



TRABALHO FINAL

MESTRADO INTEGRADO EM MEDICINA

Clínica Universitária de Oftalmologia

Fuji Sign in Central Serous Chorioretinopathy: case series and literature review

Joana Maria Gomes Santos

Orientado por:

Prof.^ª Doutora Sara Vaz-Pereira

Coorientado por:

Dr.^ª Joana Medeiros Pinto

maio' 2024

O Trabalho Final é da exclusiva responsabilidade do seu autor, não cabendo qualquer responsabilidade à FMUL pelos conteúdos nele apresentados.

Abstract

Introduction: Central serous chorioretinopathy (CSC) is a common chorioretinal disease that is characterized by the presence of pachychoroid and subretinal fluid (SRF) in the macula, which, when persistent, leads to retinal damage and, ultimately, impaired visual function. It primarily affects young men, between 20 and 60 years old, although it is seen occasionally in older patients and females, and it is typically classified into two main subtypes, acute and chronic CSC (cCSC). Acute CSC (aCSC) is a self-limited condition with generally good recovery of visual acuity within three months, however little is known about the characteristics that can help to predict which patients may experience spontaneous SRF resolution and do not progress to cCSC. The Fuji sign is a novel morphological feature on optical coherence tomography (OCT) in which SRF has a triangular shape resembling the Japanese Mount Fuji and its presence may predict spontaneous SRF resolution.

Purpose: To review patients with CSC and explore tomographic signs that may predict spontaneous SRF resolution, namely the presence of the Fuji sign.

Methods: Retrospective case series and literature review. All patients underwent complete ophthalmologic examination and multimodal imaging with OCT, fundus autofluorescence and in selected cases fluorescein angiography.

Results: Four Caucasian men with a mean \pm SD age of 47.75 \pm 9.44 years were included, with a mean \pm SD follow-up time of 8 \pm 3.94 months. Two patients (50%) reported sporadic use of topical steroids within 3 months before the baseline visit and one patient had a pigment epithelial detachment (PED) before (25%). The right eye (OD) was the most affected eye (75%). One patient presented with aCSC (25%), while the other three had cCSC (75%). On OCT all patients had pachychoroid (100%), macular neurosensory detachment (100%) and SRF (100%). One patient had non-central PED (25%) and 1 had central PED (25%). The Fuji sign was present in 3 patients (75%), 2 in the OD and 1 in the left eye. Amongst patients with a positive Fuji Sign, spontaneous resolution occurred in 1 patient, resolution with eplerenone in 1 patient and resolution

with laser treatment in 1 patient. The patient with a negative Fuji Sign required laser treatment for resolution of the SRF.

Conclusions: Identifying predictive markers in CSC could significantly impact patient care and research. While the positive Fuji sign is notable, its presence alone does not ensure spontaneous resolution, underscoring the necessity for further research into additional markers to enhance treatment decisions and patient outcomes.

Keywords: Central Serous Chorioretinopathy; Fuji Sign; Optical Coherence Tomography; Spontaneous Resolution; Subretinal Fluid.

Resumo

Introdução: A Coriorretinopatia Serosa Central (CSC) é uma doença coriorretiniana comum que se caracteriza pela presença de paquicoroide e líquido sub-retiniano (SRF) na mácula, que, quando persistente, conduz a dano retiniano e, conseqüentemente, a alterações da função visual. Afeta principalmente homens jovens, entre 20 e 60 anos, embora seja identificada ocasionalmente em doentes mais idosos e no sexo feminino, e é tipicamente classificada em dois subtipos principais, a CSC aguda (aCSC) e crônica. A CSC aguda é uma condição autolimitada com geralmente boa recuperação da acuidade visual em três meses, porém pouco se sabe sobre as características que podem ajudar a prever quais os doentes que podem apresentar resolução espontânea do SRF e não evoluir para CSC crônica (cCSC). O sinal de Fuji é uma nova característica morfológica na tomografia de coerência ótica (OCT), na qual o SRF tem uma forma triangular semelhante ao Monte de Fuji japonês e a sua presença pode prever a resolução espontânea do SRF.

Objetivo: Analisar doentes com CSC e explorar sinais tomográficos que possam prever a resolução espontânea do SRF, nomeadamente a presença do sinal de Fuji.

Métodos: Série de casos retrospectivos e revisão da literatura. Todos os doentes foram submetidos a exame oftalmológico completo e a avaliação multimodal que incluiu OCT, autofluorescência do fundo ocular e, em casos selecionados, angiografia fluoresceínica.

Resultados: Quatro homens caucasianos com uma idade média \pm DP de 47,75 \pm 9.44 anos foram incluídos, com um tempo de seguimento médio \pm DP de 8 \pm 3,94 meses. Dois doentes (50%) relataram uso esporádico de esteroides tópicos nos 3 meses anteriores à visita inicial e um doente já teve descolamento do epitélio pigmentar (PED) antes (25%). O olho direito (OD) foi o mais afetado (75%). Um doente apresentou aCSC (25%), enquanto os outros 3 apresentaram cCSC (75%). Na OCT, todos os doentes apresentaram paquicoroide (100%), descolamento neurosensorial macular (100%) e SRF (100%). Um doente apresentou PED não central (25%) e 1 apresentou PED central (25%). O sinal de Fuji estava presente em 3 doentes (75%), 2 no OD e 1 no olho esquerdo.

Entre os doentes com sinal de Fuji positivo, a resolução espontânea ocorreu em 1 doente, resolução com eplerenona em 1 doente e resolução com tratamento a laser em 1 doente. O doente com sinal de Fuji negativo necessitou de tratamento a laser para resolução do SRF.

