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Is anterior segment OCT superior to slit-lamp biomicroscopic examination for Kayser Flesicher ring in Wilson's disease?

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Abstract. – OBJECTIVE: Detection of the Kayser-Fleischer (KF) ring in the diagnostic scoring and treatment follow-up of Wilson's Disease (WD) is important. Slit lamp (SL) biomicroscopic examination has traditionally been used in the evaluation of the KF ring. The role of Anterior Segment Optical Coherence Tomography (AS-OCT), which is used in various corneal diseases, in the detection of KF rings has attracted attention in recent years. In our study, we tried to demonstrate the effectiveness of AS-OCT in detecting the KF ring by comparing it with SL biomicroscopic examination.

PATIENTS AND METHODS: 64 of 356 patients followed in our outpatient clinic due to WD were included in the study in the order of their admission to the outpatient clinic. The KF ring was evaluated in both eyes by SL-biomicroscopic examination and AS-OCT. Ophthalmic examination, and findings were performed by the same physician.

RESULTS: Age range was 18-67 years, mean 33.06±10.83 years, gender was 39.1% (n: 25) female. At the time of diagnosis, the mean age was 19.48 ± 9.36 years, range was minimum 5 years and maximum 51 years. Clinical presentation was mixed type involvement n: 18 (28.1%), hepatic involvement n: 32 (50%), neurological involvement n: 14 (21.9%). The follow-up period was 2-257 months (74.6±76.16). The presence of KF ring was evaluated together with both AS-OCT and slit-lamp examination, the presence of KF could be detected in both AS-OCT and SL biomicroscopic examination in 10 patients (15.6%), in 12 (18.8%) of the cases KF ring is positive in AS-OCT but was negative in Slit-lamp biomicroscopic examination, in 65.6 (n: 42) of the cases OCT and slit-lamp biomicroscopic examination results were negative.

CONCLUSIONS: The sensitivity of AS-OCT in detecting the KF ring was higher than the slit-lamp biomicroscopic examination. AS-OCT can detect early stage of KF rings in Wilson's Disease patients, so that diagnosis and treatment accuracy can be evaluated effectively.

Key Words:
Wilson's disease, Optical coherence tomography, KF ring.

Introduction

Wilson's disease (WD) was first defined by Samuel Alexander Kinnier Wilson in 1912. In this disease, both liver and neurological involvement may occur, and its relationship with copper was discovered in 1913[1]. WD is an autosomal recessive genetic illness defined as hepatolenticular degeneration. The genetic transmission of WD has been detected in more than 500 mutations in the ATP7b gene in chromosome 13[2]. Globally, the prevalence of WD is one to 30,000 live births.

The clinical range of WD is wide because impaired biliary copper excretion leads to the accumulation of copper in several organs, most notably in the liver, brain, and corneas[3]. The liver is the first organ in which copper accumulates in the WD. As a result of this accumulation, different clinical situations may be observed. Liver involvement can range from asymptomatic aminotranspherasis elevation to cirrhosis, resulting in liver transplantation. Acute fulminant liver failure may occur in approximately 5% of WD cases[3,4].

The neurological involvement of WD is another form of clinical application. Most patients with neurologic WD fall into one of several categories: dysarthric, dystonic, tremulous, pseudosclerotic (tremor with or without dysarthria), or Parkinsonian disease[5]. Usually, only one of these symptoms may be observed initially. Still, with the progression of the disease, complex combinations of neurologic symptoms may develop. Although

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a broad spectrum of clinical symptoms occurs due to the accumulation of copper in the liver, brain, and corneas, the diagnosis is challenging if WD is not suspected. Since the WD diagnosis cannot be based on a single clinical or laboratory finding, a scoring system was developed to reach the diagnosis at an international meeting held in Leipzig[6]. This scoring system included both clinical and laboratory testing, and the results yielded three categories of patients: those in whom other diagnoses should be considered, those in whom further diagnostic testing is needed, and those in whom there is certainty regarding the diagnosis. Life expectancy in patients diagnosed with WD is not different from the average population of patients treated in the presymptomatic period. Therefore, the early diagnosis of WD is critical for the survival of WD patients[7].

