Ophthal Focus
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Dear Doctor,
Greetings from Micro Labs Limited. We are happy to bring you 'Ophthal Focus' which contains latest and interesting news in the field of Ophthalmology.

This issue contains

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Endothelial Failure and Rejection In Corneas Recipients Of The Same Donor

INTRODUCTION:

The lack of a significant difference in graft outcome for FED and PBK corneal transplants between paired and unpaired donors may be due to a homogeneous donor pool.

The cornea, unlike other tissues or organs, is a relatively privileged site for transplantation in its healthy state due to the absence of blood and lymphatic vessels (except for the marginal corneal arcades) and a relative scarcity of mature antigen presenting cells. Despite this, corneal graft failure is still common, with 79% and 59% 5-year graft survival rates for Fuchs endothelial dystrophy (FED) and pseudophakic bullous keratopathy (PBK), respectively. Corneal transplants fail primarily due to endothelial failure because these cells do not divide and rely on the donor endothelium for survival. Endothelial graft failure is frequently caused by corneal graft rejection and/or recipient inflammation. [1] Graft rejection and failure are affected by both donor and recipient factors. Many recipient risk factors for rejection are well known, such as young recipient age, number of previous transplants, vascularisation, previous rejection episodes, and the indication and type of transplant. [2] Endothelial cell density (ECD), donor age, and H-Y incompatibility have also been shown to play variable roles in graft rejection and failure. Many donor factors such as race, lens status, harvesting and preservation techniques have been studied, but the evidence is often conflicting. [3] The demographics and endothelial outcomes of 'paired' corneal transplants were compared to 'unpaired' single corneal donor transplants and donors who donated both corneas but for a different indication or regraft in this study. An association between the cause of failure and the type of rejection was also investigated for each patient of paired donor transplants. Other donor factors, such as donor age, ECD, and gender mismatch, were also investigated to see if they were associated with an increased risk of endothelial graft failure and rejection. In addition to the donor factors that were recorded, an unknown donor effect was fitted to account for unexplained donor to donor variation and any correlation between pairs of corneas from the same donor.

METHODS:

Fuchs endothelial dystrophy (FED) and pseudophakic bullous keratopathy (PBK) patients who had their first corneal transplant were studied. Patients who received corneas from donors who donated both corneas for the same indication were classified as'paired.' Gray's test was used to compare the cumulative incidence of endothelial failure and rejection in the 'paired' and 'unpaired' groups 5 years after transplant. Cox regression models were used to see if there was a link between donor characteristics (endothelial cell density (ECD), age, and gender) and endothelial graft failure and rejection.

RESULTS:

There were 10,838 patients studied, with 1536 (14%) being paired. The unpaired group was made up of 1837 (69%) recipients of single corneal donors and 7465 (69%) donors who donated both corneas for another reason. Unpaired single cornea donors had a lower ECD. After adjusting for transplant factors, there was no significant difference in endothelial graft failure or rejection

between paired and unpaired groups for FED or PBK, nor for donor ECD, age, sex, or paired donation.

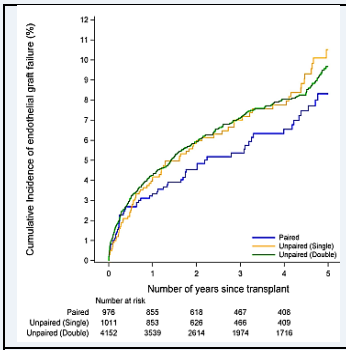

Figure 1 Cumulative incidence of endothelial graft failure in fed recipients.

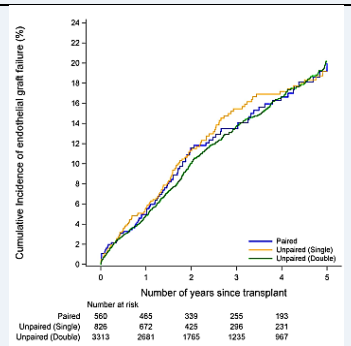

Figure 2 Cumulative incidence of endothelial graft failure in PBK recipients. PBK, pseudophakic bullous keratopathy.

