Original Article

Macular Telangiectasia Type 2: Long-Term Disease Progression and Management of Complications

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Abstract

Objectives: To evaluate the long-term progression of macular telangiectasia type 2 (MacTel) using a standardized classification system and to assess the incidence, progression, and management strategies of complications such as macular neovascularization (MNV) and macular hole (MH).

Materials and Methods: This retrospective study analyzed the medical records of patients diagnosed with MacTel at a tertiary referral center in Türkiye from January 2004 to February 2025. Patients with a minimum follow-up of 3 years and no confounding macular pathologies were included. Data collection included best corrected visual acuity (BCVA), multimodal imaging (optical coherence tomography [OCT], fundus autofluorescence, fluorescein angiography), and demographic variables. Disease severity was classified using the MacTel Classification System developed by Chew et al. Longitudinal changes in BCVA and OCT parameters were statistically analyzed.

Results: A total of 184 eyes from 94 patients (mean age: 63.89±9.98 years; mean follow-up: 79.27±50.69 months) were included. A significant decline in BCVA was observed ($p<0.001$). MNV was present in 29 eyes (15.8%), with 18 receiving intravitreal anti-vascular endothelial growth factor (anti-VEGF) therapy (mean injections: 5.89±3.72). While post-treatment BCVA showed improvement ($p<0.001$), long-term visual outcomes were not significantly different from baseline ($p=0.213$). MH formation occurred in 8 eyes (4.3%), with 6 undergoing successful surgical closure. Structural retinal changes, including ellipsoid zone disruption and pigmentation, significantly progressed over time ($p<0.001$).

Conclusion: MacTel demonstrates a progressive decline in visual and structural integrity over extended follow-up. While anti-VEGF therapy offers short-term benefits for MNV, its long-term efficacy remains limited. MH development, though rare, poses a significant challenge, with variable surgical outcomes.

Keywords: Macular telangiectasia type 2, macular neovascularization, macular hole

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Introduction

Macular telangiectasia type 2 (MacTel), also known as idiopathic juxtafoveal telangiectasia, is a progressive bilateral retinal disorder. The condition typically manifests in individuals over the age of 40 and is more prevalent in females.[1] The characteristic retinal pathology of MacTel typically begins in the parafoveal temporal region and progresses superiorly and nasally, often with loss of retinal transparency, discontinuity of the ellipsoid zone (EZ), and the presence of right-angled venules (RAVs). As the disease progresses, complications such as macular neovascularization (MNV), central pigmentation, and full-thickness macular hole (MH) may develop, reflecting the progressive and degenerative nature of the disease.[2,3] Though identified in the 1980s, the natural progression and underlying etiology of MacTel remain poorly understood despite its significant impact on vision. Knowledge regarding the disease's long-term course and causative mechanisms is also limited.[4]

Complications such as MNV and MHs are associated with the progression of the disease. The development of MNV in particular can lead to significant visual loss. While short-term clinical studies have demonstrated the benefit of anti-vascular endothelial growth factor (anti-VEGF) therapies in the treatment of MacTel-associated MNV, the long-term efficacy of these interventions has not yet been fully determined.[5] Meanwhile, the occurrence of MHs, although very rare, poses a significant challenge; considerable heterogeneity in functional and anatomical outcomes has been reported following surgical treatment.[6] Given the slow and long-term nature of the

condition, it is essential that longitudinal studies are conducted to delineate the disease's progression and evaluate the long-term efficacy of therapeutic modalities.

The objective of this study was to examine the natural progression of MacTel over an extended period of time and to propose a management strategy for the associated complications.

Materials and Methods

A retrospective analysis of medical records was performed at a tertiary referral center in Türkiye, with the approval of the Ethics Committee of Hamidiye Scientific Research, University of Health Sciences (approval number 12/4, date: 17.10.2024). The study was executed in accordance with the Declaration of Helsinki. The requirement for informed consent was not applicable to this retrospective study, as it employed anonymized archival data.

Medical records from January 2004 to February 2025 were evaluated. The sample included individuals diagnosed with MacTel with a minimum of 3 years of follow-up data. Patients with concomitant macular pathologies that could interfere with the assessment of MacTel, and those whose diagnosis was uncertain due to overlapping clinical features were excluded from the study. Patients with a history of tamoxifen use were also excluded to avoid potential diagnostic overlap with tamoxifen-associated retinopathy. Additionally, patients with media opacities that impeded the acquisition of high-quality optical coherence tomography (OCT) scans for reliable analysis were not included.

