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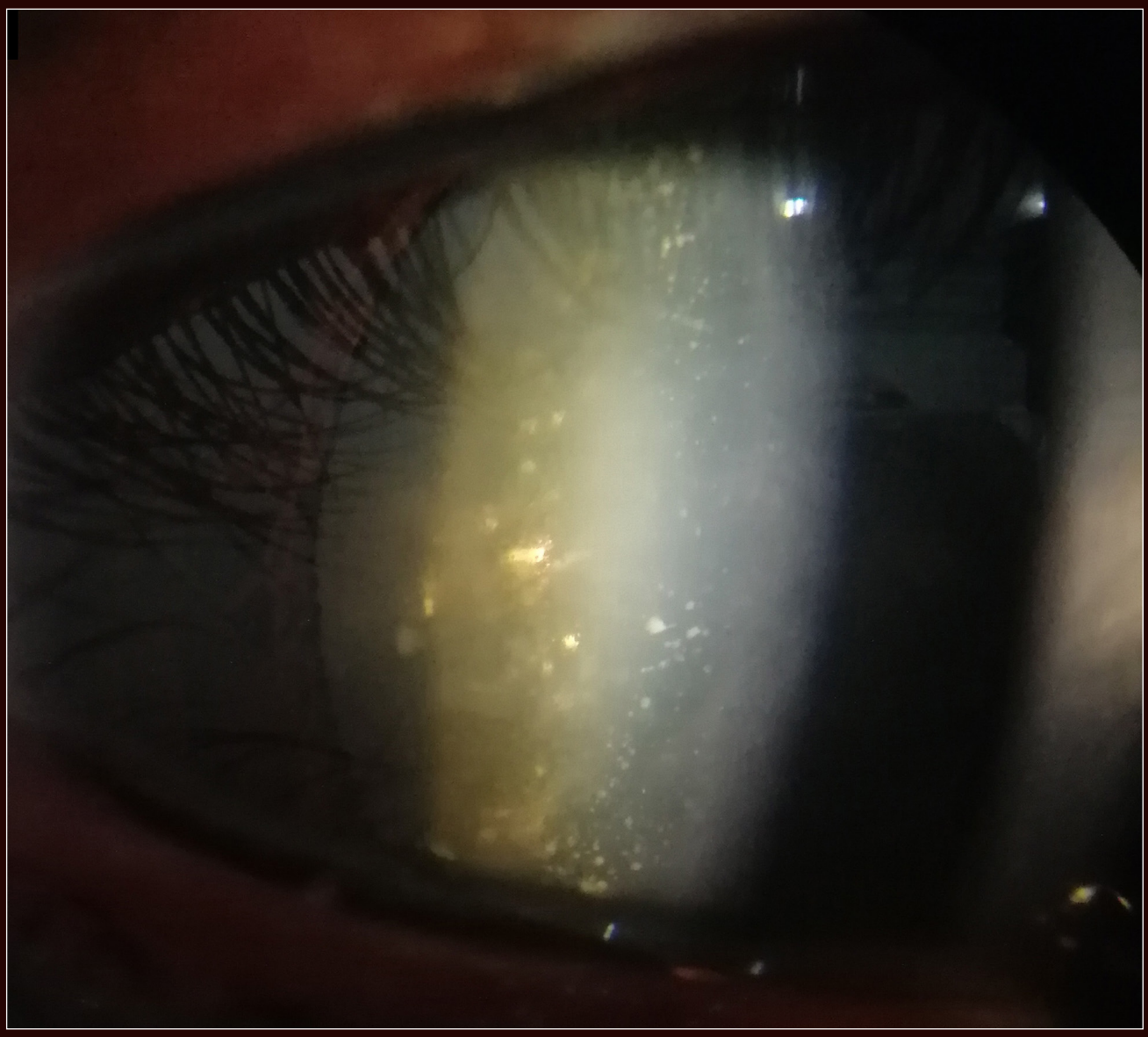

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ARTICLE ORIGINAL

Tomographic macular changes due to silicone oil in rhegmatogenous retinal detachments

Modifications maculaires tomographiques dues à l'huile de silicone dans les décollements de la rétine rhegmatogènes.

