg which required anti-glaucoma medication. Both fundi showed progression to proliferative diabetic retinopathy and complete pan-retinal photocoagulation was performed (Figure 4). She had optimum IOP control on a single ant glaucoma medication (latanaprost 0.005%) throughout her pregnancy so the medication was withheld 6 weeks post-partum.

She delivered a healthy baby girl, birthweight of 3000g without complications. Ocular examination till 10 weeks post-partum (6 months post-dexamethasone implant) revealed both eyes had VA of 6/9, with quiescent PDR and no recurrence of DME.

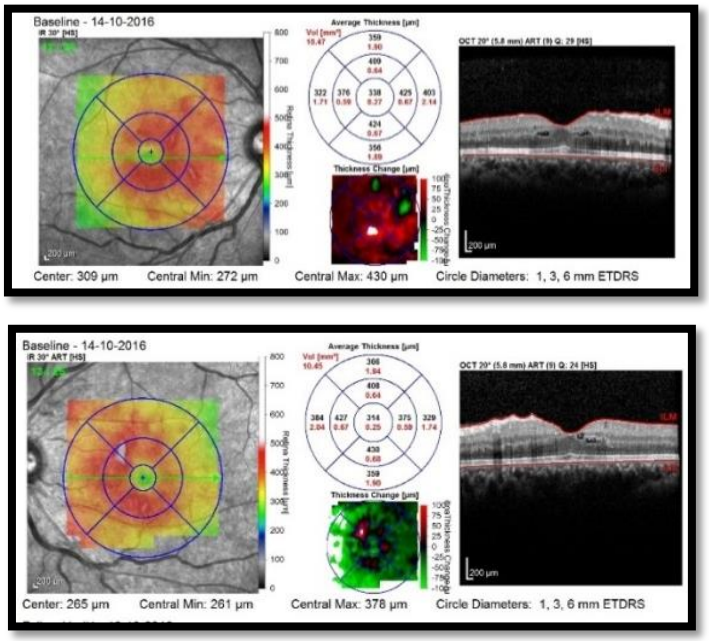

Fig-1: SD-OCT images at initial visit A: The right eye at initial visit. Central retinal thickness (CRT) of 338 µm with minimal cystoid changes; B: The left eye at initial visit. CRT of 314 µm with minimal cystoid changes. BCVA was 6/9(RE) and 6/6(LE) at initial visit