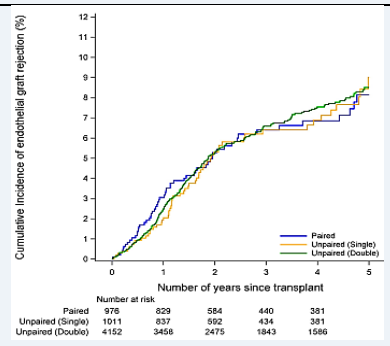

Figure 3 Cumulative incidence of endothelial graft rejection in fed recipients.

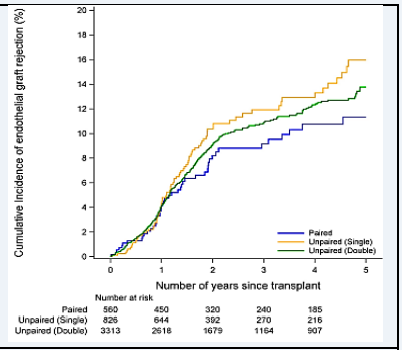

Figure 4 Cumulative incidence of endothelial graft rejection in PBK recipients. PBK, pseudophakic bullous keratopathy

DISCUSSION:

The donor tissue's quality is an important factor in corneal graft survival. As a result, standards are established to ensure that donor tissue issued by eye banks meets quality assurance standards such as ECD above a certain threshold, endothelial cell quality, and corneal clarity. Although this is speculative, it may account for the lack of significant donor effects in age and ECD within the ranges used for these variables. The researchers were also unable to investigate donor factors such as diabetes and other known donor characteristics because this information is not collected in the registry.

Although there is little evidence of an effect of ECD on graft survival for an ECD of more than 2300 cells/mm^2. [2,3] ECD is the most critical donor factor in determining graft survival. This would support the study's finding of no significance for ECD. Lower ECDs for unpaired single cornea donors may explain why the other cornea was discarded. While unpaired single cornea donors had slightly higher rates of endothelial rejection and failure, there was no significant difference in these outcomes between the unpaired and paired groups, implying that single and paired cornea donors were comparable, but more research is needed.

Donor age has been extensively studied as a potential factor in graft survival and has been linked to graft failure and rejection in varying degrees. In over 24000 grafts, a study found evidence of an adverse effect of donor age of 80 years or older on graft survival following PK. Graft survival after DSAEK and DMEK appears to be better in donors under the age of 40 and 50. [4]

Mismatches in donor and recipient gender or H-Y have been found to affect graft outcome depending on the type of transplant and indication. However, in our study, there was no link between gender mismatch and endothelial rejection or survival in paired transplants.

CONCLUSION:

Overall, the study found no donor factors associated with endothelial rejection or survival; paired and unpaired transplants had very similar outcomes. However, there was a borderline significant donor effect for endothelial graft survival in FED patients, implying that there may be donor factors that have not been identified and require further investigation. The number of cases with the same cause of failure or rejection was very small, so there was no similarity in each transplant outcome.

The general lack of difference in endothelial outcomes between paired and unpaired FED and PBK transplants could be attributed to a homogeneous donor pool.

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A Comparative Clinical Study of Lacrimal Gland Injection of Platelet Rich Plasma for the Treatment of Severe Dry Eye

INTRODUCTION:

The tear film is responsible for providing the necessary moisture and lubrication to maintain both vision and comfort. [1] TFOS/DEWS II defines dry eye disease (DED) as "a multifactorial ocular surface disease characterised by a loss of tear film homeostasis and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles." [2]