Conclusões: Identificar marcadores preditivos em CSC poderia impactar significativamente os tratamentos e a literatura. Embora o sinal de Fuji positivo seja notável, a sua mera presença não garante resolução espontânea, destacando a necessidade de mais pesquisas sobre marcadores adicionais para aprimorar decisões de tratamento e prognóstico.

Palavras-Chave: Coriorretinopatia Serosa Central; Sinal de Fuji; Tomografia de Coerência Ótica; Resolução Espontânea; Líquido Sub-retiniano.

Index

Abstract.....	5
Resumo	7
List of Tables	11
List of Figures	13
Introduction	17
Description of the Condition.....	17
Definition	17
Classification	18
Epidemiology	18
Etiology and Pathophysiology	18
Clinical Features and Diagnostic.....	19
Fuji Sign in Optical coherence tomography	19
Methods.....	23
Results.....	25
Case Report 1	25
Case Report 2	26
Case Report 3	27
Case Report 4	28
Summary of Cases	29
Discussion.....	31
Conclusions	33
Acknowledgments	35
References.....	37

List of Tables

Table 1. Pachychoroid Spectrum Disorders of the Macula	17
Table 2. Clinical and multimodal imaging characteristics of central serous chorioretinopathy patients during follow-up.....	29

List of Figures

Figure 1. The “Fuji sign” 20

Figure 2. Optical coherence tomography from two patients with chronic central serous chorioretinopathy. 23

Figure 3. Multiple OCT Images of OD from patient 1 with aCSC over approximately 9 months follow-up. 25

Figure 4. Serial OCT images of the OD from patient 2 with cCSC over approximately 5 months follow-up. 27

Figure 5. Serial OD OCT images from case 3 over approximately 14 months follow-up. 28

Figure 6. Multiple OCT images of the OS from case 4 with cCSC over approximately 4 months follow-up. 29

Acronyms

aCSC: Acute central serous chorioretinopathy

cCSC: Chronic central serous chorioretinopathy

CMT: Central macular thickness

CRT: Central retinal thickness

CSC: Central serous chorioretinopathy

DLS: double-layer sign

ELM: External limiting membrane

FA: Fluorescein angiography

FAF: Fundus Autofluorescence

IOP: Intraocular pressure

NSD: neurosensory detachment

OD: *Oculus dexter*

OS: *Oculus sinister*

OCT: Optical coherence tomography

PDT: Photodynamic therapy

PED: Pigment epithelial detachment

PRN: *Pro re nata*

RPE: Retinal pigment epithelium

SRF: Subretinal fluid

VA: Visual acuity

Introduction

Several studies have demonstrated that central serous chorioretinopathy (CSC) is part of a spectrum of pachychoroid disorders, including pachychoroid pigment epitheliopathy, pachychoroid neovascularopathy and pachychoroid aneurysmal type 1 choroidal neovascularization, which seem to constitute a continuous pathological process (Cheung *et al.*, 2019). In this context, Siedlecki *et al.* have proposed reclassifying the spectrum of choroidal diseases into five successive subtypes (Siedlecki *et al.*, 2019), as explained in Table 1.

Table 1. Pachychoroid Spectrum Disorders of the Macula

0	Uncomplicated pachychoroid
I	Pachychoroid pigment epitheliopathy
II	Central serous chorioretinopathy
III	Pachychoroid neovascularopathy
IIIa	With neurosensory detachment (overlap with central serous chorioretinopathy)
IIIb	Without neurosensory detachment
IV	Pachychoroid aneurysmal type 1 choroidal neovascularization (formerly polypoidal choroidal vasculopathy)

Description of the Condition

Definition

CSC is a common degenerative disease of the choroid and retina that causes impaired visual function. It is characterized by a macular neurosensory detachment (NSD) due to the presence of subretinal fluid (SRF), resulting from dysfunction of the retinal pigment epithelium (RPE) and hyperpermeability and thickening of the underlying choroid – pachychoroid (van Rijssen *et al.*, 2019).

Classification

This condition is commonly classified into two subtypes: acute CSC (aCSC), which usually resolves spontaneously within 2-3 months, and chronic CSC (cCSC), which takes longer than 3 or 6 months to resolve. The classification of this condition is based on the time required for resolution of SRF, making it temporally defined. However, there is no consensus on the exact time frame that distinguishes between acute and chronic forms (Kaye *et al.*, 2020).

Epidemiology

It mostly affects men, between 20 and 60 years old (van Rijssen *et al.*, 2019). There is an annual incidence rate of 10 per 100 000 in men with cCSC, making it six times more common in men compared to women (Wong *et al.*, 2016). Race is also a factor in CSC, with Caucasians, Hispanics, and Asians being more commonly affected, while African Americans are relatively less affected (Desal *et al.*, 2003).

This overview is essential because CSC is a widespread and vision-threatening disease, with high prevalence, following conditions like age-related macular degeneration, diabetic retinopathy, and retinal vein occlusion (Das & Das, 2017).

Etiology and Pathophysiology

The etiology of CSC has remained a mysterious disease since its initial description by Von Graefe due to the uncertainty surrounding its etiology. Von Graefe first described it in 1866 (Von Graefe, 1866) as central syphilitic retinitis, and since then, other descriptions have included capillarospastic central retinitis, central angiospastic retinopathy, central serous retinopathy, and central serous pigment epitheliopathy (Kaye *et al.*, 2020). Finally, the term central serous chorioretinopathy was introduced by several investigators due to the prominent choroidal involvement in the disease process (Cheung *et al.*, 2019).