The diagnosis of MacTel was made based on the presence of characteristic clinical features identified through biomicroscopic examination, fluorescein angiography (FA), and OCT. The presence of diabetes mellitus (DM) and hypertension was confirmed by the current use of prescribed medications.

The following data were collected: age, sex, baseline and final best corrected visual acuity (BCVA) measured using Snellen, follow-up time (months), and diagnoses of DM and hypertension. Fundus photography, FA, fundus autofluorescence (FAF), and OCT images from baseline and final visits were assessed. Snellen BCVA was converted to logarithm of the minimum angle of resolution (logMAR) units for statistical analysis. Fundus photographs obtained during routine clinical examinations were captured using the TRC 50DX retinal camera (Topcon, Tokyo, Japan). OCT, FAF, and FA images acquired with the Spectralis HRA system (Heidelberg Engineering, Heidelberg, Germany) were retrospectively analyzed from records.

OCT imaging was employed to evaluate structural features, including pigmentation, hyperreflectivity, the inner limiting membrane (ILM) drape sign, hyporeflective cavities, disruption of the EZ, and measurements of subfoveal choroidal thickness (SFCT) and central macular thickness. SFCT was measured using enhanced depth imaging OCT scans. SFCT was manually delineated from Bruch's membrane to the inner scleral surface beneath the fovea using Heidelberg Spectralis software. FA was employed to evaluate late leakage, while FAF images were analyzed for the presence of focal hypo-autofluorescence—indicative of pigment migration—and increased FAF signal in the foveal area.

The classification of patients with MacTel was based on the MacTel Classification System, developed by Chew et al.[3] as part of the MacTel Project. This standardized 7-grade system was applied to eyes with a confirmed diagnosis using multimodal ocular imaging, including OCT, FAF, FA, and color fundus photography. Disease severity was stratified according to key imaging biomarkers associated with decline in visual acuity, such as EZ loss, pigmentary changes, and OCT hyperreflectivity. Eyes classified as Grade 0 exhibited diagnostic features of MacTel without significant risk factors for vision loss, whereas higher grades (1–6) corresponded to increasing structural disruption and functional impairment. Furthermore, the development of full-thickness MHs and MNV was assessed using OCT, FA, and/or OCT angiography. EZ integrity was assessed using OCT with Heidelberg Eye Explorer software (Heyex, version 6.0.13.0, Heidelberg Engineering). The B-scan traversing the foveal center was selected, and EZ break length was measured in micrometers.

Statistical Analysis

Statistical analyses were performed using SPSS version 24 (IBM Corp., Armonk, NY, USA). Continuous variables were tested for normality using the Shapiro-Wilk test. Normally distributed variables were expressed as mean ± standard deviation (SD), while non-normally distributed variables were presented as median (interquartile range). Categorical variables were summarized as frequencies and percentages. Categorical variables were analyzed using the chi-squared or Fisher's exact test, as appropriate. Longitudinal changes in BCVA and OCT parameters were evaluated using the paired t-test for normally distributed data or the Wilcoxon signed-rank test for non-normally distributed data. A p value <0.05 was considered statistically significant.

Results

A total of 184 eyes from 94 patients were analyzed with a mean follow-up period of 79.27±50.69 months. The minimum follow-up duration was 3 years. The male-to-female ratio was 35 (37.2%) to 59 (62.8%). The mean age of the study cohort was 63.89±9.98 years. DM was present in 37 patients (39.4%) and hypertension in 30 (31.9%). Eight patients (8.51%) were identified as having mild non-proliferative diabetic retinopathy (DR). Proliferative DR was not observed in any of the patients.

The mean logMAR BCVA at presentation was 0.47±0.41. The most frequently observed clinical findings were loss of retinal transparency (91.8%) and the presence of RAVs (90.8%) (Figure 1). However, it should be noted that the assessment of retinal transparency was not discernible in a subset of patients due to confounding factors, such as the presence of MNV and pigmentary plaques. Other common clinical findings included the presence of hyporeflective retinal cavities (60.9%), the

ILM drape sign (50%), OCT hyperreflectivity (34.2%), and hyperreflective retinal pigment clumps (23.9%). In 125 of 135 eyes with available FA examinations, leakage was observed in the late stages. A total of 142 eyes were evaluated with FAF imaging. Hypofluorescence was identified in 47.18% (n=67) and hyperfluorescence in 52.82% (n=75) of these eyes.