Failure to diagnose WD with a single clinical parameter result in clinical practice difficulties. Still, approximately 50% of patients diagnosed with WD have the classic clinical symptoms observed in patients with decreased serum ceruloplasmin, and detectable Kayser-Fleischer (KF) rings in corneas. Therefore, detecting the KF ring constitutes a unique and essential finding in WD, since it is vital in diagnosis scoring. KF is based on the accumulation of copper in the Descement's membrane (DM) of the cornea and can be seen with a slit lamp (SL). The presence of the KF ring confirms the release of free copper into the bloodstream[8]. KF rings have been reported in 90% of patients with neurologic involvement, and nearly 50% have shown hepatic involvement[9,10]. The KF ring condition is almost always bilateral. First, it begins in the superior portion of the organ, then it spreads to the inferior parts of the corneas. Finally, it becomes circumferential[11]. The KF ring, which can be seen even with the naked eye when there is excessive copper accumulation, has an important place in diagnosing and evaluating adherence to WD treatment[12].

Because of the necessity to use lifelong treatment regularly, compliance with treatment is an important problem for patients with WD. The KF ring may reappear in patients who do not follow treatment. Therefore, it is essential to regularly monitor the ocular status of patients[13,14].

As stated by the American Association for the Study of Liver Diseases (AASLD) and by the European Association of the Study of Liver Disease (EASL) guidelines, KF ring detection requires the presence of an experienced ophthalmologist[3,4]. KF ring detection with SL has been the gold standard for many years[15]. Gullstrand invented the SL in 1911. The KF ring is observed using diffuse illumination in SL and a direct focal examination. KF ring detection is observed as golden-brown, brown-green, green-yellow, golden-yellow, bronze, or reddish-brown coloring of the DM in the peripheral limbal area of the cornea[16]. The intensity of the KF ring seems to be correlated with WD severity.

Anterior segment optical coherence tomography (AS-OCT) imaging is a test that can be used to evaluate the anterior chamber of the eye and diagnose the KF ring. This method allows visualization and assessment of anterior segment ocular features, such as the tear film, cornea, conjunctiva, sclera, rectus muscles, anterior chamber angle structures, and lens. Izatt et al[17] were the first to introduce AS-OCT to detect the KF ring in 1994. AS-OCT is a noncontact examination method. The examination time is lower than 20 seconds for each eye. On AS-OCT, the KF ring seems like a hyperreflective layer at the periphery of the cornea.

A comparison between biomicroscopic examination with SL and AS-OCT in evaluating the presence of KF in WD has been made in limited case studies. Based on these data, we assessed the presence of the KF ring in biomicroscopic examinations with SL and AS-OCT imaging in patients who were followed up after the diagnosis of WD. Therefore, this study aimed to evaluate whether AS-OCT is superior to SL in detecting the KF ring in patients diagnosed with WD showing neurological, hepatic, and mixed-type involvement.

Material and Methods

The Internal Review Board approved the study protocol at the Medical University of Istanbul. Informed consent was obtained from all patients who participated in this study.

Patients' Selection

356 patients with established WD diagnoses were followed by Istanbul University, Istanbul Faculty of Medicine Gastroenterology Department. Among them, 64 were enrolled in the study during their outpatient clinic visits.

Patient Data

All demographic data of the patients were recorded. Such data comprised disease involvement. (e.g., hepatic, neurologic, mixed-type involvements), presentation of the disease, family history, symptom duration, treatment duration,

parameters related to the WD diagnosis, presence of cirrhosis, and duration of the treatment they were using.

Ophthalmic Examination

A complete ophthalmic examination was performed in each participant, consisting of visual acuity testing, bilateral anterior segment evaluation using the SL examination, and dilated fundus examination to assess optic discs and peripheral retina. The KF ring presence was evaluated during the appointment with an SL (Haag Streit BQ 900, magnification 25x) and AS-OCT using the SPECTRALIS Anterior Segment Module (Spectralis OCT, Heidelberg Engineering, Heidelberg, Germany), with a CL-line scan of 8 mm length (horizontal and vertical). The cornea image was located between the two red-guided lines, and the "auto" scan was selected.

The KF ring was evaluated in both eyes of patients with SL and AS-OCT. The same physician performed ophthalmic examinations and findings. The ophthalmologist who evaluated the ocular findings was unaware of the clinical information of the patients.