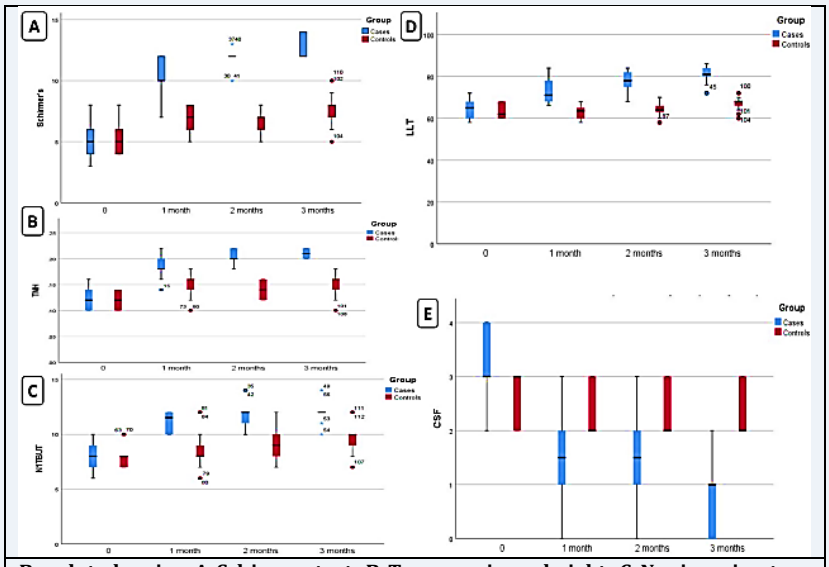
Injection of PRP into the lacrimal gland is a simple, safe, and effective technique for treating severe dry eye, as evidenced by improvements in tear film parameters measured subjectively and objectively. More research is needed to standardise the technique and confirm these findings.

The use of human blood as a source of a wide range of cell-based or protein-based therapeutic products is regarded as a critical component in regenerative medicine, and platelet-derived preparations rich in growth factors are now being used for a variety of therapeutic applications such as tissue repair, wound healing, and regeneration. The use of blood-derived products such as platelet rich plasma (PRP) and autologous serum (AS) is regarded as a new treatment modality for severe dry eye because it can enrich the ocular surface with growth factors as well as anti-inflammatory cytokines. One of the primary distinctions between PRPs and AS is that platelets are not enriched during AS production, whereas platelets are enriched at least twice the platelet concentration in peripheral blood in PRP. [3] Growth factors such as epidermal growth factor (EGF), transforming growth factor (TGF), fibroblast growth factor (FGF), platelet derived growth factor (PDGF), nerve growth factor (NGF), and insulin-like growth factor (IGF), as well as cytokines and chemokines, can be stored as granules in vesicles by platelets. [4] The current study is a non-randomized interventional consecutive study that evaluated the efficacy of autologous PRP injection into the lacrimal gland as a treatment tool in severe forms of chronic DED.

METHODS:

The study included 28 eyes from 14 patients with severe DED who were diagnosed with Sjogren syndrome in this retrospective interventional clinical study.

At days 0, 30, 60, and 90, each patient received a unilateral lacrimal gland injection of PRP, while the other eye served as a control group, receiving preservative-free eye drops. The study objectively assessed parameters such as non-invasive tear breakup times (NIBUT), tear meniscus height (TMH), lipid layer thickness (LLT), Schirmer test I, corneal fluorescein staining (CFS), and meiboscore at baseline, 1month, 2months, and 3months.



Boxplot showing A Schirmer test, B Tear meniscus height, C Noninvasive tear breakup times, D Lipid layer thickness and E Corneal fuorescein staining at baseline compared to 1, 2, and 3months in the injected eye group and control group

RESULTS:

The average age was 43.4±.7.85 years. When different parameters were compared, baseline data revealed a non-significant difference between the injected eye group and the control group. There were significant differences between the two groups after 1 and 3 months of follow up in terms of NITBUT, TMH, LLT, CFS, and Schirmer test, with p 0.001 in favour of the PRP group.

DISCUSSION:

The primary goal of DED treatment is to restore ocular surface and tear film homeostasis by breaking the disease's vicious cycle. The main cause of aqueous tear deficient DED is a decrease in LG secretion. With signs of inflammation, it may become a target for the immune system. This can occur as a result of autoimmune diseases (Sjögren's syndrome), organ transplantation (graft versus host disease), or simply ageing.

