Graefe's Archive for Clinical and Experimental Ophthalmology (2022) 260:3779–3780
https://doi.org/10.1007/s00417-022-05848-7

EDITORIAL (BY INVITATION)

In vivo confocal microscopy for eyes with Behçet's disease: a missing piece of the puzzle

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Received: 17 September 2022 / Revised: 17 September 2022 / Accepted: 21 September 2022 / Published online: 29 September 2022

The invention of the in vivo confocal microscopy (IVCM), a noninvasive imaging and diagnostic tool, enables morphological and quantitative analysis of ocular surface microstructure in a layer-by-layer fashion [1]. One of its versatile applications is that IVCM allows the detection of corneal nerves, including the sub-basal nerve plexus. The sub-basal nerve plexus runs parallel to the ocular surface, at the level above the Bowman's layer, presents as hyper-reflective linear structures [1, 2]. Another important application is its ability to quantify the corneal endothelium, which has comparable results with specular microscopy [3]. IVCM has become an important diagnostic tool in the armamentarium of the corneal specialists.

Behçet's disease (BD) is a disease with recurrent inflammation characterized by recurrent oral aphthous ulcers, genital ulcers, and uveitis with hypopyon [4]. It will affect the eyes with presentation of retinal vasculitis and relapsing and remitting panuveitis [5]. The commonly used criteria to diagnose BD is the International Study Group (ISG) Criteria, namely The International Criteria for Behçet's Disease (ICBD) [6], while Standardization of Uveitis Nomenclature (SUN) Working Group recently published another guideline of diagnosing BD [7]. Both criteria emphasized on ocular inflammation, while there was a lack of information of ocular surface in these criteria.

Ocular surface disease is an important yet mostly neglected perspective in taking care of BD patients with ocular involvement [8]. Population-based study found an increasing risk of keratopathy in uveitic patients [9]. Studies revealed that a significant decrease of tear break-up time and goblet cell counts, as well as increased squamous conjunctival metaplasia in ocular BD [10, 11]. On the other hand, researchers found that peripheral neuropathy and optic neuropathy are very rare in BD [12]. Therefore, there is a gap in the knowledge of BD for researchers to fill.

In this issue, Dikmetas and co-authors have presented the results of a prospective study evaluating eyes of BD using IVCM. When comparing BD patients with and without ocular involvement, their result showed that sub-basal nerve plexus density was significantly lower, and nerve tortuosity was significantly higher in the BD with ocular involvement group. Similar results regarding the decrease of endothelial cell density in BD patients have been reported using specular microscopy [13] and ICVM [14], as well as increased corneal thickness in the BD patients using ultrasound pachymetry [15]. The current study confirmed these results using IVCM and further expanded the knowledge by increasing the study population, by adding second control group as BD without ocular involvement and also by shining a light on the sub-basal nerve plexus tortuosity. This study could be the missing piece to the puzzle, and this study also highlights the heterogeneity of BD.

However, there remains unanswered issues. The IVCM finding suggested an association of the change in nerve plexus/corneal endothelium and BD with ocular involvement. Whether the change of nerve plexus and endothelium is the causative factor of ocular surface disease, or vice versa, remains unknown. The study did not reveal how many of the participants had ocular surface disease, which might be a potential selection bias of this study.

We believe this paper might open a new perspective to study the BD with ocular disease, while the results should be interpreted cautiously. Because only time can tell the cause-and-effect relationship, we suggested more prospective observation studies with longer follow-up in the both groups is needed to echo the results of this study.

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