Statistical Analysis

The sample size of this study was calculated to evaluate eye findings in WD patients using AS-OCT and SL biomicroscopic examination methods. A power analysis was determined by at least 80% and type 1 error 5% for each variable. Kolmogorov-Smirnov ($n > 50$) and Skewness-Kurtosis' tests were used to check whether the continuous measurements in the study were normally distributed. Because the measurements were normally distributed, parametric tests were applied. Descriptive statistics for the variables in the study were expressed as mean, standard deviation (SD), minimum, maximum, number (n), and percent (%). An independent *t*-test was used to compare continuous measurements according to categorical groups. A Chi-square test was used to determine the relationships between the categorical variables. Furthermore, *p*-values of less than 0.05 were considered statistically significant. The SPSS ver. 26 (IBM Corp., Armonk, NY, USA) statistical package was used to analyze the data.

Results

A total of 64 WD patients were included in the study. The patients were evaluated with sequential AS-OCT and SL biomicroscopic examinations for both eyes. The age range of the patients was 18-67 years, with a mean age of 33.06 ± 10.83 (SD) years. 25 patients (39.1%) were female. At the time of diagnosis, the mean age was 19.48 ± 9.36 years. The range of the minimum and maximum ages of WD detection was 5-51 years. The clinical presentation of WD was mixed-type involvement in 18 patients (28.1%). Hepatic involvement was observed in 32 patients (50%), and neurological involvement was observed in 14 patients (21.9%). The follow-up period was 2-257 months (74.6 ± 76.16).

The mean age of the patients with hepatic manifestations was 32.49 years (35 ± 12.63). The mean age of the patients with neurological manifestations was 31.88 years (16 ± 10.34). The mean age of the patients with mixed-type involvement was 31.87 years (23 ± 9.082). A total of 31.3% (n = 20) of the patients were in the cirrhotic stage upon admission. WD was observed in the other family members of 30.91% of the patients (n = 17). The presence of KF rings was detected in both AS-OCT and SL biomicroscopic examinations in 10 patients (15.6%). For 12 (18.8%) patients, the KF ring cases were positively detected with OCT, but were negative in the SL biomicroscopic examination. Finally, KF ring detection was negative in both AS-OCT and SL biomicroscopic examination results for 65.6% of the patients (n = 42).

The demographic characteristics of the patients submitted to AS-OCT and SL biomicroscopic examination results are shown in Table I. The KF ring on AS-OCT was visualized as an intense hyperreflective band at the level of DM in the peripheral cornea (Figure 1).

Using McNemar's test, there was a tendency in the entire cohort for subjects seemingly not presenting a KF ring in the SL examination having a KF ring when examined with AS-OCT. Copper deposits forming the KF ring, undetectable during the SL examination, were revealed using the AS-OCT technique in an additional 12 subjects ($p < 0.001$). This result is a confirmation of the improved AS-OCT evaluation accuracy compared to the SL examination commonly used as a standard of care. Therefore, the sensitivity of AS-OCT in detecting the KF ring was higher than that of the SL biomicroscopic examination ($p = 0.001$) (Table II, Figure 2). Considering the involvement pattern, the probability of the KF ring being detected with the AS-OCT technique in neurological involvement was 71.4% (n: 10), 22.8% (n: 5) in mixed involvement, and 21.9% (n: 7) in hepatic

Table I. Demographic features of the Wilsons Disease.

	N		%	
Gender	Female		25	39.1%
	Male		39	60.9%
KF results	KF is negative in both slit-lamp biomicroscopy and AS-OCT		42	65.6%
	KF ring is positive in AS-OCT, negative in slit-lamp biomicroscopy		12	18.8%
	KF positive in AS-OCT and slit-lamp biomicroscopy		10	15.6%
KF result İn AS- OCT	Negative		42	65.6%
	Positive		22	34.4%
KF result İn the slit-lamp	Negative		54	84.4%
biomicroscopy	Positive		10	15.6%
Family History	(-)		38	69.1%
	(+)		17	30.9%
Involvement	Liver		32	50.0%
	Mixt		18	28.1%
	Neurologic		14	21.9%
Liver cirrhosis in presentation	(-)		44	68.8%
	(+)		20	31.3%
Liver Biopsy	(-)		23	40.4%
	(+)		34	59.6%

Table II. Relationship between KF in slit-lamp biomicroscopy and KF in AS-OCT.