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Keywords
rhegmatogenous retinal detachment, silicone oil, optical coherence tomography, silicon retinopathy

Abstract

Purpose. To identify tomographic microstructural macular changes before and after silicone oil removal (SOR) in patients undergoing rhegmatogenous retinal detachment (RRD) surgery, and to correlate these findings to the final visual acuity.
Methods. Sixty eyes that underwent vitrectomy with silicone oil (SO) tamponade were included. Full ophthalmological examination with best-corrected visual acuity (BCVA) evaluation was performed, as well as Spectral-Domain optical coherence tomography (SD-OCT) scan, before SOR, 1 month and 3 months postoperatively. The microstructural changes identified in the OCT images were compared before and after SOR. Tomographic findings were correlated with the final BCVA.
Results. Under SO tamponade, SD-OCT revealed evidence of macular changes: epiretinal membrane (ERM) in 25 eyes (62.5%), cystoid macular oedema (CME) in 10 eyes (25%), internal retinal folds in 15 eyes (37.5%) mostly associated with epiretinal membrane; and persistence of sub-retinal fluid (SRF) in 3 eyes (7.5%). A longer tamponade with silicone oil (average of 8 months) was significantly correlated with more pronounced changes in tomographic macular microstructure (p<0.001). After SOR, we found an almost complete resolution of tomographic changes. Visual acuity was significantly improved for eyes with ERM and CME after SOR (p= 0.017). It was associated with a decrease in central retinal thickness. Restoration of photoreceptor's layer and external limiting membrane (ELM) was obtained in 32/40 eyes having, in that case, the best final BVCA.
Conclusion. Silicone oil has a damaging effect on the retinal microstructure. The introduction of the SD-OCT played a role to identify implicated mechanisms, for a better management and prevention. Our work focused on various macular microstructural changes caused by SOT. Its duration was an important factor influencing retinal changes and final visual recovery.

Mots-clés
décollement de rétine rhegmatogène, huile de silicone, tomographie par cohérence optique, rétinopathie liée au silicone

Résumé

Objectif. Identifier les modifications tomographiques de la microstructure maculaire avant et après l'ablation du l'huile de silicone chez les patients subissant une chirurgie du décollement de la rétine rhegmatogène et à corréler ces résultats à l'acuité visuelle finale.
Patients et méthodes. Soixante yeux ayant subi une vitrectomie avec tamponnement par huile de silicone ont été inclus. Un examen ophtalmologique complet avec évaluation de la meilleure acuité visuelle corrigée (MAVC) a été réalisé, ainsi qu'une tomographie par cohérence optique (SD-OCT), avant ablation de l'huile de silicone (AS), 1 mois et 3 mois après l'opération. Les changements microstructuraux identifiés dans les images OCT ont été comparés avant et après ablation de l'huile de silicone. Les résultats tomographiques ont été corrélés avec la MAVC finale.
Résultats. Sous tamponnement de l'huile de silicone, le SD-OCT a révélé des signes de modifications maculaires : membrane épirétinienne (MER) dans 25 yeux (62,5 %), œdème maculaire cystoïde (OMC) dans 10 yeux (25 %), plis rétiniens internes dans 15 yeux (37,5 %) principalement associé à la membrane épirétinienne ; et persistance du liquide sous-rétinien dans 3 yeux (7,5 %). Un tamponnement plus long avec l'huile de silicone (moyenne de 8 mois) était significativement corrélé à des modifications plus prononcées de la microstructure maculaire tomographique (p<0,001). Après AS, nous avons trouvé une résolution presque complète des modifications tomographiques. L'acuité visuelle était significativement améliorée pour les yeux avec ERM et CME après AS (p = 0,017), elle était associée à une diminution de l'épaisseur centrale de la rétine. La restauration de la couche des photorécepteurs et de la membrane limitante externe (ELM) a été obtenue dans 32/40 yeux ayant, dans ce cas, la MAVC finale.
Conclusion. L'huile de silicone a un effet néfaste sur la microstructure rétinienne. L'introduction du SD-OCT a joué un rôle pour identifier les mécanismes impliqués, permettant la prévention de ces altérations et une meilleure prise en charge. Notre travail s'est concentré sur divers changements de la microstructure maculaire causés par le tamponnement par l'huile de silicone. Sa durée était un facteur important influençant les changements rétiniens et la récupération visuelle finale.