Tear hyposecretion in Sjögren syndrome can be caused by an autoimmune infiltration as well as lacrimal gland destruction. The use of blood derivatives is an alternative approach that is gaining popularity in regenerative medicine due to its ability to stimulate tissue healing. We objectively assessed the effect of LG injection of PRP on various ocular surface parameters such as NIBUT, TMH, LLT, Meibography, CFS, and Schirmer test throughout the study period and compared it to baseline and control group data. OSDI was used to select cases with severe dry eye using subjective assessment. Significant improvements in the tested ocular surface parameters matched previous published studies. [5]

More recently, a 2019 study included patients with severe DED diagnosed as Sjogren syndrome. Patients were given either PRP or hyaluronic acid eye drops and were monitored for 90 days. PRP improved tear parameters such as OSDI, corneal staining, the mean Schirmer value, and TBUT at day 90, according to the study. This is consistent with this studys findings. [6]

When specific tissue regeneration is required, injection is a common therapeutic approach. It has been used in tissue regeneration due to the activity of several growth factors that can stimulate stem cell proliferation. [7]

The beneficial effect of PRP injection into the LG may be supported by its positive effect on the glandular cells of the liver via a direct effect on hepatocytes, as well as an indirect antifibrotic effect and a protective effect against hepatocyte apoptosis. The current advances in stem cell biology and bioengineering technologies have increased the demand for restoring lacrimal gland function, and injection of PRP in LGD appears to be a novel proposed treatment in this field. Despite the scarcity

of published data, we believe that PRP injection has a promising role in the treatment of DED. To the best of the study's knowledge, this is the first study to use an ocular surface analyzer to evaluate the enrolled patients.

CONCLUSION:

In conclusion, PRP injection in severe DED induced a positive effect on different ocular surface parameters, including the quantity and quality of tear lacrimal volume, as well as a better restoration of ocular surface homeostasis, and may open new avenues for treatment and a better understanding of DED pathophysiology. This suggests that platelets and derived products will continue to play an important, if not growing, role in clinical treatments.

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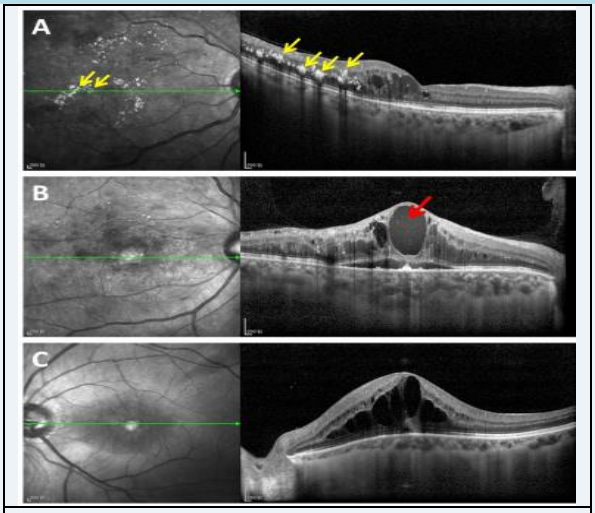
An Observational Study of Hyperreflective Foci in Macular Edema Due to Multiple Etiologies Using Spectral Domain Optical Coherence Tomography.

INTRODUCTION:

Macular edema (ME) is a leading cause of vision loss in a wide range of diseases, including metabolic, vascular, and inflammatory retinal disease. [1] According to reports, macular edema is present in more than 20% of diabetic patients 20 years after diagnosis, 5%-15% of patients with retinal vein occlusion, and 20%-35% of patients with uveitis. [2] SDOCT (spectral-domain optical coherence tomography) is a noninvasive retinal imaging technique that is currently used to diagnose retinal diseases such as macular edema. SD-OCT generates high-resolution retinal microstructure images, which aid in the diagnosis and monitoring of macular edema. On SD-OCT scans, ME typically appears as hypo-reflective cystoid spaces. However, in some patients, hyper-reflective dots can be seen scattered throughout all

SD-OCT detected HRF in DME patients more frequently than in BRVO-ME, CRVO-ME, or UME patients. HRF occurrence was related to the frequency of hard exudates. HRF is thought to be caused by the deposition of macromolecular exudates in the retina, which is thought to be a precursor to hard exudates.

