

Fleck Retina Syndrome ในประเทศไทย

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บทคัดย่อ

การศึกษาผู้ป่วย fleck retina syndrome ในโรงพยาบาลศิริราช เป็นเวลา 6 ปี (ระหว่างปี พ.ศ. 2546-2552) พบผู้ป่วยทั้งหมด 67 ราย มีผลการตรวจจักษุที่ครบถ้วนและนำมาศึกษาได้ 48 ราย โดยพบเป็นผู้ป่วยเพศชาย 19 ราย และเพศหญิง 29 ราย อายุเฉลี่ย 35 ± 19.15 ปี ผู้ป่วย 12 รายมาพบแพทย์ด้วยอาการมองเห็นในที่มืด ในจำนวนนี้ 11 รายตรวจพบว่าคลื่นไฟฟ้าของจอตามีค่าลดลงมากจนถึงบันทึกไม่ได้ และได้รับการวินิจฉัยว่าเป็นโรค retinitis punctata albescens และมีเพียงผู้ป่วย 1 รายที่มีลักษณะคลื่นไฟฟ้าของจอตาที่จำเพาะในการวินิจฉัยโรค fundus albipunctatus ผู้ป่วย 36 ราย ตรวจพบว่ามี fleck ที่จอตาโดยการมองเห็นในที่มืดปกติ ในจำนวนนี้ 25 ราย ตรวจพบความผิดปกติหรือแผลเป็นบริเวณจุดรับภาพชัด และได้รับการวินิจฉัยว่าเป็น Stargardt's disease ผู้ป่วย 5 รายไม่พบความผิดปกติของจุดรับภาพชัด ได้รับการวินิจฉัยเป็น fundus flavimaculatus และผู้ป่วยอีก 6 รายพบ fleck กระจายทั่วจอตาตรงกลาง ได้รับการวินิจฉัยเป็น familial drusen อาจมีหรือไม่มี ความผิดปกติของการมองเห็นในที่มืด ลักษณะของ fleck ที่จอตา ร่วมกับการตรวจคลื่นไฟฟ้าของจอตา จะช่วยในการวินิจฉัยโรคในกลุ่ม fleck retina syndrome เพื่อประโยชน์ในการพยากรณ์โรค และการดูแลรักษาที่เหมาะสมต่อผู้ป่วย **จักษุเวชสาร 2017; กรกฎาคม-ธันวาคม 31(2): 55-65.**

คำสำคัญ: อาการมองเห็นในที่มืด, คลื่นไฟฟ้าของจอตา, fleck retina syndrome, retinitis punctata albescens, fundus albipunctatus, Stargardt's disease, fundus flavimaculatus, familial drusen

ผู้นิพนธ์ทั้งหมดไม่มีส่วนเกี่ยวข้องหรือผลประโยชน์ใดๆ กับผลิตภัณฑ์ที่ได้กล่าวอ้างถึงในงานวิจัยนี้

Fleck Retina Syndrome in Thailand



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Abstract

Purpose: To study presenting symptoms, signs, and electroretinographic findings of patients diagnosed with fleck retina syndrome in Siriraj Hospital, Bangkok, Thailand.

Design: Retrospective chart review.

Methods: 67 charts of patients diagnosed with fleck retina syndrome during 2003 - 2009 were reviewed. Demographic data including gender, age, visual acuity, underlying diseases, presenting symptoms, signs and electroretinographic (ERG) patterns were recorded. Nineteen charts were excluded due to incomplete data. In total 48 cases were analyzed.