Introduction

Silicone oil was introduced for retinal detachments in the 1960's as an internal tamponade. Early investigators were concerned that extended contact of silicone oil (SO) with the retina could cause toxicity. Silicon retinopathy was described as microstructural changes [1] involving the deterioration of visual function despite an anatomical recovery ad integrum. These changes were poorly identified despite complete silicone oil removal (SOR). Ohira and al. [2] showed that emulsified silicone oil injected into rabbit eyes appeared in the inner layers of the retina as early as one week after injection. Previous reports have suggested high intraocular pressure as a possible infiltration mechanism of SO into the retina [3,4]. Earlier histological studies have shown that intraocular SO

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induces irreversible changes in ocular tissues, especially the retina. Due to the lack of clinically proven silicon retinopathy in the years succeeding animal experiments, many have questioned whether these changes were related to the toxicity of SO. Through advances in retinal scanning techniques, we are actually able to identify emulsified silicone in the retina. The development of optical coherence tomography (OCT) [5], non-invasive, reproducible and easy-to-use imaging, has made possible a precise exploration of different retinal layers changes.
The aim of our study was to identify tomographic microstructural macular changes before and after SOR in patients operated for rhegmatogenous retinal detachment (RRD), and to correlate them to the final visual recovery.

Patients et methods

The study was carried out under the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Hedi Rais Institute of Ophthalmology of Tunis, Tunisia. A retrospective spectral domain optical coherence tomography (SD-OCT) scan review was conducted for 60 eyes of 60 consecutive patients who underwent uncomplicated 23-gauge pars plana vitrectomy with 1,300-centistokes SO tamponade for RRD between January 2019 and December 2019.
All patients were operated by the same surgeon, using the 23-gauge pars plana vitrectomy. A complete central and peripheral vitrectomy was performed with posterior mechanical vitreous detachment. After stabilization of the posterior pole by injection of Perfluorocarbon Liquid (PFCL), we proceeded to laser retinopexy of the tear(s) and PFCL-silicone oil exchange for all patients. Silicone oil was removed by pars plana approach when the eyes were confirmed to have an attached retina a permanent exclusion of tear(s).

The collected data included demographic characteristics, ophthalmological findings: best-corrected visual acuity (BCVA) evaluated on Snellen chart and converted to LogMAR, anterior segment exam with corrected ocular pressure, and fundus examination. SD-OCT was performed by the Heidelberg© Spectral Domain OCT looking for epiretinal membrane (ERM), cystoid macular oedema (CME), central macular thickness (CMT), macular folds as well as a complete examination of the external retinal layers. All informations were collected preoperatively, at months 1, 3, and 6 after SOR.
The statistical analysis used SPSS software, version 20.0, Microsoft Corporation, USA. Qualitative data were expressed in frequencies and percentages. Quantitative findings were expressed as mean ± standard deviation (SD) for parametric data. To compare categorical data, we used the Chi-square test ($\chi 2$) or the exact Fisher test. All tests were considered significant for a value of $p<0.05$.

Results

Sixty eyes of 60 consecutive patients were included in our study, with 42 males (sex ratio=7/3). The average age was 53.4 ± 14.7years. The mean duration of SO tamponade was 7.5 ± 2 months. All patients completed 6 months of follow up after silicon oil removal. Ten eyes were pseudophakic and 22 went through a combined procedure including phacoemulsification with intraocular lens implantation associated with SOR. Twenty-eight eyes had SOR on a transparent lens. None of our patients had a secondary endo-ocular procedure. Tomographic macular changes under SO tamponade were registered for 40 eyes/60 (66.67%): ERM was detected in 25 eyes (62.5%) (**figure 1a**) and CME in 10 ones (25%) (**figure 1b**). Inner retinal folds were diagnosed in 15 eyes (37.5%) associated to ERM in 12 eyes (**figure 1c**). SRF persisted in 3 eyes (7.5%) (**figure 1d**).