Several risk factors for active CSC development have been identified, such as corticosteroid usage, elevated diastolic blood pressure, psychological stress, behavioral traits (Jain *et al.*, 2022), pregnancy, and endogenous Cushing's syndrome (Kaye *et al.*, 2020).

Clinical Features and Diagnostic

In acute presentation, patients usually complain about symptoms related to the NSD in the macular area: blurred vision with a relative central scotoma, metamorphopsia, moderate dyschromatopsia, micropsia, hypermetropization and reduced contrast sensitivity (Wang *et al.*, 2008).

The presence of a NSD is a sign of the acute form and the fluid usually is transparent, but occasionally can become turbid due to subretinal fibrin deposition. This fibrin sometimes gets organized to cause subretinal fibrosis, in the chronic form, leading to permanent drop in vision (Das & Das, 2017).

Diagnosis is generally straightforward, based on clinical and characteristic tomographic findings such as the presence of pachychoroid, SRF, RPE changes, and pigment epithelial detachments (PEDs). These can be observed using imaging techniques like optical coherence tomography (OCT), fundus autofluorescence (FAF) or fluorescein angiography (FA).

Fuji Sign in Optical coherence tomography

OCT is a valuable tool for diagnosing and monitoring CSC patients because it can detect and quantify pathological changes. It provides fast, high-quality, and non-invasive imaging of the retina, making it the gold standard modality for CSC follow-up (Kaye *et al.*, 2020).

One of the primary observations made by OCT is the presence of SRF, which accumulates in the macula and can also be observed in multiple areas. Another significant finding in OCT imaging is the identification of PEDs, which are commonly seen

in cases of cCSC. OCT imaging enables the identification of various types of PEDs, including dome-shaped and irregular PEDs. These PEDs exhibit a distinct appearance with hyper-reflective content overlying a thin hyper-reflective layer, forming a characteristic double-layer sign (DLS), a sign of choroidal neovascularization (Kaye *et al.*, 2020).

Recently, a new tomographic sign has been identified in CSC (Pérez-García *et al.*, 2023). The Fuji sign observed using OCT is a morphological feature that shows potential in predicting the spontaneous resolution of SRF in patients with CSC. Characterized by a distinctive SRF shape resembling the Mount Fuji (Pérez-García *et al.*, 2023), its presence can help identify CSC patients more likely to experience spontaneous resolution of SRF without treatment. This information aids in determining appropriate management strategies, such as active monitoring.

This sign is observed when the shape of the SRF, as visualized on OCT, resembles the summit of Mount Fuji in Japan (Figure 1) (Feenstra *et al.*, 2022).

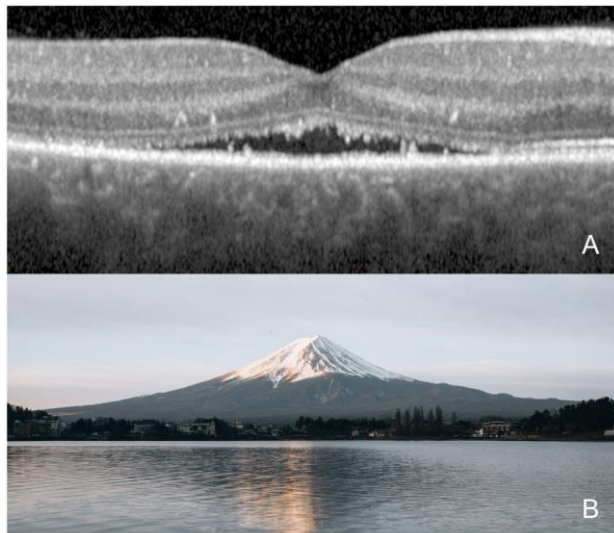


Figure 1. The “Fuji sign”: the contour of SRF on an OCT scan of a patient with cCSC resembling Mount Fuji. **A.** A standard-depth imaging OCT scan of a 35-year-old man with cCSC at baseline visit of the study. Spontaneous resolution had occurred 2 months after this OCT scan was taken. **B.** Note how the shape of the SRF on OCT and the concave lines of the external limiting membrane above resemble the slope of the mountain (Feenstra *et al.*, 2022).

The pachychoroid refers to the appearance of a thickened choroid with dilated vessels. It is associated with CSC, given the initial event in disease pathogenesis is thought to be choroidal vessel dilation and hyperpermeability (Kaye *et al.*, 2020).

We aim to review patients with CSC and explore tomographic signs that may predict spontaneous SRF resolution, with a particular focus on the presence of the Fuji sign.

Methods

Literature review and retrospective case series of 4 patients diagnosed with CSC and subfoveal SRF.

All patients underwent through a complete ophthalmologic examination, which included multimodal imaging techniques such as OCT, FAF and in selected cases FA. Additionally, a comprehensive medical history was obtained from all patients, including steroid use within 3 months before the baseline visit.

In the first step of the assessment, all images were carefully reviewed to determine the presence or absence of the Fuji sign, following the instructions indicated by Feenstra *et al.* (Feenstra *et al.*, 2022). In their research, to determine the presence of the Fuji sign they used a triangular geometric approach involving three key lines. The first line was a vertical one, from the innermost part of the ellipsoid zone to the Bruch membrane. The second line was a horizontal one, the base of the triangle. It was drawn halfway and perpendicular to the first line. The 2 legs of the triangle were drawn from the external limiting membrane (ELM), at the apex of the SRF, to the 2 points where the baseline intersected with the ELM. The Fuji sign was considered present when the ELM aligned precisely with either the intersection or lied beneath the two legs of the triangle (as depicted in Figure 2) (Pérez-García *et al.*, 2023).

