Comment on: Rebound inflammation after an intravitreal injection in Vogt–Koyanagi–Harada syndrome

Sir,
I read with interest the article “Rebound inflammation after an intravitreal injection in Vogt–Koyanagi–Harada syndrome” by Ranjan et al.[1] They attributed the inflammatory response to the stimulation of T-lymphocytes by uveal melanocytes after injections of dexamethasone and bevacizumab through pars plana.

Literature is replete with reports of sporadic and “herd” ocular inflammation associated with bevacizumab.[2,3] While in theory, ocular autoimmunity can be triggered or boosted with injuries, a micro injury by needle may not release enough doses of putative autoantigens, to be processed and presented by an antigen-presenting cell to T-lymphocytes. Further, a “stirred-up” immune system would then target both eyes and evoke at least a mild inflammatory flare up in the other eye. In contrast, lipopolysaccharide endotoxin contamination during preparation of doses by pharmacy or operating room staff is a possibility that explains unilateral inflammation. Recognition of lipopolysaccharides through Toll-like receptor 4 causes macrophages to produce large quantities of potent cytokines, such as interleukin-1, tumor necrosis factor, and colony-stimulating factors. Lipopolysaccharides also cause polyclonal activation of B-cells and stimulate natural killer cells and other cell types to produce γ-interferon.[4] This case had an unusual increase in the subretinal fluid and exudative detachment though both the fluid and intraretinal cystic spaces pre-existed. Inflammatory cascades triggered by above cytokines can explain this. Apart from the autoimmunity and endotoxin, the other remotely possible cause could be higher immunogenicity of bevacizumab due to presence of both crystallizable fragment Fc and antibody-binding fragment Fab, or degradation due to disruption of cold chain/exposure to light, and consequent anti-idiotype phenomenon generating antibodies to bevacizumab.

It would be interesting to know if this patient was a lone user of bevacizumab or the drug was shared among several patients; if so, did other recipients exhibit any sign of inflammation?

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Conflicts of interest
There are no conflicts of interest.

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