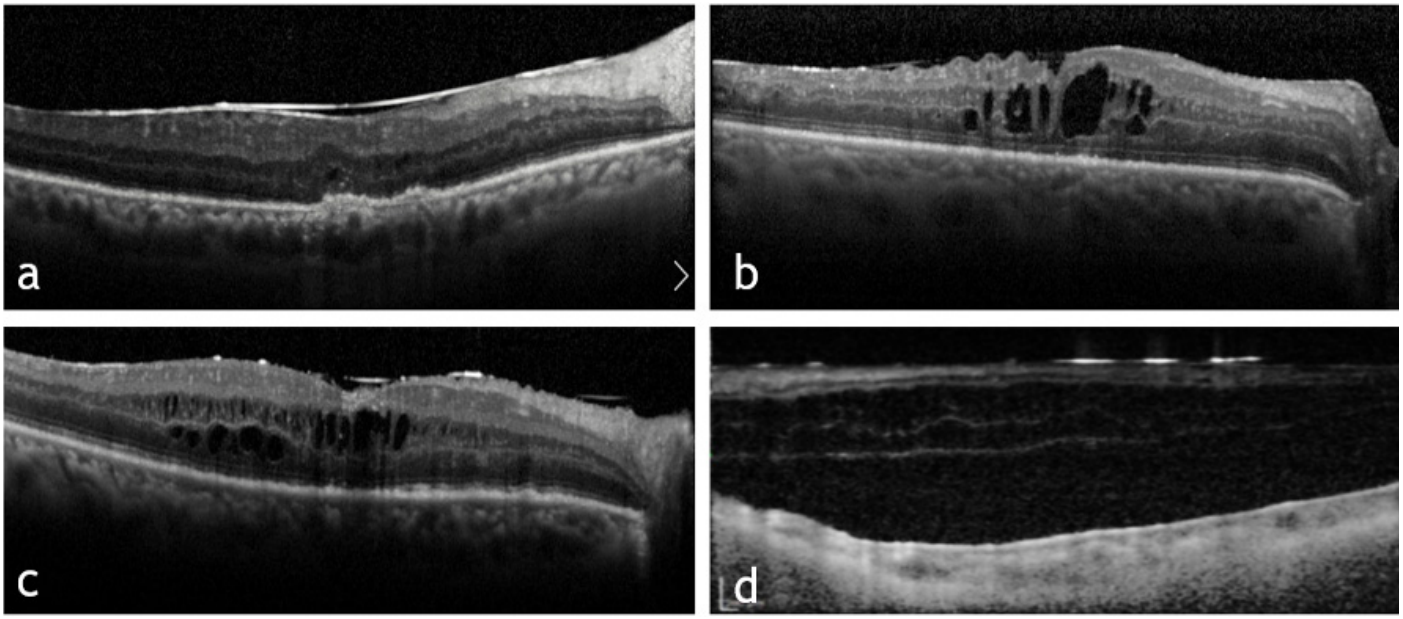

Figure 1. Microstructural changes under silicone oil: (a) tractional epiretinal membrane, (b) inner retinal folds and macular oedema, (c) cystoid macular oedema, (d) persistent subretinal fluid.

Central foveal thickness (CFT) was 341.52 ± 150.47 µm in eyes with macular changes against 162.22µm±91.41µm in eyes without macular changes. The CFT was greater in eyes with CME or persistent SRF (average macular thickness up to 620µm).
On the other hand, a longer tamponade with the silicone oil (duration>6 months) was statistically correlated with more pronounced changes in tomographic microstructures. In fact, we found that 100% eyes with ERM (25eyes) have had silicone oil for more than four months and an increase in macular thickness and CME has been observed after a tamponade period of more than 6 months (**Table I**).
After SOR, the average of CFT was 243.72 ± 131.09µm with no statistically significant difference from the baseline (p=0.079). Macular changes before and after SOR are summarized in **Table II**. Although the persistence of ERM after SOR, we have noticed the repair of retinal folds and the vanishing of tractions

(**figure 2 a, b**). The resolution of CME was correlated to the decrease of CMT (**figure 3 a, b**). The SOR allowed the restitution of external retinal layers as well as external limiting membrane and IS/OS line (**figure 4 a, b**).

Table I. Correlation between tamponade period and tomographic microstructure changes.