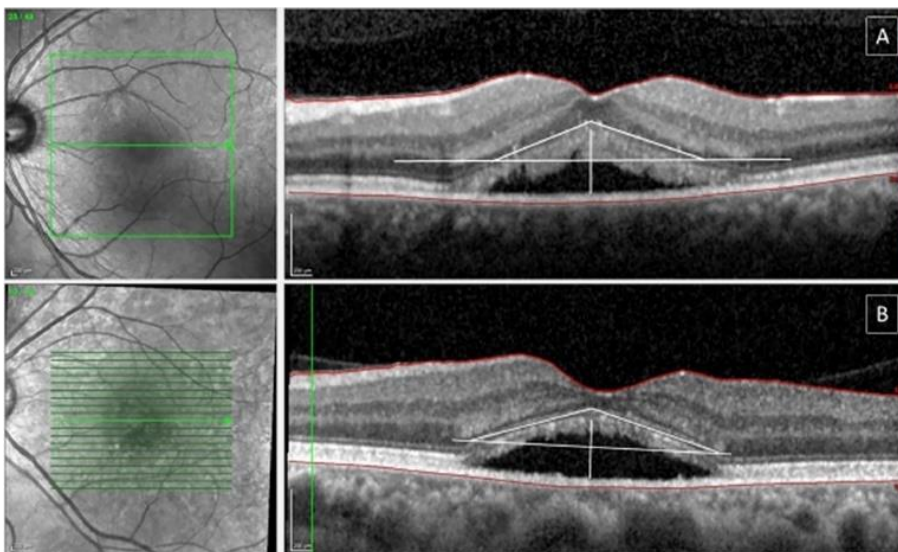


Figure 2. OCT from two patients with cCSC. **A.** Positive Fuji sign: appreciate the ELM overlapping the line from the ELM at the apex of the SRF to the point in which the ELM intersects with the

horizontal line. **B.** Negative Fuji sign: the ELM is above the sides of the triangle (Feenstra et al., 2022).

Results

Four patients with CSC and foveal NSD were included and are described below.

Case Report 1

A 41-year-old Caucasian man with sporadic use of topical corticosteroids in the external auditory canal and a previous tomographic diagnosis of a PED in his right eye (OD) was observed at the emergency department due to recent onset of a central scotoma in the same eye.

On examination, OD visual acuity (VA) was 4/10, while the left eye (OS) had a VA of 8/10. Intraocular pressure (IOP) readings for both eyes were recorded, respectively 21 mmHg OD and 15 mmHg OS. Anterior segment biomicroscopy was unremarkable. Fundus examination revealed a central NSD in OD, confirmed by OCT, with a central macular thickness (CMT) of 530 μm , a positive Fuji sign (Figure 3) and pachychoroid in accordance with CSC.

The patient's management plan included ongoing surveillance through subsequent consultations until the presence of SRF was completely resolved, as evident in the panel C of Figure 3. Additionally, the patient was also advised to discontinue topical corticosteroids, if possible, to minimize the risk of recurrence in CSC.

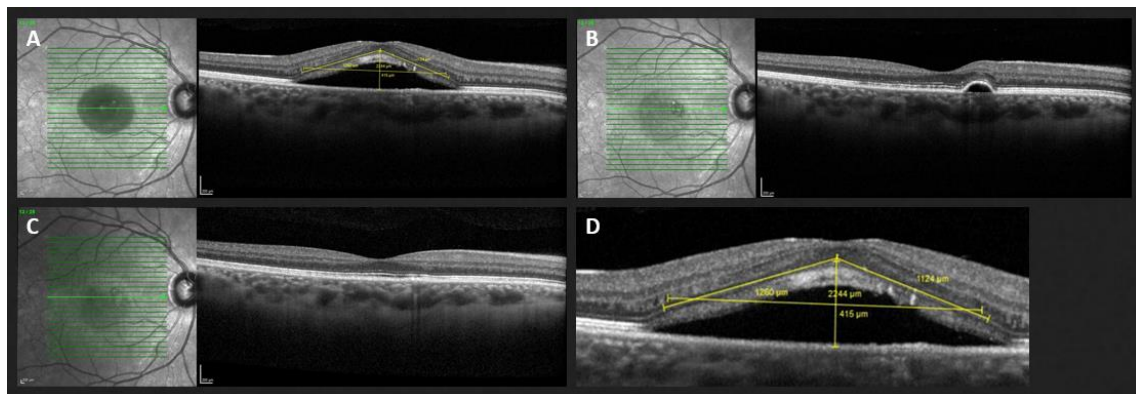


Figure 3. Multiple OCT Images of OD from patient 1 with aCSC over approximately 9 months follow-up. **A.** Positive Fuji sign: appreciate the ELM overlapping the line from the ELM at the apex of the SRF to the point in which the ELM intersects with the horizontal line (baseline). **B.** Note the

decrease in SRF and significant improvement and the presence of one PED nasal to the fovea (3 months follow-up). **C.** Absence of SRF and complete resolution at 9 months follow-up. **D.** Close-up of the measurement of the Fuji sign. The yellow arrows shows the ELM overlapping the line from the ELM at the apex of the SRF to the point in which the ELM intersects with the horizontal (baseline), resulting in a positive Fuji sign.

Case Report 2

A 56-year-old otherwise healthy Caucasian man, with *pro re nata* (PRN) use of topical corticosteroids on the skin and a personal ophthalmological history of hyperopia had been previously followed in other institution due to CSC. His symptoms included blurry vision and decreased VA in OD accompanied by significant difficulty in focusing on objects, which had worsened over 2 months.