Table 1 illustrates the classifications of patients at baseline and final visit according to the MacTel Classification System developed by Chew et al.[3] Table 2 compares the clinical and imaging findings obtained at baseline and final visit.

In the baseline examination, 155 (84.2%) of the analyzed eyes exhibited non-proliferative MacTel. Meanwhile, 29 (15.8%)

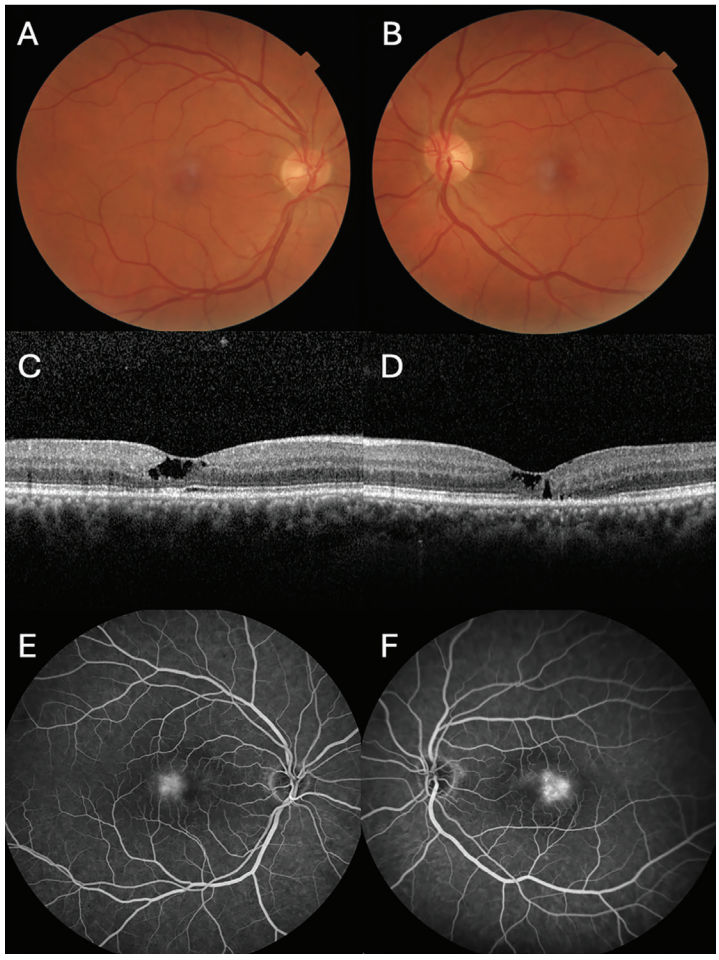

Figure 1. Fundus photographs (A, B), optical coherence tomography (OCT) images (C, D), and fluorescein angiography (E, F) of a patient with macular telangiectasia type 2. The fundus images reveal a loss of retinal transparency temporal to the fovea, accompanied by angiographic leakage. OCT images demonstrate hyporeflective cavities in both the inner and outer retina. A central hyporeflective inner retinal cavity is observed at the foveal center, with an overlying internal limiting membrane drape

Table 1. Distribution of eyes classified according to the MacTel Classification System (Chew et al.[3]) at baseline and final visits

Stage	Classification of macular telangiectasia type 2 (MacTel)	Number of eyes at baseline visit (%)	Number of eyes at final visit (%)
0	No EZ break/no pigmentation/no OCT HR	26 (14.1)	17 (9.2)
1	Non-central EZ break/no pigment/no Oct HR	30 (16.3)	10 (5.4)
2	Central EZ break/no pigment/no OCT HR	62 (33.7)	49 (26.6)
3	Non-central pigment/no, non-central or central EZ loss/no OCT HR	4 (2.2)	8 (4.3)
4	OCT HR/EZ break (either central or non-central)/no pigment	37 (20.1)	29 (15.8)
5	Central pigment/no exudative neovascularization/EZ present or not gradable	9 (4.9)	42 (22.8)
6	Neovascularization (exudative) ± central pigment	16 (8.7)	29 (15.8)