	< 4 months	4-6 months	6-9 months	> 9 months	P value***
ERM*	0/25	6/25	14/25	25/25	<0.001
thickening of the central retina	0/40	0/40	23/40	37/40	0.032
CME**	0/10	2/10	8/10	10/10	0.047

*: ERM: epiretinal membrane; **: cystoid macular oedema; ***p value: statistically significative <0.05.

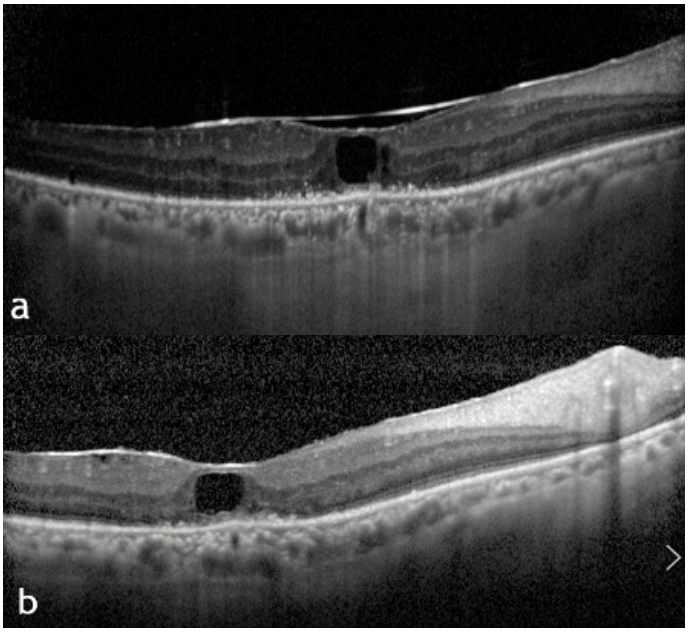

Figure 2. Macular changes before and after silicon oil removal: (a) large central cyst associated to epiretinal membrane (ERM) before silicone oil removal. (b) after silicone oil removal, we noticed the reduction of macular thickness and relaxation of retinal cyst despite the ERM.

Functionally, the BCVA under SO ranged from 1/100 (counting finger to 30 cm, 2 LogMAR) to 3/10 (0.52 LogMAR), with an average of 1/10 (1 +/- 0.43 LogMAR). After SOR, the BCVA has been evaluated at 1, 3 and 6 months. The mean BCVA were, respectively 0.88 ± 0.33; 0.69 ± 0.44, and 0.48 ± 0.79 LogMAR. Final BCVA (6 months after SOR) was positively correlated with the integrity of external retinal layers (p<0.001).
Patients with ERM did not show a statistically significant improvement in visual acuity after SOR (p=0.97). After resorption of the CME, patients showed an improvement in visual acuity with a gain of one line on the Snellen score, without being statistically significant (p=0.32).

Discussion

In this study, macular microstructural changes such as macular ERM, inner retina folds, CME, and SRF were identified by SD-OCT under SO tamponade. Globally, these retinal findings were diagnosed in 40 eyes (66.67%) through an average period of 7.5 months. Postoperative visual improvement occurred parallel to the resolution of macular microstructural changes following the removal of the SO.

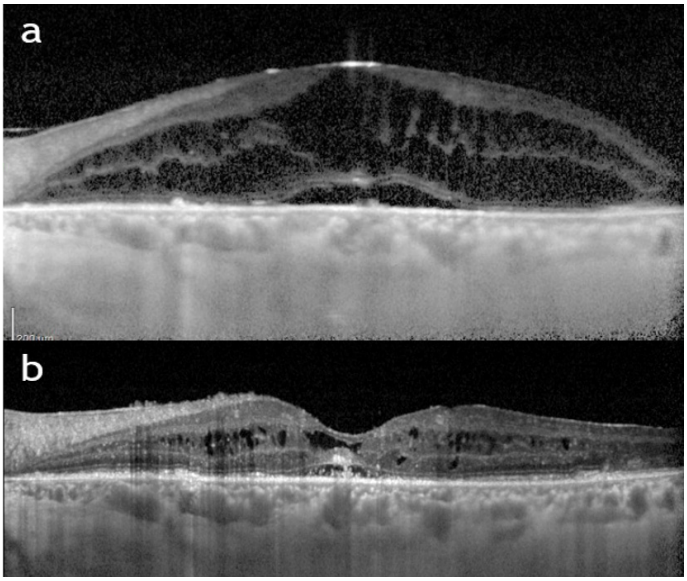

Figure 3. Evolution of cystoid macular oedema after silicone oil removal: (a) under silicone oil: significant cystoid macular oedema and serous retinal detachment, (b) after silicon oil removal: central macular thickening and recovery of photoreceptor's layer.