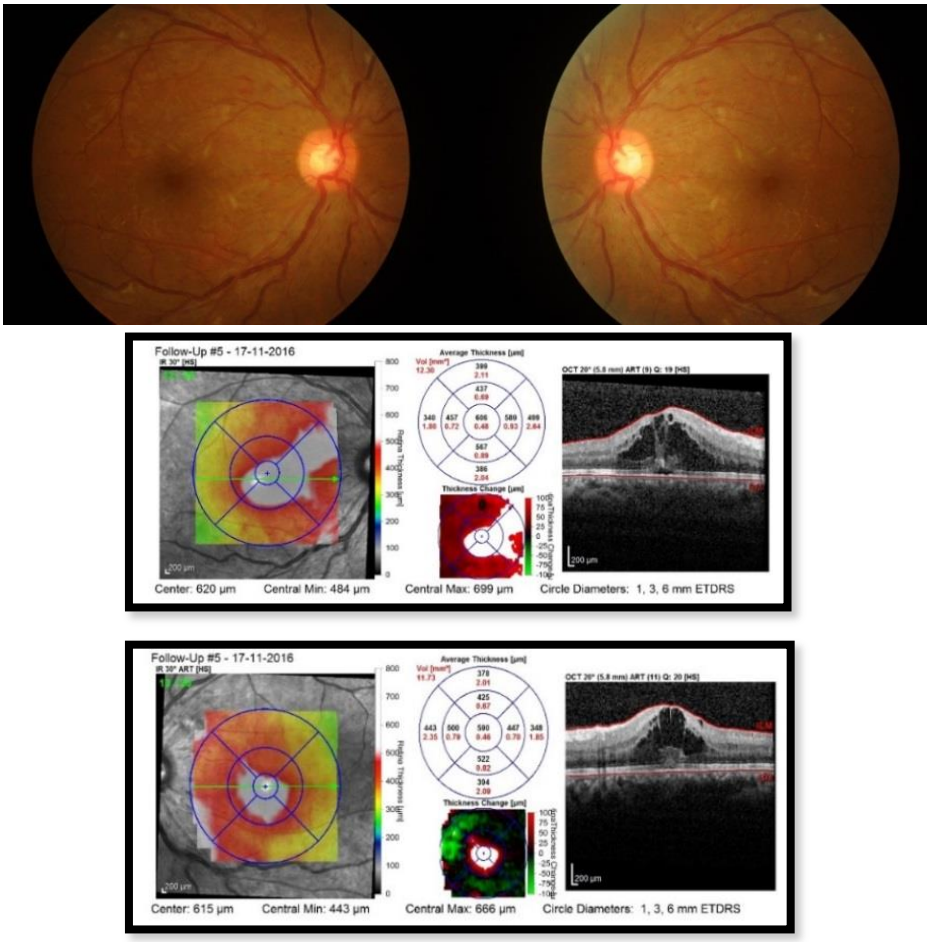

Fig-2: Follow-up fundus photograph A & B: Both eyes showed progression to severe NPDR with DME at 16 week POG. Serial SD-OCT images. C: Right eye increasing of CRT of 606 µm with intraretinal fluid. D: Left eye increasing of CRT of 590 µm with intraretinal fluid. BCVA was 6/60(RE) and 6/60(LE) with worsening of DME respectively

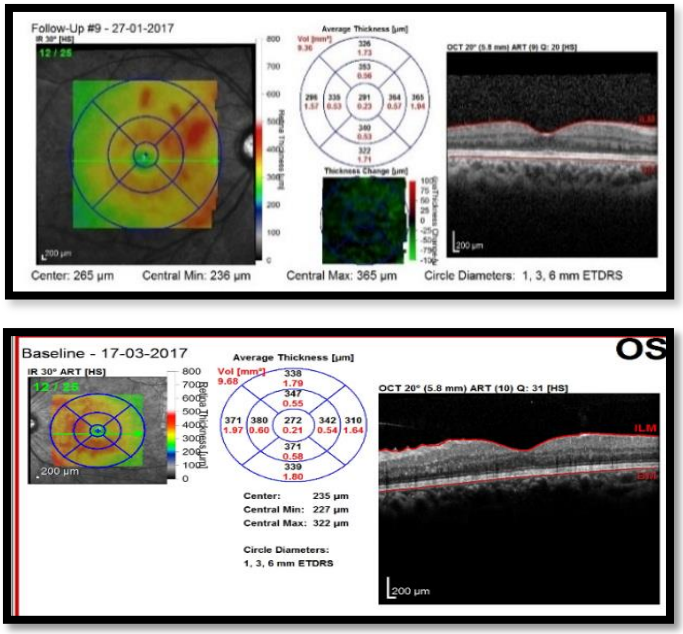

Fig-3: SD-OCT images A: Right eye showed complete resolution of DME with CRT 291 µm at 1 month post RE Intravitreal Ozurdex; B: Left eye showed complete resolution of DME with CRT 291 µm at 1 month post LE Intravitreal Ozurdex