			KF results in AS-OCT		
			Negative	Positive	*p
KF results in slit-lamp biomicroscopy	Negative	N	42	12	**.001**
		%	77.8%	22.2%	
	Positive	N	0	10	
		%	0.0%	100.0%	

*Statistically significant level for p is <0.05. Significance level according to Mc Nemar's test results.

Table III. Relationship between "Involvement pattern" and KF status with AS-OCT and slit-lamp biomicroscopy.

		Pattern of involvement						
		Liver		Mixt		Neurologic		
		N	%	N	%	N	%	p
KF results in AS-OCT	Negative	25	78.1%	13	72.2%	4	28.6%	.004
	Positive	7	21.9%	5	22.8%	10	71.4%	
SL biomicroscopic examination	Negative	29	90.6%	16	88.9%	9	64.3%	.064
	Positive	3	9.4%	2	11.1%	5	35.7%	

*Statistically significant level for p is <0.05. Significance level according to Chi-square test results.

involvement. The probability of detecting a KF ring with AS-OCT was statistically significant for neurological involvement (p=0.004). The detection rate of the KF ring using the SL biomicroscopic examination in neurological involvement was 35.7% (n: 5), 11.1% in mixed involvement (n: 2), and 9.4% (n: 3) in hepatic involvement (p=0.064) (Table III). There was no statistical difference when the demographic characteristics of the patients (e.g., age, age at diagnosis, age of symptoms, delayed diagnosis, and follow-up period) were compared according to their CF sta-

Table IV. Comparison of patient characteristics "according to KF result.

	KF RESULTS	Mean	Std. Dev.	*p
Age	Negative in both examination	34.86	11.74	.143
	Positive in AS-OCT, negative in Slit-lamp biomicroscopy	28.08	7.73	
	Both positive	31.50	8.37	
Age at diagnosis	Negative in both examination	20.80	9.99	.296
	Positive in AS-OCT, negative in Slit-lamp biomicroscopy	17.33	8.40	
	Both positive	16.33	6.75	
Age at onset of symptoms	Negative in both examination	18.63	11.60	.345
	Positive in AS-OCT, negative in Slit-lamp biomicroscopy	14.75	10.25	
	Both positive	13.78	7.93	
Diagnosis delay (years)	Negative in both examination	1.03	2.50	.660
	Positive in AS-OCT, negative in Slit-lamp biomicroscopy	.50	.80	
	Both positive	1.33	1.73	
Follow up years	Negative in both examination	82.84	77.17	.192
	Positive in AS-OCT, negative in Slit-lamp biomicroscopy	37.09	48.89	
	Both positive	86.56	91.72	

*Statistically significant level for p is <0.05. Significance levels according to one-way ANOVA test results.

tus (e.g., positive only in the SL biomicroscopic examination, positive in both SL biomicroscopic examination and AS-OCT, and positive only in AS-OCT) (Table IV).

Discussion

The KF ring is an essential diagnostic for WD diagnosis and follow-up criteria for evaluating drug compliance and treatment response. SL has been used for many years to assess KF ring presence. An experienced ophthalmologist is recommended to perform an SL biomicroscopic examination, as defined by the EASL guidelines. The KF ring starts from the vertical pole of the cornea and accumulates deeper, becoming circular[18]. Although SL biomicroscopic methods have traditionally been used to detect the KF ring, AS-OCT imaging, used to treat corneal diseases, has recently been evaluated to detect KF rings.

In AS-OCT, the KF ring is observed as a hyperreflective layer on the anterior segment of the posterior cornea. The detection of the KF ring with AS-OCT has been evaluated by a few studies in the literature[18-21]. Mittanamalli et al[18] detected the presence of the KF ring with AS-OCT, naked eyes, and SL in six WD patients[18], and this study was the first observation of the KF ring in WD patients using AS-OCT. In the study mentioned above, the observation of the KF ring on AS-OCT was validated by a second ophthalmologist, a medical gastroenterologist, a surgical gastroenterologist, and a neurologist to check for inter- and intraobserver variability. If an early KF ring is missed with both SL and AS-OCT techniques because of hyperreflectivity at the level of DM, the ophthalmologist can return to observing the KF ring with SL. After detecting the first