In Bae's series, retinal damages were identified in 41.3% of cases [6]. The direct incrimination of SO in the persistence of SRF is discussed. Under SO tamponade the incidence of SRF persistence was reported to be about 15% [6,7]. In our study, it was observed in 7.5% of cases and the follow-up revealed a complete resolution of submacular fluid in 2 eyes after 3 months from SOR. Bae and al. reported SRF resorption in all eyes after 6 months [6]. The association and causal relationship between SO and SRF persistence requires further investigations to be established.

Table 2. Evolution of microstructural changes before and after silicone removal.

Microstructural changes	Under silicon oil tamponade	3 months after silicon oil removal
ERM + retinal folds (n,%)	28	22 *
CME (n,%)	10 (16.66%)	2 (3.33%)
SRF persistence (n,%)	3 (5%)	1 (1.66%)
Restoration of IS/OS line (n,%)	5 (8.33%)	7 (11.66%)
Restoration of external limiting membrane (n,%)	6 (10%)	11 (18.33%)
Average retinal thickness (µm)	261.54 ± 130.77	243.72 ± 131.09 **

ERM: epiretinal membrane, CME: cystoid macular oedema; SRF: subretinal fluid, IS/OS: inner segment/ outer segment.
(*): disappearance especially of retinal undulations and traction; ERM still persists after silicone oil removal.
(**): Decrease in retinal thickness observed, correlated with the disappearance of the cystoid macular oedema.

Epiretinal membrane is the most widely-recorded complication in the literature (reported in 20 to 88.9% of cases) [6,8]. We had observed ERM in 62.5% of patients. Its formation is a common event after RRD surgery and is considered as a macular manifestation

of proliferative vitreoretinopathy (PVR). Epiretinal membrane is the most widely-recorded complication in the literature (reported in 20 to 88.9% of cases) [6,8]. We had observed ERM in 62.5% of patients. Its formation is a common event after RRD surgery and is considered as a macular manifestation of proliferative vitreoretinopathy (PVR). Although ERM can also being observed after scleral buckling, but its incidence is increased in eyes undergoing pars plana vitrectomy, with an estimated prevalence of 6-35% [6,9,10]. The pathogenesis of ERM consequent to RRD repair consists of the migration of RPE and inflammatory cells from the peripheral breaks to the surface of the macular internal limiting membrane. The inflammatory mechanism is mostly involved [6,11]. SD-OCT provides the positive diagnosis in most cases [6] by showing hyper-reflectivity, located at the SO retinal interface. This aspect is easy to detect after SO removal. Our results showed several cases of macular ERM combined with inner retinal folds (12 patients).

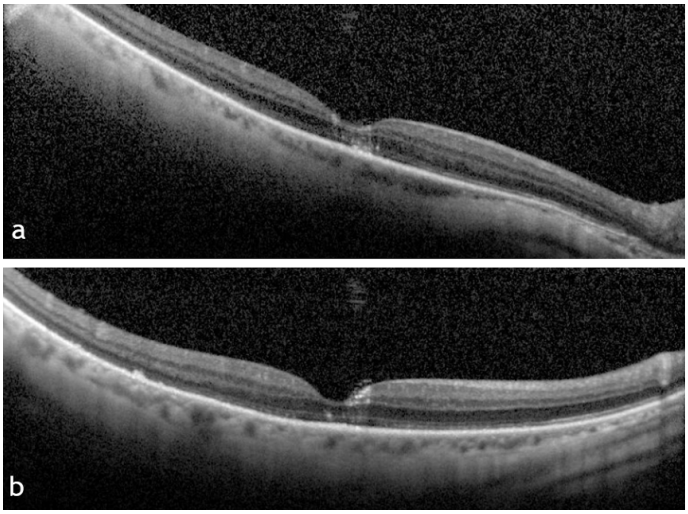

Figure 4. Recovery of inner retinal layers after silicone oil removal: (a) multiple micro cysts in inner macular layers before silicone oil removal, (b) normal foveal depression and resorption of micro cysts after silicone oil removal.