On observation conducted 7 months after the beginning of symptoms, the following findings were noted: best corrected VA in OD was 8/10, while in OS was 10/10. IOP and slit-lamp examination were unremarkable. Funduscopy showed a loss of fundus tessellation and no other abnormalities in OS but the OD had an altered foveal reflex. OCT of OD showed pachychoroid, a non-central pigment epithelium detachment, a CMT of 336 μm and the presence of macular SRF, as evident in the panel A of Figure 4, with a negative Fuji sign, since the ELM was above the sides of the triangle.

FA identified a leakage point in the superior nasal macular area. The management included thermal laser on the leaking point. At 2 months follow-up, after thermal laser, there was complete resolution of SRF, with a CMT of 236 μm , and resolution of symptoms, as evident in the panel D of Figure 4.

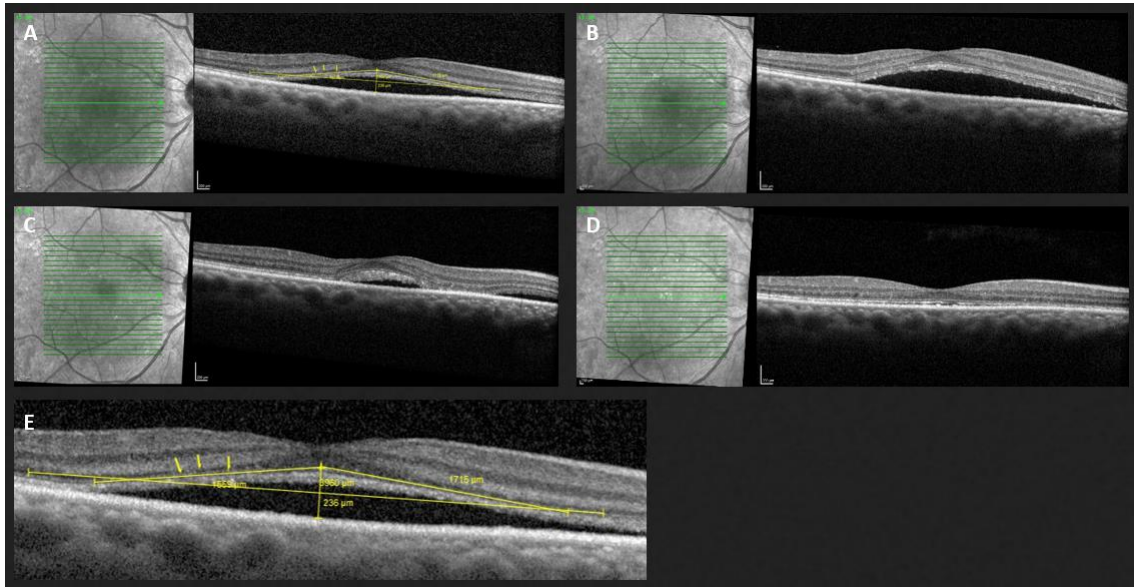


Figure 4. Serial OCT images of the OD from patient 2 with cCSC over approximately 5 months follow-up. **A.** Negative Fuji sign: the ELM is above the sides of the triangle (7 months after presentation of CSC). **B.** Decrease in SRF (8 months after presentation). **C.** Persistence of SRF at 10 months follow-up. **D.** Absence of SRF and resolution (2 months after thermal laser). **E.** Close-up of the measurement of the Fuji sign. The yellow arrows shows the ELM above the sides of the triangle, resulting in a negative Fuji sign.

Case Report 3

A 58-year-old Caucasian man, with a personal ophthalmic history of myopia and no other relevant medical history was observed. CSC was detected in OD, with worsening during subsequent visits. Best corrected VA was 5/10 OD and 10/10 OS. IOP was 16 mmHg bilaterally and the anterior segment showed no abnormalities. Funduscopy examination revealed an upper temporal hypopigmented area near the fovea in OD and a hypopigmented area superior to the fovea in OS. The OCT showed in OD a subfoveal NSD, an area of outer retinal layer disorganization superotemporal to the fovea, a PED, and pachychoroid, as evident in panel A of Figure 5, with a positive Fuji sign; OS showed pachychoroid.

The management plan included surveillance through scheduled follow-up appointments. Photodynamic therapy (PDT) was recommended for OD due to persistent SRF but, because of PDT unavailability, eplerenone 50 mg/day was tried for 8 months.

There was total resolution of SRF 14 months after the diagnosis of CSC (7 months after the beginning of eplerenone) (Figure 5D) and the VA improved to 10/10.