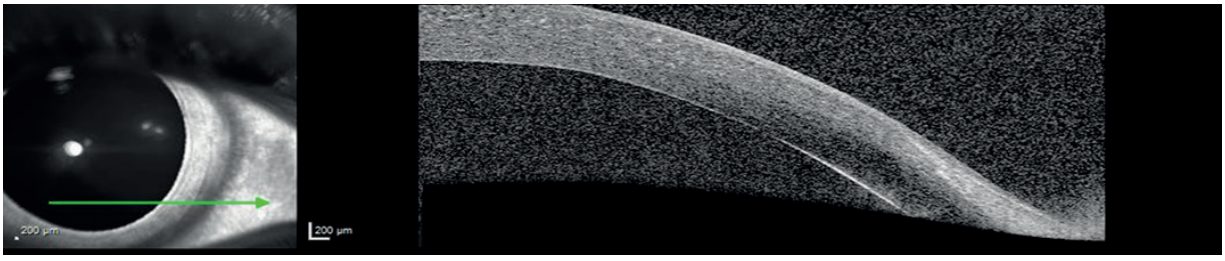

Figure 1. Anterior Segment Optical Coherence Tomography (AS-OCT).

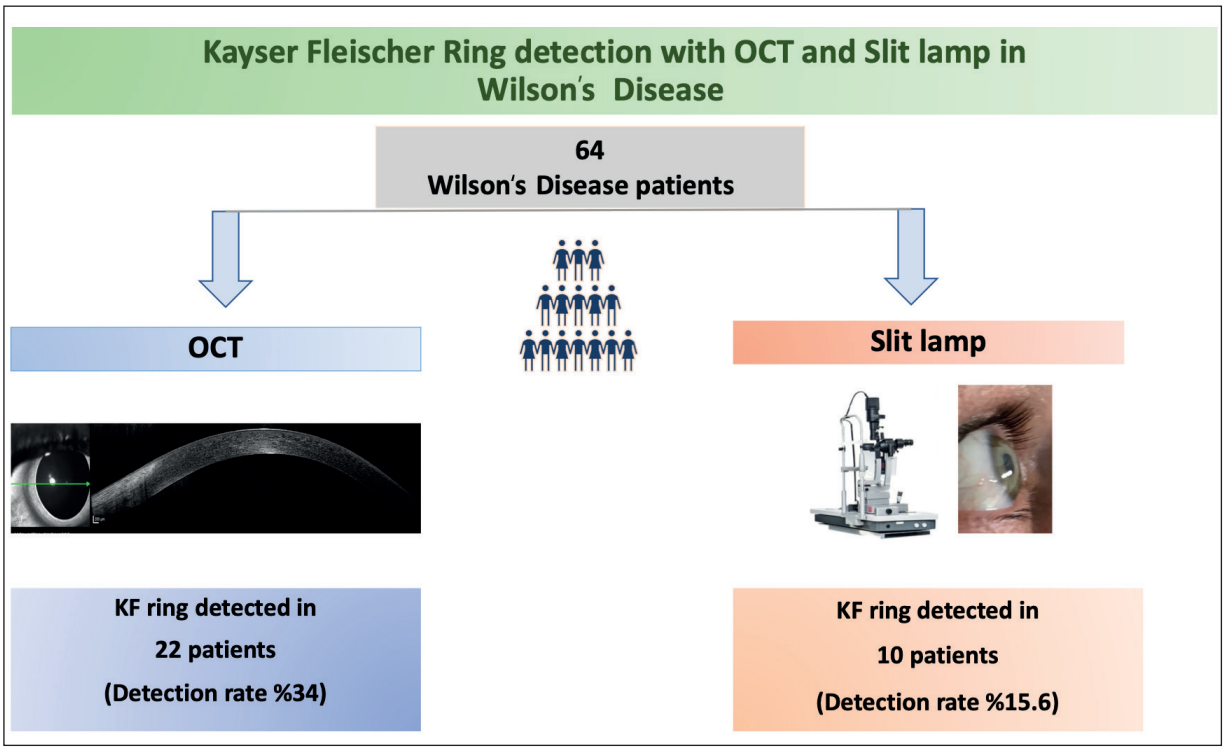

Figure 2. Results of 64 Wilson's disease patient's KF ring examination by OCT and slit lamp (Graphical abstract).

observation, clinicians could easily identify the AS-OCT features in all pictures. Therefore, they concluded that physicians other than ophthalmologists dealing with WD would be able to see KF ring on AS-OCT. Our study aimed not at evaluating the difference between observers but at revealing the difference between experienced and inexperienced practitioners. Still, we found that the rate of KF ring detection with AS-OCT was higher, even when an experienced ophthalmologist evaluated the KF ring with SL and AS-OCT.