EZ: Ellipsoid zone, HR: Hyperreflectivity, OCT: Optical coherence tomography

presented with MNV, of which 18 had active MNV and 11 had scarred lesions. Of the 18 patients who underwent intravitreal anti-VEGF treatment for active MNV, 7 received bevacizumab (Avastin, Genentech, South San Francisco, CA, USA), 3 received aflibercept (Eylea, Regeneron Pharmaceuticals, Tarrytown, NY, USA), and 8 received ranibizumab (Lucentis, Novartis, Basel, Switzerland). The mean number of injections administered was 5.89±3.72; the mean follow-up period of these patients was 129.17±56.48 months. A comparison of baseline and post-injection visual acuity in the 18 treated patients revealed a statistically significant improvement in BCVA following intervention (baseline: 0.80±0.39; post-injection: 0.61±0.35; p<0.001). However, no significant difference was observed between baseline and final BCVA at the end of the follow-up period (baseline: 0.80±0.39; final: 0.94±0.58; p=0.213).

MH formation was observed in 8 patients during the follow-up period. Surgery was not performed in 2 patients, as visual improvement was deemed unlikely due to the presence of scarring. The characteristics, surgical procedures, and postoperative outcomes of the 6 patients who underwent surgery are presented in Table 3. Following surgery, MH closure was achieved in all patients, with improved BCVA observed in 5 patients. However, at the final follow-up visits, a decline in visual acuity was noted due to progression associated with MacTel. A representative case is presented in Figure 2.

Discussion

The present study presents a large cohort with extended follow-up durations, utilizing a multimodal imaging-based classification to assess MacTel type 2. A significant decline in BCVA was observed in the overall cohort between the baseline and final visits (p<0.001). MNV was present in 15.8% of patients, and notably, MH formation developed in 8 eyes of 8 patients (4.3%) during the follow-up period.

The proposed classification system for MacTel developed by Chew et al.[3] offers several significant advantages over previous models through the incorporation of objective, image-based criteria that directly correlate with disease progression and visual acuity loss. Utilizing SD-OCT findings such as EZ discontinuity, hyperpigmentation, and OCT hyperreflectivity, the system provides a reproducible and quantifiable method for staging. In contrast to the Gass-Blodi classification,[7] which relies primarily on vascular features, the current model emphasizes structural retinal changes that have a direct impact on visual acuity, providing increased clinical relevance. The simplified grading scale further facilitates practical use in routine ophthalmic examinations, enabling earlier detection and more accurate prognostication.[3] Its adoption in recent studies underscores its growing recognition and clinical applicability.[2,8,9]

As demonstrated by Chew et al.[3], the central EZ break is a critical factor contributing to reduced visual acuity. In the present study, 30.4% of patients were classified as stage 0 or 1,

Table 2. Comparison of optical coherence tomography findings and best-corrected visual acuity at baseline and final visits

	Baseline visit	Final visit	p value
Mean logMAR visual acuity (Snellen equivalent)	0.47±0.41	0.64±0.48	**<0.001***
Central macular thickness (μm)	247.93±36.84	243.16±54.66	0.193*
Subfoveal choroidal thickness (μm)	294.84±61.64	290.97±64.44	0.298*
Ellipsoid zone break length (μm)	1087.06±873.35	1514.53±1015.64	**<0.001***
Pigmentation (n, %)	44 (23.9%)	96 (52.2%)	**<0.001¶**
Hyperreflective retinal dots (n, %)	63 (34.2%)	93 (50.5%)	**<0.001¶**
Hyporeflective retinal cavities (n, %)	112 (60.9%)	93 (50.5%)	**<0.001¶**

*Paired t-test, ¶Fisher's exact test, logMAR: Logarithm of the minimum angle of resolution

Table 3. Patient characteristics, surgical procedures, and postoperative outcomes for macular holes associated with macular telangiectasia type 2

Patient ID	Age	Sex	Preop BCVA (logMAR)	Surgery	Postop BCVA (logMAR)	Final BCVA (logMAR)	Final outcome	Follow-up time (months)
1	60	M	0.69	Free ILM patch graft	0.39	1.00	Closed	36
2	80	F	1.00	Temporal inverted ILM flap	0.69	0.69	Closed	42
3	84	F	1.30	Free ILM patch graft	0.69	1.00	Closed	47
4	74	M	0.69	ILM peeling	0.52	0.79	Closed	82
5	62	F	0.52	Free ILM patch graft	0.22	0.22	Closed	180
6	67	F	0.52	Temporal inverted ILM flap	0.52	1.30	Closed	45