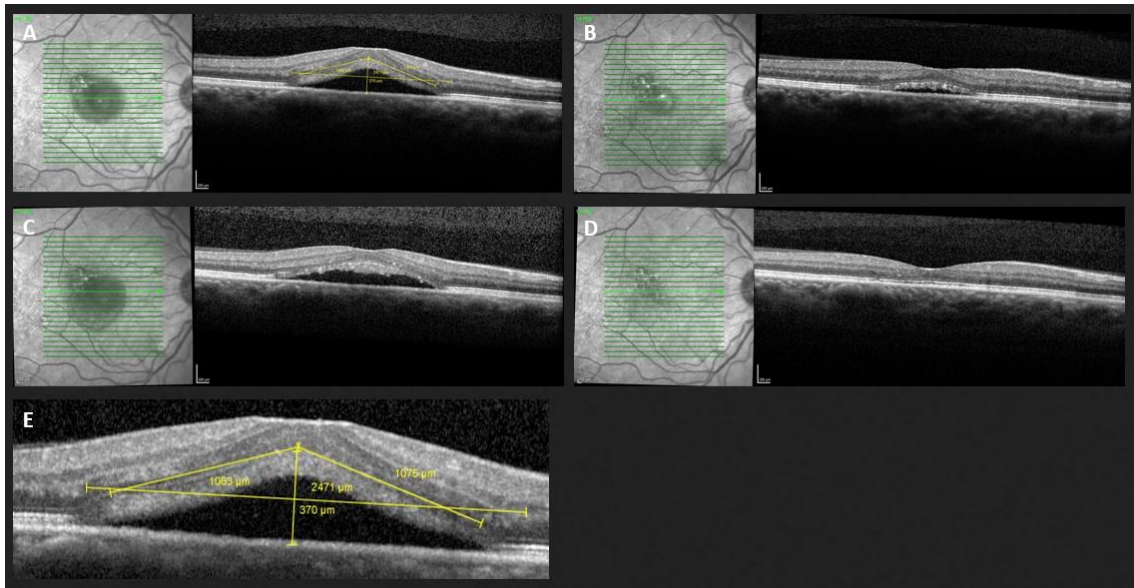


Figure 5. Serial OD OCT images from case 3 over approximately 14 months follow-up. **A.** Positive Fuji sign: appreciate the ELM under the lines from the ELM at the apex of the SRF to the point in which the ELM intersects with the horizontal line (baseline). **B.** Decrease in SRF (1 month follow-up after the diagnosis of CSC). **C.** Increase in SRF (7 months follow-up after the diagnosis of CSC). **D.** Absence of SRF and resolution (14 months follow-up after the diagnosis of CSC and 7 months follow-up after the beginning of eplerenone). **E.** Close-up of the measurement of the Fuji sign. The yellow arrows shows the ELM overlapping the line from the ELM at the apex of the SRF to the point in which the ELM intersects with the horizontal (baseline), resulting in a positive Fuji sign.

Case Report 4

A 36-year-old Caucasian man with no regular medications and no pertinent personal ophthalmic or medical history, had been attending ophthalmology appointments elsewhere for OS CSC. On observation, conducted 6 months after the beginning of symptoms, the following findings were noted: corrected VA was 10/10 OD and 6/10 OS and funduscopy showed loss of fundus tessellation for both eyes. The OCT of the OS revealed pachychoroid, persistence of SRF and a central NSD with CMT of 463 μm, as evident in the panel A of Figure 6, that illustrates a positive Fuji sign.

FA revealed no abnormalities in the OD, while in the OS confirmed a leakage point superior to the macula. At 7 months follow up, the management included thermal laser on the leak point in the OS, resulting in decreased SRF, as evident in the panel B of Figure 6. Subsequently, 2 months after, it showed complete resolution, (Figure 6C), with a CMT of 283 μm , and a VA recovery to 10/10.

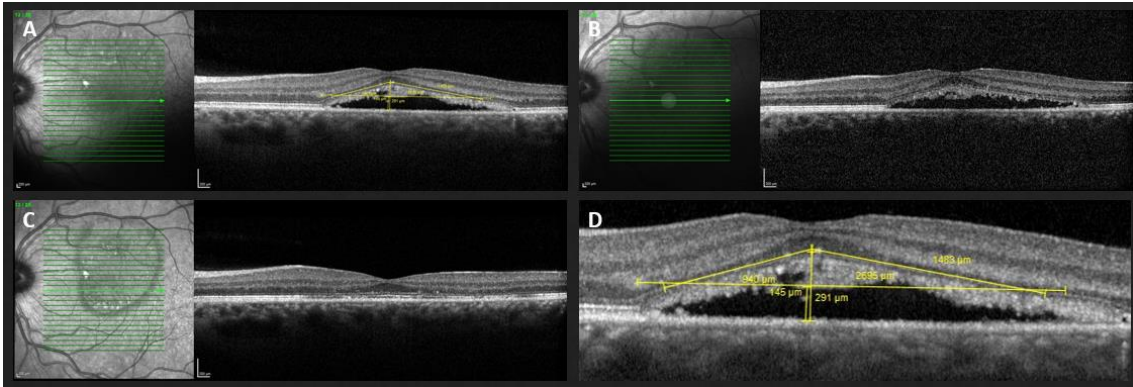


Figure 6. Multiple OCT images of the OS from case 4 with cCSC over approximately 4 months follow-up. **A.** Positive Fuji sign: appreciate the ELM under the lines from the ELM at the apex of the SRF to the point in which the ELM intersects with the horizontal line (6 months after presentation of CSC). **B.** Decreased in SRF (7 months after presentation of CSC). **C.** Absence of SRF and resolution (2 months after laser treatment). **D.** Close-up of the measurement of the Fuji sign. The yellow arrows shows the ELM overlapping the line from the ELM at the apex of the SRF to the point in which the ELM intersects with the horizontal (baseline), resulting in a positive Fuji sign.

Summary of Cases

The clinical and multimodal imaging characteristics of the 4 CSC patients included are summarized in Table 2. Patients mean \pm SD age was 47.75 \pm 9.44 years, and all patients were Caucasian men. Mean follow-up \pm SD time was 8 \pm 3.94 months. Two patients (50%) reported sporadic use of topical steroids within 3 months before the baseline visit and one patient had a PED before (25%). The right eye was the most affected eye (75%). One patient presented with acute CSC (25%), while the other three had chronic CSC (75%).

The OCT findings observed across the 4 cases of these patients varied. All patients had pachychoroid (100%), NSD (100%) and SRF (100%). One patient had non-central PED (25%) and 1 had central PED (25%). The Fuji sign was present in 3 patients

(75%), 2 in the OD and 1 in the OS. Amongst patients with a positive Fuji Sign, spontaneous resolution occurred in 1 patient, resolution with eplerenone in 1 patient and resolution with laser treatment in 1 patient. The patient with a negative Fuji Sign required laser treatment for resolution of the SRF.