Broniek-Kowalik et al[19] evaluated 29 patients with WD (17 women) and 29 control groups for the presence of a KF ring[19]. The AS-OCT and SL techniques were compared with the control group in that study. A KF ring was detected in 15 patients using AS-OCT. No KF ring was found in these cases with the SL biomicroscopic examination. According to their results, AS-OCT has been superior to SL biomicroscopic examination in detecting the KF ring. Their results support the use of AS-OCT as a diagnostic procedure. Better objectivity and accuracy are offered when using AS-OCT compared to the SL examination at the diagnostic stage and during the monitoring changes in the KF ring during medical therapy. This finding is essential to assess the efficacy and patient compliance.

One of the advantages of AS-OCT over SL during the detection of the KF ring can also be attributed to the trace copper deposits forming the KF. Such deposits are predominantly found at the Schwalbe line in the anterior chamber angle within Descemet membrane. Since the angle view is hidden by the corneal limbus, copper deposits are not detected in standard SL anterior segment assessments. Such deposits become visible only after they extend beyond the contour of the limbus.

In our study, the grayscale hyperreflective layer of copper was determined to accumulate most from the superior and inferior portions of the cornea zones. Such zones can be defined as early copper accumulation, which means that AS-OCT could detect the KF ring earlier than SL examination. This was similar to what was found by Broniek-Kowalik et al[19].

Our results and those found in other studies[20] support that in suspected cases of WD, features of the KF ring observed with AS-OCT serve as alerts for clinicians to perform a careful SL examination to look for early KF ring. AS-OCT can also be used to evaluate the density of the KF

ring, which can reflect the severity of the disease according to its high density. Nevertheless, we did not consider it for this purpose in our study. As mentioned before, the KF ring may disappear with treatment. The reappearance of KF is a suggestion that the patient does not follow the treatment, so detecting the KF ring with AS-OCT can be another indication for the evaluation of treatment compliance[20].

Another indication of the best performance of AS-OCT over SL in detecting the KF ring is mentioned in the literature[21]. AS-OCT can be applied if it is inappropriate to evaluate young children with an SL biomicroscopic examination because of a neurological deficit. Rathi et al[21] published a case study to detect the KF ring in AS-OCT in neurological WD in 2017. They suggested performing AS-OCT under challenging cases. The authors speculate that, given its resolution, reproducibility, and repeatability, AS-OCT may be a valuable adjunct for sequentially monitoring therapeutic responses and making diagnoses in doubtful WD cases[21].

In our literature review, our study constitutes one of the most comprehensive studies evaluating the efficacy of AS-OCT in detecting KF rings. AS-OCT technology has been successfully utilized for anterior segment evaluation, offering several clinically relevant applications. The capabilities of this technology allow for non-contact imaging, detailed visualization, and analytics of the anterior segment structures of the human eye on one device. These structures include the cornea, anterior chamber, iris, and lens. AS-OCT is now routinely used in all ophthalmology clinics. The KF ring detection rates increased with AS-OCT over SL, even when experienced ophthalmologists in KF performed the exam. The advantage of AS-OCT over SL is that it can detect patients in the early stages of WD.

Conclusions

As a conclusion, in suspected cases, hyperreflectivity of the deep corneal layer in the periphery on AS-OCT serves as an alert to clinicians to perform a careful SL examination to search for an early KF ring.

Ethics Approval

The Internal Review Board approved the study protocol at the Medical University of Istanbul.

Informed Consent

Informed consent was obtained from all patients who participated in this study.

Availability of Data and Material

Data and materials can be reached by corresponding author's permission.

Conflicts of Interest

The authors declare no conflicts of interest.

Authors' Contributions

AÇÖ and KD designed and conceived the project. AÇÖ wrote the manuscript. ŞB, AOI and Bİ were responsible for eyes examination.BÇ, RA, Zİ, MKS contributed to collecting data. FA, FB, SK, KD, AÇÖ were responsible for drafting and revision of the manuscript for important intellectual content of the article.