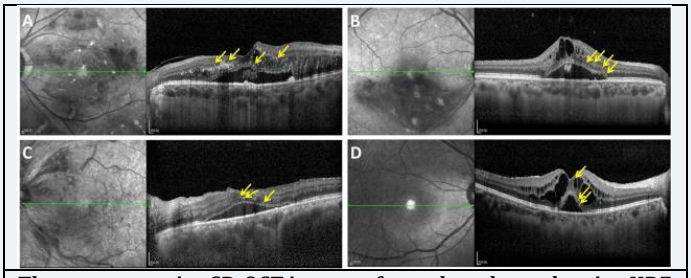
retinal layers, particularly around the intra-retinal cystoid spaces, which are referred to as hyper-reflective foci (HRF). [3] HRF has been detected in macular edema caused by diabetes, retinal vein occlusion, uveitis, age-related macular degeneration, and other diseases. This study examined the relationship between the number of HRF and hard exudates in diabetic retinopathy (DR), branch retinal vein occlusion (BRVO), central retinal vein occlusion (CRVO), and uveitis. Along with HRF, the cyst's enhanced internal reflectivity was investigated. Furthermore, the correlations between HRF and the characteristics of hard exudates in DME patients were investigated in order to better understand the properties and origin of HRF.



Representative SD-OCT images of macular edema secondary to diferent etiologies. A Diabetic macular edema (DME), hard exudates are seen in the retina (yellow arrows), manifesting as irregular dense and hyperrefective signals, mainly distributed in the outer plexiform layer, accompanied by a posterior hyporefective shadow, and corresponding exudate lesions can be seen in infrared fundus images. B DME, the signal in the edema cyst was enhanced (red arrow), showing that the refectivity in the edema cyst was higher than that in the vitreous. C Uveitic macular edema (UME), no obvious hard exudates or enhanced internal refectivity of the cyst was observed, no high-density lesion was observed in the corresponding infrared fundus images, and the refectivity of the contents in the cyst was equivalent to that in the vitreous

METHODS:

This was a retrospective study. SD-OCT images were examined to investigate macular microstructural features such as the number and distribution of HRF and hard exudates, as well as the internal reflectivity of the cysts. The differences in microstructural features between groups, as well as the correlations between the number of HRF and other parameters, were investigated.



The representative SD-OCT images of macular edema showing HRF in diferent diseases. The HRF can be seen in the retinas (yellow arrows) (A) Diabetic macular edema (DME). B Branch retinal vein occlusion-macular edema (BRVO-ME). C Central retinal vein occlusion-macular edema (CRVO-ME). D Uveitic macular edema (UME)

RESULTS:

This study included 101 eyes with ME from 86 diabetics (diabetic macular edema, DME) patients, 51 eyes from 51 patients with ME secondary to branch retinal vein occlusion (branch retinal vein occlusion-macular edema, BRVO-ME), 59 eyes from 58 central retinal vein occlusion (central retinal vein occlusion-macular edema, CRVO-ME) patients, and The number of HRF, frequency of hard exudates, and enhanced internal reflectivity of the cysts differed significantly between groups. The number of HRF was significantly higher in the DME group than in the other groups.

DISCUSSION:

The study analyzed SD-OCT images obtained from patients with macular edema caused by DR, BRVO, CRVO, and noninfectious uveitis. The frequency of hard exudates and enhanced reflectivity in edema cysts in the DME group was significantly higher than in the BRVO-ME, CRVO-ME, and UME eyes, according to our findings. The HRF number in DME eyes was significantly higher than in the

other groups, whereas the lowest HRF number was found in UME eyes. The presence of hard exudate is associated with the number of HRF in each retinal layer in eyes with DME.