Table 2. Clinical and multimodal imaging characteristics of patients during follow-up

Patient	1	2	3	4
Age (years)	41	56	58	36
Gender	Male	Male	Male	Male
Ethnicity	Caucasian	Caucasian	Caucasian	Caucasian
Follow up time (months)	9	5	14	4
Steroid use	Yes, sporadic	Yes, sporadic	No	No
Laterality (eye)	Right	Right	Right	Left
CSC subtypes	Acute	Chronic	Chronic	Chronic
Fuji Sign	Positive	Negative	Positive	Positive
Eplerenone use	No	No	Yes	No
Laser treatment	No	Yes	No	Yes
Spontaneous resolution	Yes	No	No	No
Resolution of the SRF	Complete	Complete	Complete	Complete

CSC, central serous coriorretinopathy; SRF, subretinal fluid

Discussion

The presence of a Fuji sign has been described as tomographic marker with potential to predict the spontaneous resolution of SRF in patients with CSC (Feenstra *et al.*, 2022). Among the 4 patients in this study, 3 exhibited a positive Fuji sign and from those 3, only one experienced spontaneous resolution without treatment (25%), the one with aCSC, which aligns with the anticipated higher occurrence of spontaneous resolution in acute cases. The lower rate of SRF resolution in cCSC cases was anticipated, since the findings of the Feenstra *et al.* study revealed that in untreated disease for more than 4 months, complete SRF resolution after 12 months occurred in just 30% of patients with a positive Fuji sign, in a sample of 38 patients with cCSC, previously untreated and in the placebo treatment.

The present study included two patients that underwent laser treatment (one with negative and one with positive Fuji Sign) and one patient that received eplerenone (with a positive Fuji Sign). It is important to note that in the Feenstra *et al.* study, the Fuji sign was also observed in 13.2% of treated patients. Despite controversies surrounding the effectiveness of eplerenone, whether it truly has any effect or if resolution would have occurred spontaneously, the Iqbal *et al.* article revealed that the treatment with eplerenone failed to decrease SRF height and does not bring any significant improvement in the VA of patients, additionally it had some mild adverse effects that include hypertension, abdominal cramps, nausea, and migraine (Iqbal *et al.*, 2021).

Although treatment can often accelerate visual recovery in CSC, it is important to understand that it does not guarantee the optimization of the final visual outcome. Nonetheless, early intervention is recommended in cases where prompt restoration of vision is crucial for vocational purposes or if untreated CSC has previously resulted in unfavorable visual outcomes in the other eye (Wong *et al.*, 2016). The Pérez-García *et al.* study (Pérez-García *et al.*, 2023), comprising 130 patients with cCSC, reported a global SRF resolution rate of 75.55% with PDT. However, only 58.3% (7/12) of those with a positive Fuji sign showed improvement post-PDT, suggesting that the Fuji sign does not

predict therapy response. Notably, Fuji sign is an uncommon OCT finding in cCSC and does not correlate with enhanced PDT outcomes.

CSC is a highly heterogeneous and multifactorial entity, influenced by factors not explored in this work or the Feenstra *et al.* study. These unexplored factors, such as stress levels, psychological profile, genetic predisposition, corticosteroid treatments, refractive error, or the recently described scleral thickness and intervortex venous anastomosis, could explain the observed differences (Pérez-García *et al.*, 2023).

In many instances, spontaneous resolution and improvement in VA are attainable. Nevertheless, even when VA is restored to 20/20 or higher, some patients may continue to experience residual changes. The factors associated with declining VA include persistence of RPE detachment or SRF, recurrent episodes and the emergence of submacular choroidal neovascularization (Quintão *et al.*, 2023).

The present study has limitations such as its retrospective nature, limited sample size, finite follow-up duration and the treatments used. However, it underscores the multifactorial nature of CSC, emphasizing the need for additional comprehensive investigations given its limited sample size. While the Fuji sign can be easily identified in clinical practice through measurements, its practical utility seems limited, as it did not provide significant insight or clarity.

Conclusions

In conclusion, identifying predictive markers would have significant implications for clinical practice, patient management, and further research. The purpose of this study was to review patients with CSC and examine tomographic signs, particularly the presence of the Fuji sign, as potential predictors of SRF resolution.

Overall, the positive Fuji sign in 75% of CSC cases was considered a relevant tomographic marker. However, due to the small sample size, drawing definitive conclusions is limited, and the isolated presence of the Fuji sign did not guarantee spontaneous resolution. Furthermore, recognizing additional factors, such as psychological profile, genetic predisposition, corticosteroid treatments, and other potential markers, highlights the complexity of CSC and the necessity for a holistic approach to its diagnosis and management.

Moving forward, efforts should be directed toward larger-scale studies with longer follow-up periods, standardized treatment protocols, and comprehensive assessment of patient characteristics. Such endeavors are crucial in elucidating the role of the Fuji sign and other potential markers in predicting treatment response and long-term visual outcomes in CSC patients. By addressing these gaps in knowledge, we can enhance our ability to tailor individualized treatment strategies and optimize visual outcomes for patients affected by this multifaceted condition.

Acknowledgments

Firstly, I would like to express my gratitude to Prof. Doutora Sara Vaz-Pereira and Dr. ^a Joana Medeiros Pinto for their invaluable time, guidance, support, and knowledge in developing this work. Their support, knowledge, and expertise were indispensable for the success of this thesis project. I am thankful for the opportunity to work on this thesis project in their area of expertise.