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References

1) Wilson SAK. Progressive lenticular degeneration: a familial nervous disease associated with cirrhosis of the liver. Brain 1912; 34: 20-509.
2) Tao TY, Gitlin JD. Hepatic copper metabolism: insights from genetic disease. Hepatology 2003; 37: 1241-1247.
3) EASL Clinical Practice Guidelines: Wilson's disease. European Association for Study of Liver J Hepatol 2012; 56: 671
4) Roberts EA, Schilsky ML. Diagnosis and treatment of Wilson disease: an update. Hepatology 2008; 47: 2089-2111.
5) Lorincz MT, Ann NY. Neurologic Wilson's. Acad Sci 2010; 1184: 173.
6) Ferenci P, Karel C, Georgios L, Georgina MV, Stuart T, Irmin S, Michael S, Diane C, Frieder B. Diagnosis and phenotypic classification of Wilson disease. Liver Int 2003; 23: 139-142.
7) Anna C, Tomasz L, Petr D., Peter F, Svetlana L, Valentina M, Janusz KR, Karl HW, Michael LS. Wilson disease. Nat Rev Dis Primers 2018; 4: 21.
8) Wiebers DO, Hollenhorst RW, Goldstein NP. The ophthalmologic manifestations of Wilson's disease. Mayo Clin Proc 1977; 52: 409-416
9) Steindl P, P Ferenci, H P Dienes, G Grimm, I Pabinger, C Madl, T Maier-Dobersberger, A Herneth,

B Dragosics, S Meryn, P Knoflach, G Granditsch, A Gangl. Wilson's disease in patients presenting with liver disease: a diagnostic challenge. Gastroenterology 1997; 113: 212.

10) Gow PJ, R A Smallwood, P W Angus, A L Smith, A J Wall, R B Sewell. Diagnosis of Wilson's disease: an experience over three decades. Gut 2000; 46: 415.
11) Innes JR, Strachan IM, Triger DR. Unilateral Kayser-Fleischer ring. Br J Ophthalmol 1986; 70: 469-470.
12) Ala A, Ann PW, Keyoumars A, James SD, Michael LS. Wilson's disease. Lancet 2007; 369: 397-408.
13) Mittanamalli SS, Pineda R. Anterior segment optical coherence tomography to look for Kayser-Fleischer rings. Pract Neurol 2017; 17: 222-223.
14) Schilsky M. Goldman-Cecil Medicine -Volume Set, 26th Edition,2020, 1385-1388.
15) Telinius N, Ott P, Hjortdal J. Detection of Kayser–Fleischer ring using Scheimpflug imaging. Acta Ophthalmol 2017; 95: 248-249.
16) Rio-Cristobal A, Martin R. Corneal assessment technologies: current status. Surv Ophthalmol 2014; 59: 599-614.
17) Izatt JA, Hee MR, Swanson EA, Lin CP, Huang D, Schuman JS, Puliafito CA, Fujimoto JG. Micrometer scale resolution imaging of the anterior eye in vivo with optical coherence tomography. Arch Ophthalmol 1994; 112: 1584-1589.
18) Mittanamalli SS, Advithi R, Kavitha A, Sharat PR, Sachin D, Sita J, Bajibhi S. Evaluation of Kayser-Fleischer ring in Wilson disease by anterior segment optical coherence tomography. Indian J Ophthalmol 2017; 65: 354-357.
19) Broniek-Kowalik K, Dzieżyc K, Litwin T, Członkowska A, Szaflik JP. Anterior segment optical coherence tomography (AS-OCT) as a new method of detecting copper deposits forming the Kayser-Fleischer ring in patients with Wilson disease. Acta Ophthalmol 2019; 97: e757-e760.
20) Sridhar MS. Cornea in Wilson Disease: Kayser Fleischer Ring & Beyond. Global Journal of Medical Research: Diseases 2017; 17; Issue 2 Version 1.0.
21) Rathi A, Brijesh T, Nripen G, Prafulla KM. Optical coherence tomography of the Kayser-Fleischer ring: an ancillary diagnostic tool for Wilson's disease in children. BMJ Case Reports 2017; 2017: bcr-2017-220007.