Retinal folds can be observed from the first few days after vitrectomy and can be recognized by indirect ophthalmoscopy as straight or curvilinear retinal wrinkles on an intact choroid. Retinal folds affect the inner layers of the retina and preserve the outer ones [12]. Contraction of the ERM over time causes tractions and wrinkles on the superficial retina, which eventually form complete fold. Surgical peeling of ERMs may be necessary to flatten the inner retinal folds. The benefits of combined surgery for ERM have been documented in the literature [6]. In order to reduce the incidence of ERM cases, many authors have proposed prophylactic peeling of ILM during vitrectomy for RRD, with good results [13]. In this study, the removal of SO helped to complete dissolving of the retinal undulations. Bae [6] documented that after SOR, ERM decreased from 26.1% to 4.3% after 6 months of follow-up. The ERM was still persistent after silicone removal but we rather observed the disappearance especially of retinal folds and traction caused by ERM.

The effect of SO on CME still uncertain, although eye inflammation has been reported to play a major role, especially after trauma, cryotherapy or SRF drainage. The concentration of angiogenic factors in the silicone-retinal CME interface has been reported. Conversely, CME has not been linked to preoperative macular condition or duration of RRD [14,15]. The reported incidence varies from 19.6% to 47% [6,16]. The proportion of CME was 25% in our study under SO tamponade. Currently, the incidence of CME has been significantly reduced with the prophylactic use of topical non-steroidal anti-inflammatory drugs (NSAIDs) before surgery [17]. Besides, obvious cases spontaneously regress in up to 76% of cases within two years. In unresolved cases, topical corticosteroids and NSAIDs, systemic acetazolamide, and intravitreal steroids have been used, with different success rates [18,19].

The influence of the silicone oil tamponade on the outer retinal layers remains unclear. In enucleated eyes, Knorr has observed that retina showed after RRD, independent of the use of silicone oil, a loss of inner and outer segments of photoreceptors and ganglion cells, thinning and rarefaction of all other retinal layers [20]. Reports in the literature, in this regard, are controversial and while some studies reported that the use of silicone oil tamponade caused thinning in the inner retinal layers but not in the outer retinal layers, others reported the opposite [21,22]. Lee documented that silicone oil tamponade had a significant effect on the postoperative decrease in thickness of all retinal layers, except for the photoreceptor layer [23]. Furthermore, the fact that SO could be involved in such damages has not been excluded. Some lipophilic substances have been identified in the silicone extracted from the eye after the SOR procedure [24]. Some macular pigments are lipophilic and can dissolve in silicone oil. Besides, it has been documented that SO produces vacuoles in the photoreceptor outer segments and shortening of the horizontal and bipolar processes [25]. Migration of phagocytosed emulsified oil bubbles by macrophages might be another mechanism for subretinal migration of SO [26].

In this study, SOR allowed the reconstitution of the outer layers of the retina (IS/OS line in 2 eyes and ELM in 5 eyes). For Durrani and al. IS/OS line disruption was noted in 20 eyes with SO and only 10 eyes after SOR [27]. The same study reported that eyes with these disruptions under SO had a significantly longer duration of tamponade.

Conclusion

Outer retinal layers are known to be closely associated with visual prognosis. Our results are in line with this view. In our study, significant improvement of visual acuity paralleled the recovery of macular microstructural changes after SO removal. The final visual acuity in our study (6 months after SOR) depended mainly on the integrity of the external retina. Future multicentric studies need to be carried out with larger study groups to engage these observations.

Conflicts of interest

There is no conflict of interest regarding the publication of this article.

Funding and acknowledgments

None.

Availability of Data and Material

The data supporting the findings of this study are available from the corresponding author on request.

Authors' contribution

All authors contributed to the study conception, design, material preparation, data collection, and analysis. The first draft of the manuscript was written by Dr. Hsouna Zgolli, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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