I'd also like to express my gratitude to Prof. Doutor Carlos Marques Neves, Head of the Ophthalmology Department at Faculdade de Medicina da Universidade de Lisboa (FMUL) for generously allowing the project, providing access to department facilities, and facilitating patient contact. The favorable conditions offered by the department significantly contributed to the ongoing development of this thesis.

Furthermore, I appreciate FMUL for the years of medical and academic education, offering opportunities for growth from a high school student to a medical student.

Lastly, I would like to express my heartfelt thanks to my family and friends for their unwavering support, enthusiasm, and inspiration since the inception of my dream to become a doctor. They continuously provide me with the strength to pursue and achieve my goals.

References

- Cheung, C. M., Lee, W. K., Koizumi, H., Dansingani, K., Lai, T. Y. Y., & Freund, K. B. (2019). Pachychoroid disease. In *Eye (Basingstoke)* (Vol. 33, Issue 1, pp. 14–33). Nature Publishing Group. <https://doi.org/10.1038/s41433-018-0158-4>
- Das, S., & Das, D. (2017). Central serous chorioretinopathy (CSC). *Scientific Journal of Medical & Vision Research Foundations*, 35(3), 10–20. https://sankaranethralaya.org/pdf/publication/insight_october_2017.pdf
- Desal, U. R., Alhalel, A. A., Campen, T. J., Schiffman, R. M., Edwards, P. A., & Jacobsen, G. R. (2003). Ford Health System are comparable in African Americans and Caucasians. In *J Natl Med Assoc* (Vol. 95).
- Feenstra, H. M. A., Hensman, J., Gkika, T., Lipkova, V., Hoyng, C. B., Diederens, R. M. H., Schlingemann, R. O., Downes, S. M., van Dijk, E. H. C., & Boon, C. J. F. (2022). Spontaneous Resolution of Chronic Central Serous Chorioretinopathy: “Fuji Sign.” *Ophthalmology Retina*, 6(9), 861–863. <https://doi.org/10.1016/j.oret.2022.04.023>
- Iqbal, F., Iqbal, K., Inayat, B., Arjumand, S., Ghafoor, Z., Sattar, W., & Abbas, K. (2021). Eplerenone Treatment in Chronic Central Serous Chorioretinopathy. *Cureus*. <https://doi.org/10.7759/cureus.18415>
- Jain, M., Mohan, S., & Van Dijk, E. H. C. (2022). Central serous chorioretinopathy: Pathophysiology, systemic associations, and a novel etiological classification. In *Taiwan Journal of Ophthalmology* (Vol. 12, Issue 4, pp. 381–393). Wolters Kluwer Medknow Publications. <https://doi.org/10.4103/2211-5056.362601>
- Kaye, R., Chandra, S., Sheth, J., Boon, C. J. F., Sivaprasad, S., & Lotery, A. (2020). Central serous chorioretinopathy: An update on risk factors, pathophysiology and imaging modalities. In *Progress in Retinal and Eye Research* (Vol. 79). Elsevier Ltd. <https://doi.org/10.1016/j.preteyeres.2020.100865>
- Pérez-García, P., Oribio-Quinto, C., Gómez-Calleja, V., Moreno-Morillo, F. J., Burgos-Blasco, B., & Fernández-Vigo, J. I. (2023). Fuji sign: Prevalence and predictive power to photodynamic therapy in chronic central serous chorioretinopathy. *Photodiagnosis and Photodynamic Therapy*, 42. <https://doi.org/10.1016/j.pdpdt.2023.103316>
- Quintão, T., Furtado, M. J., & Vaz-Pereira, S. (2023). *25 Perguntas e Respostas sobre Paquicoroide* (AOGER - Associação de Oftalmologistas para o Estudo da Retina, Ed.; 1st ed.). GER - Grupo de Estudos da Retina.
- Siedlecki, J., Schworm, B., & Priglinger, S. G. (2019). The Pachychoroid Disease Spectrum—and the Need for a Uniform Classification System. In *Ophthalmology Retina* (Vol. 3, Issue 12, pp. 1013–1015). Elsevier Inc. <https://doi.org/10.1016/j.oret.2019.08.002>
- van Rijssen, T. J., van Dijk, E. H. C., Yzer, S., Ohno-Matsui, K., Keunen, J. E. E., Schlingemann, R. O., Sivaprasad, S., Querques, G., Downes, S. M., Fauser, S., Hoyng, C. B., Piccolino, F. C., Chhablani, J. K., Lai, T. Y. Y., Lotery, A. J., Larsen, M., Holz, F. G., Freund, K. B., Yannuzzi, L. A., & Boon, C. J. F. (2019). Central serous chorioretinopathy: Towards an evidence-based

treatment guideline. In *Progress in Retinal and Eye Research* (Vol. 73). Elsevier Ltd.
<https://doi.org/10.1016/j.preteyeres.2019.07.003>

Von Graefe, Albrecht. (1866). Ueber centrale recidivierende retinitis. *Graefes Arch Clin Exp Ophthalmol*, 12(12), 211–215.

Wang, M., Munch, I. C., Hasler, P. W., Prünke, C., & Larsen, M. (2008). Central serous chorioretinopathy. In *Acta ophthalmologica* (Vol. 86, Issue 2, pp. 126–145).
<https://doi.org/10.1111/j.1600-0420.2007.00889.x>

Wong, K. H., Lau, K. P., Chhablani, J., Tao, Y., Li, Q., & Wong, I. Y. (2016). Central serous chorioretinopathy: What we have learnt so far. In *Acta Ophthalmologica* (Vol. 94, Issue 4, pp. 321–325). Blackwell Publishing Ltd. <https://doi.org/10.1111/aos.12779>