DME pathogenesis is caused by a number of factors, including an increase in inflammatory conditions, changes in vascular structure, BRB breakdown, and Müller cell degeneration. [4] A study used a machine learning algorithm to distinguish DME from pseudophakic cystoid macular edema based on SD-OCT characteristics. HRF was one of the significant markers. [5] The HRF signal intensity is reported to be lower than that of the RPE layer and closer to that of the retinal nerve fibre layer (RNFL). [6]

The current study defined HRF signal intensity as the same as RPE layer, and the minimum diameter of HRF was set to 10 m to avoid missing smaller HRFs. Even though HRF were carefully counted, certain bias is unavoidable, as mentioned in other reports; for example, the selected section of analysis was limited to the central horizontal SD-OCT B-scan. Automatic analysis of SD-OCT microstructural features by new computer algorithms may be an effective method to solve such problems in the future. [6]

The features of HRF in different retinal layers were studied in this study. Previous research found that HRF levels in different retinal layers correlated with different prognoses and therapeutic effects. The number of HRF at baseline in the outer retinal layer is thought to predict poorer final visual acuity after treatment. [7]

Furthermore, the study discovered increased signal within the cysts. After BRB destruction, hard exudates are thought to be the deposition of macromolecular exudates such as lipids and lipoproteins in retinal tissues. The increased signal in the edema cyst is thought to be caused by fibrinogen exudates caused by BRB destruction or inflammatory products. In this study, we discovered that the frequency of hard exudates and enhanced reflectivity in edema cysts was significantly higher in the DME group than in the other groups, which may indicate that the degree of BRB destruction was more severe in the DME group.

CONCLUSION:

Although this study concluded that HRF in DME were precursors to hard exudates, it cannot rule out the possibility that HRF in other types of macular edema, such as microglia, are inflammatory reaction products. Some researchers discovered a decrease in the number of HRF after anti-inflammatory therapy. According to the study, the reason for the regression of HRF after anti-inflammatory treatment could be that anti-inflammatory treatment improves the BRB and reduces vascular permeability damage, resulting in a decrease in the number of HRF.

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A Case Report of Bilateral Choroidal Osteomas in an Elderly Woman

A case of an elderly woman with bilateral choroidal osteomas was presented. A 84-year-old Caucasian woman was referred to our hospital for a follow-up visit despite being asymptomatic and lacking clinical features suggestive of choroidal osteoma. Both eyes had a suspected lesion on the fundus examination. A B-scan ultrasound revealed bilateral highly reflective calcified lesions within the choroid, as well as an obvious cone of shadow, indicating choroidal osteoma. Additional tests have been performed to confirm the diagnosis. Although the literature describes choroidal osteoma as a more common one-sidedness and typical manifestation in adolescence, this case report describes bilateral choroidal osteomas in an elderly woman.

INTRODUCTION:

Choroidal osteoma is a benign ossifying disorder in which mature cancellous bone forms in the choroid. The exact cause of the disease is unknown, and the disease is extremely rare. It is most common in women between their second and third decades of life, and the majority of cases are unilateral and localised near the optic disc. There are no known risk factors. It appears as orange-yellow to yellow-white lesions with a distinct margin and blood vessels overlying them on fundus examination. The colour of the lesion is determined by the degree of depigmentation of the overlying retinal pigment epithelium (RPE). The diagnosis is primarily clinical and is based on the appearance of the lesion during a posterior pole examination; however, additional diagnostic studies are required to support the diagnosis. The most diagnostic techniques are ocular ultrasound and CT, which reveal the bony nature of the tumour. Choroidal neovascularization (CNV) and/or photoreceptor loss, as well as choroidal and RPE atrophy associated with decalcification, are the most common causes of visual loss in these patients. [1]

CASE REPORT:

This is a case of an 84-year-old Caucasian woman who is asymptomatic and has no clinical features of choroidal osteoma. Her clinical systemic history revealed no renal or parathyroid disorders, but she was only being treated for systemic hypertension. Her ocular history revealed no evidence of trauma or clinically significant intraocular inflammation. Four years prior, she had bilateral cataract surgery and was monitored for glaucoma at a different facility. She was referred to our hospital for a second opinion on her glaucoma.