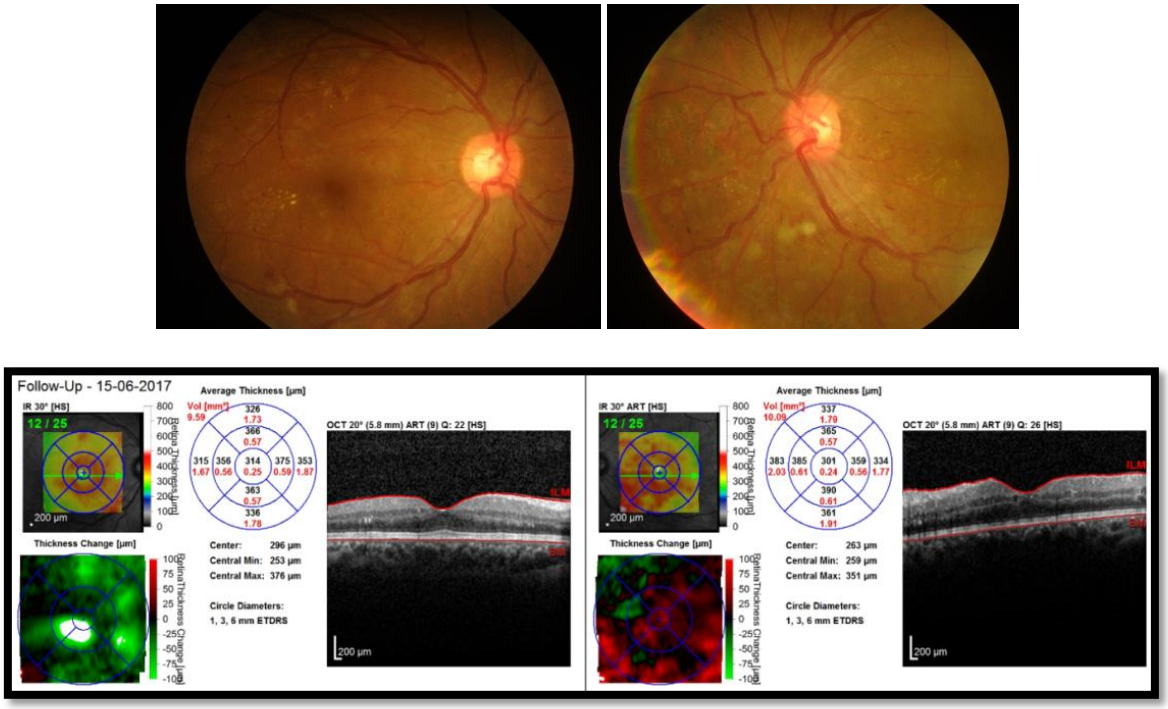

Fig-4: Follow-up fundus photograph 6 weeks post-partum. A & B: Both eyes treated PDR with laser photocoagulation scars and resolved DME. Serial SD-OCT images 6 weeks post-partum. C: Right eye slight increase of CRT to 314 µm with preserved foveal contour. D: Left eye slight increase of CRT to 301 µm with minimal intraretinal fluid and preserved fovea contour. Final VA were 6/6(RE) and 6/6(LE)

DISCUSSION

Studies have shown that concentrations of VEGF in pregnant ladies are increased during the 1st and 2nd trimester; maternal hyperglycaemia will induce foetal hyperglycaemia, which results in metabolic and hormonal changes in the foetus therefore increasing the foetal oxygen demands [3]. As a response, VEGF/VEGFR-2 is important in promoting vasculogenesis and angiogenesis to prevent foetal hypoxia. Anti-VEGF was discussed but not considered in this patient as intravitreal injections such as bevacizumab to women in early pregnancy has been reported to cause miscarriages, although the exact causal relationship could not be demonstrated [4].

As for diabetic retinopathy assessment, pregnant ladies with pre-existing DM require frequent follow up as DR can progress faster. Thus, it is important treat severe NPDR in pregnancy early[5]. However, in this patient, her condition progressed to PDR despite having scattered laser photocoagulation performed. Co-management with the feto-maternal team comprising of endocrinologists and obstetricians is essential in optimisation of treatment.

The dexamethasone (DEX) implant was used in this patient because systemic exposure of steroids is minimal, and glucocorticoid medication is accepted in pregnancy for a broad range of imperative clinical indications. Moreover, glucocorticoids have been safely used in premature labour to improve lung maturation[6]. DEX implants into the eye are known to be effective for up to 4-6 months with a single injection, with minimal concentration entering systemically thus minimising systemic side effects [7]. In the BEVORDEX study, DEX showed similar efficacy to Bevacizumab and brought significant improvement of visual impairment for the treatment of DME [8]. Furthermore, intravitreal dexamethasone implants have also been FDA approved for treatment of DME.

Ozurdex can be used to treat patients who have symptomatic visual loss and foveal retinal thickening of a magnitude that would make patients eligible for intravitreal therapy in routine clinical practice. Concillado *et al.* demonstrated prompt and uniform reduction in DME following intravitreal dexamethasone implant in 5 patients during pregnancy [9]. Intravitreal triamcinolone acetonide was not considered in this case because the efficacy of Ozurdex is arguably superior [10].

In summary, this patient with DME in both eyes presented asymptomatically at her 13th week of pregnancy. Subsequent follow-up showed no spontaneous resolution but instead worsening of DME and vision. We noted a sudden decrease in VA of 6/60 bilaterally with gradual worsening of her DR status and increase in DME on SD-OCT. Intravitreal corticosteroid was chosen in this case after considering the safety and efficacy as compared to anti-VEGF. This method of treatment significantly improved the patient's vision

and resolved her DME. She required only a single injection for each eye and the effect lasted for 6 months. Raised IOP was transient and could be managed with topical medication in this patient.

CONCLUSION

Intravitreal dexamethasone implants can be beneficial in treating diabetic macular oedema in pregnancy as shown in this case.

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