F: Female, M: Male, BCVA: Best corrected visual acuity, ILM: Internal limiting membrane, logMAR: Logarithm of the minimum angle of resolution

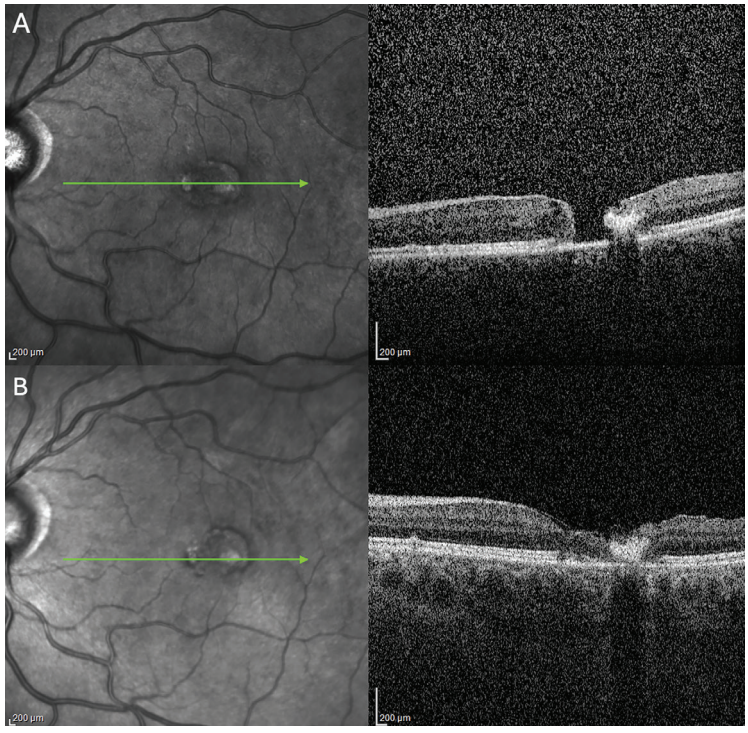

Figure 2. Optical coherence tomography (OCT) images of a macular hole associated with macular telangiectasia type 2. A) Preoperative OCT shows a full-thickness macular hole. B) Postoperative OCT at 6 months following pars plana vitrectomy with a free internal limiting membrane patch graft, demonstrating anatomical closure of the hole

characterized by the absence of central EZ break. Meanwhile, 33.7% of patients were categorized as stage 2, signifying the onset of damage to the central EZ. This distribution suggests that a significant proportion of patients sought medical consultation following the onset of visual impairment. At the final follow-up examination, 14.6% of patients remained in the early stages (stages 0 and 1), while 38.6% had progressed to advanced stages (stages 5 and 6), which are strongly associated with severe visual loss.[3]

Recent studies have reported a high prevalence of DM among patients with MacTel.[10] In our cohort, DM was identified in 37 patients (39.4%). Additionally, mild, non-proliferative DR was observed in 8 patients (8.51%), while no cases of proliferative DR were detected. Similarly, van Romunde et al.[10] reported DM in 50 patients (49%) in their MacTel sample, with mild DR observed in 22 eyes (11%). Notably, no cases of severe or proliferative DR were identified in their cohort. Sauer et al.[11] also found the rate of diabetic patients to be 35%. While previous studies have reported similar incidences, it remains unclear whether this association is coincidental or influenced by lead-time bias from routine ophthalmic screening in diabetic patients. The MacTel Project 3 addressed this issue by including age-matched controls and confirmed a significantly higher prevalence of DM among MacTel patients. Despite potential biases, current evidence increasingly supports a relationship between DM and MacTel.[10,12]

The most common clinical findings in this cohort were loss of retinal transparency (91.8%) and the presence of RAVs (90.8%). Müller cells are essential for preserving the blood-retinal barrier and providing trophic support to surrounding neurons. As these cells envelop neurons, supply nutrients, and maintain close interactions with retinal blood vessels in the outer plexiform layer, the neurodegenerative theory of MacTel proposes their dysfunction as a key factor. The resulting nutritional deprivation may play a significant role in the loss of retinal transparency frequently observed in MacTel.[13]

