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Short Communication

Role of Anti-Vascular Endothelial Growth Factor Agents in the Treatment of Coats Disease

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Abbreviations

PPV: Pars Plana Vitrectomy; RD: Retinal Detachment; SB: Scleral Buckle; VEGF: Vascular Endothelial Growth Factor.

Coats disease is a sporadic, acquired ocular condition characterized by abnormal retinal telengiectasia, sub/intra-retinal exudation and retinal detachment (RD). It is most commonly seen among young male children [1]. It is mostly unilateral but can be bilateral among adults with a systemic condition called facioscapulohumeral dystrophy. It usually presents in the first decade of life. The presenting symptoms can be diminution of vision, strabismus, lekocoria and ocular pain. Most common clinical findings are abnormal retinal telegiectasia, retinal aneurysms, subretinal and or intraretinal exudates, retinal detachment. Based on the clinical and angiographic findings, Coats disease is classified into five stages (Table 1). In stage 1, there is only peripheral retinal telengiectasia, stage 2 has stage 1 plus retinal exudates (extrafoveal [2A] or foveal [2B]), stage 3 has exudative retinal detachment (subtotal [3A] or total [3B]), stage 4 has total RD with secondary glaucoma and stage 5 is an advanced end stage disease [2].

Stage	Clinical findings	Treatment
Stage 1	Retinal telengiectasia	Observation
Stage 2	Telengiectasia + exudation	Observation+ laser photocoagulation, cryotherapy
2A	Extrafoveal exudation	Anti-VEGF agents, cryotherapy, laser photocoagulation
2B	Foveal exudation	Anti-VEGF agents, laser photocoagulation
Stage 3	Exudative RD	Anti-VEGF agents, laser photocoagulation, cryotherapy, transcleral drainage of exudates
3A	Subtotal RD	Anti-VEGF agents, laser photocoagulation, cryotherapy, transcleral drainage
3A1	Extrafoveal RD	Anti-VEGF agents, laser photocoagulation, cryotherapy, transcleral drainage
3A2	Foveal RD	Anti-VEGF agents, laser photocoagulation, transcleral drainage
3B	Total RD	Pars plana vitrectomy (PPV), sclera buckling (SB), external drainage
Stage 4	Total RD with glaucoma	PPV, SB, anti-VEGF agents, enucleation
Stage 5	Advanced end stage disease	Observation, enucleation

Table 1: Classification and treatment options depending on the stage.

PPV: Pars Plana Vitrectomy; RD: Retinal Detachment; SB: Scleral buckle; VEGF: Vascular Endothelial Growth Factor.

Over decades, various methods have evolved in the treatment of Coats disease. The goal of the treatment is to obliterate the abnormal retinal telengiectasia and aneurysmal vessels, prevent chronic subretinal exudation and/or RD, preserve the central macular function and the visual acuity, and prevent the secondary glaucoma and progress to the advanced stages. Depending on the stage of disease and patients age either single therapy or multiple treatment modalities can be advocated. The standard treatment methods prior to invention of anti-VEGF agents were observation, cryotherapy, laser photocoagulation, diathermy, intravitreal triamcinolone, sclera buckle surgery, subretinal fluid drainage, pars plan vitrectomy (PPV for RD), and enucleation (Table 1) [2-5]. In the last two decades, anti-vascular endothelial growth factors (VEGF) medicines are being given intravitreally in the management of Coats disease that act by blocking the retinal telegiectasia, aneurismal retinal vessels and control the exudation [6-12]. However, combined treatment methods including transcleral drainage of the subretinal exudation along with adjuvant anti-VEGF therapy and laser photocoagulation are being performed by many surgeons.

Vascular endothelial growth factors are naturally occurring intraocular cytokines that cause increased vascular permeability and abnormal retinal neovascularisation. Their role in the pathogenesis of diabetic retinopathy, neovascular macular degeneration, and retinal vein occlusions has been extensively studied and reported in the literature. Anti-VEGF agents [Bevacizumab (Avastin, Genetech Inc., San Francisco, CA, USA), Ranibizumab (Lucentis; Novartis Pharma AG, Basel, Switzerland, and Genentech Inc., South San Francisco, CA, USA), Pegaptanib (Macugen; Pfizer Inc.), Aflibercept (Eylea, Bayer, Leverkusen, Germany)] are being used very frequently for the above conditions. They are considered as the best adjuvant therapy in the treatment of Coats disease, depending on the stage of the disease. They not only obliterate the abnormal retinal telengiectasia and aneurysms but also reduce the subretinal/intraretinal exudation [7-14]. Zhao Q and co-authors did an interventional case control study and measured the levels of VEGF among patients with Coats disease with the congenital cataract patients. They reported that the aqueous levels of VEGF were higher among Coats disease patients than the controls. They also concluded that the levels of VEGF were more at the later stages of Coats disease (stage 3A, 3B and 4) and among those with extensive exudative RD than the earlier stages (stage 2) of disease [13]. He., *et al*. measured VEGF levels in the subretinal fluid, aqueous and vitreous of patients with Coats disease and compared them with those of rhegmatogenous retinal detachment (control group). They reported that after giving intravitreal bevacizumab, there was decrease in the macular edema and improvement in visual acuity in patients with Coats disease than the control patients and concluded that the intravitreal bevacizumab is a valuable adjuvant therapy for Coats disease [12].

Zhang L., *et al*. conducted a retrospective study on stage 3 or above patients with Coats disease using intravitreal ranibizumab and conbercept in addition to the laser photocoagulation and concluded that these agents have reduced the macular edema, subretinal exudates equivalently. They also reported improvement of the symptoms, stabilization of the visual acuity and decrease in the peripheral retinal telengiectasia. There were no adverse effects to either of the medicines in their study patients [7].

Shieh WS., *et al.* used intravitreal aflibercept in Coats disease patient with persistent macular edema despite of prior intravitreal bevacizumab injections and additional laser photocoagulation. After repeated aflibercpt injections, the macular edema has resolved with improvement in visual acuity and no recurrence of retinal exudation [8].

There are very few local side-effects or complications reported after using intravitreal anti-VEGF agents. These include mostly vitreoretinal fibrosis and tractional RD [15]. None of the studies reported any systemic complications.

Conclusion

Studies have reported the elevated levels of VEGF levels in the ocular fluids of Coats disease patients with higher concentrations at later stages than the early stages. The aim of treatment in early stages is obliteration of abnormal retinal vasculature by stopping retinal exudates to preserve vision and in advanced stages is to globe salvage. Anti-VEGF medicines have proven to be safe adjunctive agents in the treatment of Coats disease. Frequent intravitreal injections in combination with other therapeutic modalities improve the anatomic and functional outcomes. They prevent subretinal exudation and stabilize the visual acuity. But one should also remember that they can cause vitreoretinal fibrosis and tractional RD. Frequent follow-ups are necessary to monitor Coats disease patients to prevent the complications due to disease and or treatment.

Conflict of Interest

The author has no conflicts of interest in the medication or devices used in this paper.

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