Her visual acuity in both eyes was 20/20 with ipermetropic astigmatism correction; her intraocular pressure was 12 mm Hg and was treated with timolol 0.5 BID; and she was pseudophakic in both eyes. We found an optic-disc-cup-disc ratio of 0.7 in both eyes, as well as bilateral, yellowish-white lesions with well-demarcated borders located supero-temporally, distanced from the macular area, suggestive of decalcified lesions, one of 8.5 mm 5 mm 2 mm in the right eye and the other of 7 mm 4 mm 2 mm in the left eye (Fig. 1). There was no evidence of CNV or subretinal haemorrhage.

The autofluorescence of the fundus revealed two bilateral hypo-autofluorescent areas located outside the supero-temporal posterior pole edge, far from the macular area (Fig. 2). The OCT

revealed a retinal lift with slight retinal thinning and choroidal thickening with some choroidal large vessels (Fig. 3)

The Humphrey Field Analyzer II-i, programme 24-2 SITA Standard, was used to perform a visual field test, which revealed a diffuse slight reduction in sensitivity in the right eye and a superior arcuate defect in the left eye. Because osteomas must be diagnosed using multimodal imaging and ultrasonography, an ultrasound test and a CT scan were recommended. A B-scan ultrasound revealed an irregular hyper-echogenic calcified lesion in the posterior choroid, focused in both supero-temporal choroids, with acoustic shadowing resembling "pseudo-optic nerve" (Fig. 4). Her eyes' CT scan revealed an asymmetrical and irregular calcified lesion in the posterior choroid, far from the optic disc region, and focused in both supero-temporal choroids (Fig. 5).

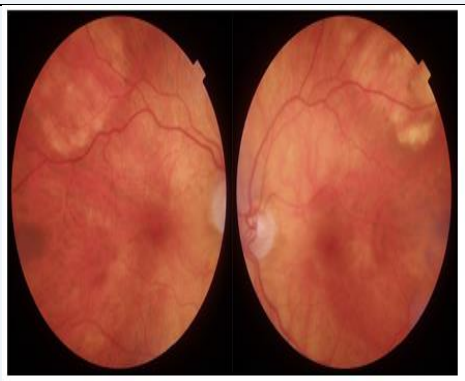

Fig. 1. Fundus photos showed bilateral yellowish-white lesions with well-demarcated borders located superotemporally; right eye on the right and left eye on the left

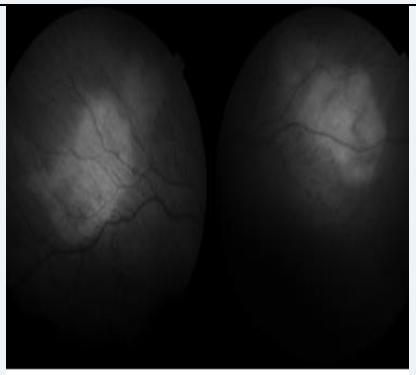

Fig. 2. The fundus autofluorescence revealed two bilateral hypo-autofluorescent areas, located outside to the supero-temporal posterior pole edge; right eye on the right and left eye on the left.