According to the Gass and Blodi[7] clinical staging system, the presence of RAVs in fundoscopy is associated with advanced MacTel (stages 3-5). However, this classification relies exclusively on morphological findings from fundoscopy and FA, without incorporating insights from advanced imaging techniques such as OCT or OCT angiography. Tzaridis et al.[14] demonstrated that multimodal imaging, particularly OCT angiography, has the capacity to detect vessels exhibiting RAV characteristics at earlier stages (1-2), thus suggesting that vascular abnormalities may manifest earlier than previously thought. Their findings also highlight the value of advanced imaging in the early detection and understanding of MacTel progression.[14] In contrast, Chung et al.[15] associated inner retinal disorganization, outer retinal cavities, and EZ disruption on OCT with the presence of RAVs, indicating a more advanced disease stage. Chandran et al.[16] further showed that multicolor imaging, particularly green

reflectance, has higher sensitivity and negative predictive value in detecting RAVs compared to traditional imaging. The authors noted that Chung et al.'s[15] reliance on fundus photography and FA may have limited early-stage detection.[16] In line with the data discussed above, RAV was one of the most common findings in our study.

Krivosic et al.[17] reported the incidence of MNV in MacTel patients to be 14%. In the present study, 29 eyes (15.8%) exhibited MNV, of which 18 had active MNV and 11 had scarred lesions in the baseline examination. Anti-VEGF injections have been reported as beneficial for short-term treatment of secondary MNV associated with MacTel. However, there is a lack of conclusive data regarding their long-term efficacy and outcomes.[5,18,19] Although we observed early improvement in visual acuity following treatment, no significant gain in BCVA was noted after approximately 10 years of follow-up, likely reflecting the progressive neurodegenerative course of the disease. Overall, our findings suggest that anti-VEGF therapy provides short-term visual benefit and may help mitigate vision loss due to MNV over the long term.

MacTel-associated MHs are rare, and their surgical management remains controversial due to inconsistent functional outcomes despite high anatomical success. In our study, MH formation occurred in eight patients, six of whom underwent surgery. Notably, MH closure was achieved in all surgically treated cases, and five patients demonstrated initial BCVA improvement. However, the long-term outcomes were adversely affected by disease progression, as indicated by a decline in BCVA at the final follow-up (ranging from 36 to 180 months). These findings are in line with previous reports indicating that ILM techniques, including inverted and free flaps, achieve high closure rates but offer limited and often inconsistent visual recovery. Our data showed that surgery achieved anatomical closure, but visual acuity improvements were not sustained, likely due to the progression of MacTel.[6,20,21]

Study Limitations

A notable limitation of this study is its retrospective design, which inherently limits the ability to control for confounding variables. In addition, due to the rarity of MacTel-associated MHs and MNV, our study includes a relatively small number of patients who underwent surgery or injection treatments. Nonetheless, this study provides significant contributions through its use of a modern, imaging-based classification that links structural changes to functional outcomes. This framework enhances clinical decision-making and supports future research into the pathophysiology of the disease and potential therapeutic interventions. With its large cohort and long follow-up period, the study also offers valuable data on secondary complications and their management, offering insight into the long-term outcomes of therapeutic interventions in MacTel.

Conclusion

While MacTel is a slow-progressing disease, only 15% of patients remain in the early stage with minimal visual loss. However, 70% of patients seek medical consultation during the later stages, which is characterized by significant visual loss. The frequent co-occurrence of DM underscores the importance of systemic evaluation in these patients. Early diagnosis, along with timely management of complications, may help delay further visual decline and improve long-term outcomes.

Ethics

Ethics Committee Approval: Ethics Committee of Hamidiye Scientific Research, University of Health Sciences (approval number 12/4, date: 17.10.2024).

Informed Consent: Retrospective study.

Declarations

Authorship Contributions

Surgical and Medical Practices: M.Ö., Ö.A., M.Ş., Concept: M.Ö., Design: Ö.A., M.Ş., Data Collection or Processing: M.Ö., R.K., İ.H., Analysis or Interpretation: Ö.A., R.K., İ.H., Literature Search: M.Ö., Ö.A., R.K., İ.H., M.Ş., Writing: M.Ö.

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