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**Preservation of Macular Structure and Function after Intravitreal Aflibercept for Choroidal Neovascularization
Associated with Serpiginous Choroiditis**

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CASE SERIES

We describe 3 patients (3 eyes) whom received treatment with intravitreal injection with aflibercept for choroidal neovascularization secondary to Serpiginous Choroiditis (SC). To the best of our knowledge, aflibercept has not been described previously for this indication in the medical literature. All patients developed classic types of choroidal neovascularization in one of their eyes and received 2-7 intravitreal injections of aflibercept (EYLEA, Regeneron, Tarrytown, NY, USA) (Table 1). Follow-up time after the first intravitreal injection ranged between 8-14 months. Horizontal macular spectral domain optical coherence tomography showed regression of choroidal neovascularization in all patients (Figure 1). Multifocal electroretinography showed severely reduced function in the macular area affected by the SC, and preserved function in the uninvolved macula, thus documenting sparing of regional macular function after treatment with aflibercept (Figure 2). Full-field electroretinography demonstrated rod and cone responses within normal limits before and after treatment (Table 1). Autofluorescence imaging demonstrated progressive reduction of inflammatory activity, seen as diminishing hyperautofluorescence, at the leading edges of the lesion, for each intravitreal injection of aflibercept (Fig. 1).

COMMENT

SC is known to be progressive and carries a guarded prognosis with respect to visual outcome. There is no solid documentation of efficacy of any of the immunosuppressive strategies used in the treatment for this condition. Due to the low frequency of SC, randomized trials are unlikely to provide answers regarding optimal immunosuppression in SC.

Herein we present 3 cases with SC in whom secondary neovascularization developed and treatment was instituted with general immunosuppression and intravitreal injections of aflibercept. Previous studies have described intravitreal ranibizumab and bevacizumab for this condition, however to the best of our knowledge, intravitreal aflibercept use has not been described previously for SC and its complications (Parodi et al. 2014, Balaskas et al. 2012, Song & Roh 2009). Among previous studies, the best documented series, using bevacizumab in 7 eyes, demonstrated improved function of at least 5 and 10 ETDRS letters in two eyes, and one eye, respectively, at the 12-month follow-up (Parodi et al. 2014). Four eyes had stable vision and one eye experienced a two-line decrease (Parodi et al. 2014). Median central macular thickness at baseline was 261 μm , decreasing to 196 μm at the 12-month examination (Parodi et al. 2014). The median number of injections was 1 in 12 months (Parodi et al. 2014). In our series, choroidal neovascularization regressed in all 3 patients, with a concomitant decrease in central retinal thickness, however 2 out of 3 patients lost vision compared to baseline (Table 1).

Albeit the pathogenesis of SC remains largely unknown, intravitreal aflibercept may have advantages over ranibizumab or bevacizumab in the treatment of neovascular complications in SC. Aflibercept binds to circulating vascular endothelial growth factors (VEGFs) and acts like a "VEGF trap". It thereby shows a more broad mechanism of action compared to the former 2 drugs, inhibiting not only vascular endothelial growth factor subtype VEGF-A, but also VEGF-B, as well as placental growth factor (PGF) (Stewart et al. 2012). Furthermore, the Fc portion of the human IgG1 immunoglobulin in the recombinant aflibercept protein may also exert favourable immunological effects which may potentially affect the disease course. In keeping with this, we were able to demonstrate areas of remaining macular function by multifocal electroretinography, in the area that was not directly affected by the SC, after treatment with aflibercept.

Limitations of the present study include small sample size, and electrophysiological studies were performed in only 1 patient. Furthermore, the given generalized immunosuppressive medication may also have local effects contributing to the regression of choroidal neovascularization, thus any treatment effects may not be attributed to aflibercept only.

In summary, although there are significant limitations as mentioned above, we present potentially promising data which require further exploration, regarding the role of intravitreal aflibercept in SC affected by secondary choroidal neovascularization.

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LEGENDS

Figure 1. Patient 1: Imaging of the left eye of a 32 year old male patient with choroidal neovascularization secondary to serpiginous choroiditis, before and after treatment with 3 monthly intravitreal injections with aflibercept. Left panel: Baseline findings. Middle panel: Findings at 1 month after the 1st intravitreal injection. Right panel: Findings at 1 month after 3 intravitreal injections.

Top: Left eye autofluorescence imaging shows a nasal hypofluorescent area and 2 temporal (superior and inferior) hyperfluorescent extensions indicating inflammatory activity in the latter. The intensity of the hyperfluorescent edges gradually diminishes over time after each intravitreal injection of aflibercept (Top middle and right).

Bottom left: Spectral domain optical coherence tomography shows cystoid edema, subretinal fluid and a deep retinal mass (its inner contour being delineated by red arrows) which represents a classical membrane, confirmed by fluorescein angiography (not shown).

Bottom middle and right: The edema and mass (red arrows) resolve after additional intravitreal injection of aflibercept.

Figure 2: Analysis of macular retinal function with multifocal electroretinography in a 36 year old male with serpiginous choroiditis and secondary choroidal neovascularization, before and at 1 month after 3 monthly intravitreal injections of aflibercept (Patient 1).

Top row: Baseline function. Left: Trace plot. Right: color coded plot. There is reduced function in the nasal macula, corresponding to the serpiginous choroiditis and the choroidal neovascularization membrane. Function is preserved in the unaffected temporal macula.

Bottom row: Macular function at 1 month after 3 monthly intravitreal injections with aflibercept. Function is reduced in the nasal macula and preserved in the temporal macula.

Table 1. Clinical data for 3 eyes (3 patients) with Serpiginous Choroiditis and secondary choroidal neovascularization treated with aflibercept.*

Patient	Gender (age)	Number of injections	Initial systemic Immunosuppression	CDVA		Optical coherence tomography centerfield thickness, μm		Multifocal electroretinography amplitudes nV/deg^2				Full-field electroretinography amplitudes μV					
				preop	postop	preop	postop	Ring 1-2		Ring 3-6		Rod		Rod-cone		Cone 30 Hz flicker	
								preop	postop	preop	postop	preop	postop	preop	postop	preop	postop
1	M (36)	7	Azathioprine 2mg/kg per day, Prednison 1 mg/kg per day, Cyclosporine 3 mg/kg per day	20/20	20/50	450	320	22	23	20	22	234	256	351	373	98	89
2	M (52)	2	Azathioprine 2mg/kg per	20/200	20/60	496	337	N/A		N/A		N/A				N/A	

			day, Prednisone 1 mg/kg per day								
3	F (61)	4	Azathioprine 10 mg per day	20/40	20/200	360	221	N/A	N/A	N/A	N/A

* CDVA=corrected distance visual acuity; Preop= within 1 week before 1st intravitreal injection with Afibercept; Postop= Follow-up time ranged between 8-14 months after the first injection, except for electrophysiological examinations in Patient 1 which were performed 1 month after the third injection; N/A= not analysed; Mg=milligram; Kg= Kilogram; µm= microns; nV/deg²=nanovolts per degree squared; µV= microvolts.