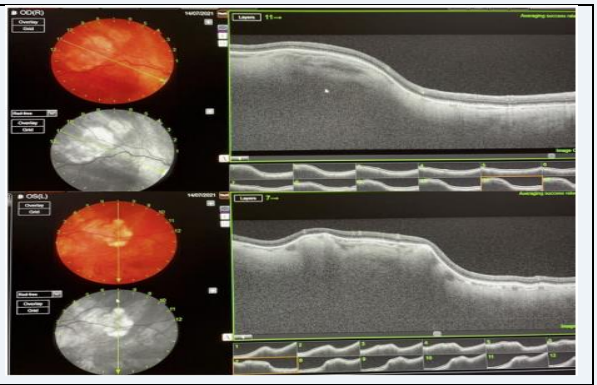

Fig. 3. OCT showed a retinal lift with a slight thinning of the retina and a choroidal thickening with some choroidal large vessels. No CNV was detected; right eye up and left eye down

Fig. 4. Irregular hyper-echogenic calcified lesion in the posterior choroid demonstrated by B-scan ultrasound; right eye on the right and left eye on the left.

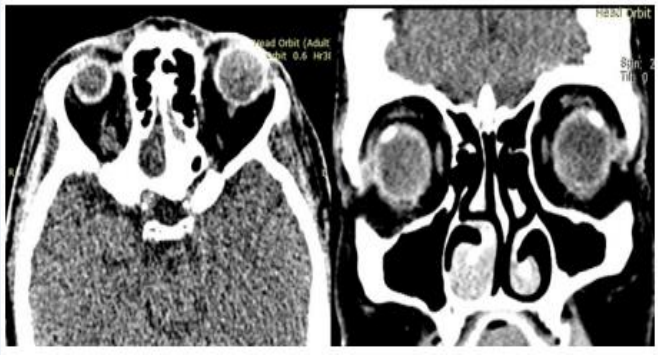

Fig. 5. Two different CT scans showed an asymmetrical and irregular calcified lesion in the posterior choroid in both supero-temporal choroids; on the right a transversal scan of the orbits, on the left sagittal scan of the orbits

DISCUSSION:

Although the literature describes choroidal osteoma as a more common one-sidedness and typical manifestation in adolescence, our case report describes bilateral choroidal osteomas in an elderly woman. The cause of choroidal osteoma is unknown.

By 10 years, the largest case series on choroidal osteoma found evidence of growth in 51% of eyes and decalcification in nearly 50% of eyes. Decalcification of choroidal osteoma was usually

associated with poor vision in their series. Decalcification is frequently associated with overlying RPE alterations and choriocapillaris atrophy, both of which can lead to photoreceptor degeneration and poor visual acuity. The decalcified portion of the osteoma had an overlying marked thinning to absent outer retina and photoreceptor layers (100%), while the calcified portion had preserved intact outer retina (95%) and intact photoreceptor layer (100%). There were no reported changes in the current case, and our patient has no vision loss. [2]

There are few treatment options for choroidal osteoma. Recently, anti-vascular endothelial growth factor drugs have been used successfully off-label to treat CNV secondary to choroidal osteoma. The condition's early detection is coincidental. Most patients present with decreased vision after significant atrophy of the retinal layers has occurred. In asymptomatic cases, proper management entails regular fundus examinations and multimodal imaging to detect the development of CNV or atrophy of retinal layers, thereby minimising vision loss. [3]

Choroidal metastasis, sclerochoroidal calcifications, amelanotic choroidal melanoma, amelanotic choroidal nevus, choroidal hemangioma, choroidal granuloma (TB, sarcoid), metastatic calcification, and dysmorphic calcification are among the differential diagnoses. The sclerochoroidal calcification in this case fits the patient's clinical characteristics because it is generally bilateral, recognised as multifocal yellowish placoid lesions in the supero-temporal and postequatorial area in asymptomatic older white individuals; however, no other ocular or systemic signs were present.

CONCLUSION:

As a result, choroidal osteoma is unique in clinics because it affects otherwise healthy eyes, as in the current patient. The case report's strengths include a rare disease process involving the choroid bilaterally without significant visual impairment, which was discovered in an elderly woman. The limitations of this case report include the lack of follow-up data because this patient had no previous visits or exams at this clinic. Six-monthly visits will be scheduled for this patient.

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