Results: Forty-eight patients (19 male and 29 female), mean age 35 ± 19.15 years (range from 11-79 years), were included. The mean visual acuity at presentation using logMAR was 0.81 ± 0.66 and 0.82 ± 0.69 for right eye and left eye, respectively. There were 12 patients (25%) presenting with fleck retina and nyctalopia, 11 patients (22.9%) were diagnosed with retinitis punctata albescens with nonrecordable ERG and 1 patient (2.1%) was diagnosed with fundus albipunctatus with prolonged dark adaptation of rod ERG. Thirty-six patients (75%) of fleck retina presented without nyctalopia, of which 25 patients (52%) were diagnosed with Stargardt's disease with decreased flicker and cone ERG. The other 5 patients (10.4%) were diagnosed with fundus flavimaculatus and 6 patients (12.5%) were diagnosed with familial drusen with minimal change in ERG.

Conclusion: Fleck retina syndrome can present with nyctalopia, blurred vision or incidental findings during routine ophthalmological examination. Electroretinography is the specific test for diagnosis of the subgroup of fleck retina syndrome. Specification of diagnosis can predict the clinical course and disease progression for each subgroup of disease. **Thai J Ophthalmol 2017; July-December 31(2): 55-65.**

Keywords: Fleck retina, Electroretinography, Fundus albipunctatus, Stargardt's disease, Fundus flavimaculatus, Familial drusen, Retinitis punctata albescens.

No Author has a financial or proprietary interest in material or method mentioned

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Introduction

The fundus appearance of multiple discrete white or yellow deep retinal lesions in various distributions and configurations has been termed “Fleck retina syndrome” in ophthalmic literature since a review in the 1960s by Krill and Klien. At first, little was known about what produced the deep retina spots, various clinical presentations were reported. In 1877, Krill¹ reported Fleck retinal disease as a hereditary retinal disease. In 1882, Mooren² introduced the entities of fleck retina that presented with night blindness, and then in 1910, Lauber divided this entity into 2 subgroups, one with congenital stationary night blindness and characteristic regular round flecks as “Fundus albipunctatus” and the progressive night blindness with immense yellowish spots as “Retinitis punctata albescens”. In 1899, Robert Walter Doyme was the first to describe the fundus picture of multiple drusen with radial distribution centered on the fovea related with dominant hereditary pattern that we now call “Dominant Familial Drusen”. This entity of Fleck retina syndrome was once named Doyme Honeycomb Choroiditis or Malattia Leventinese. The fundus picture of white-yellow fishtail or pisciform lesion from subretinal lipofuscin deposits in perifoveal area and RPE atrophy in the macula region was introduced as “Stargardt’s disease” by Stargardt in 1909, then in 1953 Franceschetti referred to the similar fishtail lesion at mid-periphery without macula involvement as “Fundus flavimaculatus”. Other rare entities of Fleck retina syndrome with or without other systemic features have been reported in the literature such as Fleck retina of Kondori.³

Full-field electroretinography (ERG) plays an important role in a diagnosis of fleck retina syndrome.

To confirm nyctalopia or night vision impairment, ERG would show a significant decrease of rod function. In the absence of nyctalopia, ERG would be expected to show normal waveform of rod function, or slight decrease of cone function if the central retina had been involved. With the combination of meticulous eye examination and careful ERG interpretation, a precise diagnosis can be established.

Siriraj Hospital, one of the largest and the oldest medical school in Thailand, has available an electrophysiologic laboratory to evaluate retinal and visual pathway function for nearly 30 years. The average number of cases undergoing the tests is approximately 600 patients per year. The number of tests for the fleck retinal syndrome averages 9 cases per year. This retrospective chart review was aimed to describe the demographic data, presenting symptoms, fundus findings and electroretinographic patterns in the 4 major subgroups of fleck retina in Thai patients and to facilitate recognition of this group of diseases by clinicians.

Methods

This study was approved by the Committee for the Protection of Human Participants in Research, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand. Written informed consent was obtained from all patients. The study was conducted in accordance with the principles and guidelines of the Declaration of Helsinki and the Good Clinical Practice (GCP) standard.

Patients diagnosed with fleck retina syndrome from the Department of Ophthalmology, Siriraj Hospital, from January 2003 to December 2009 were included in the study. The demographic data (age, gender, underlying diseases), best-corrected visual acuity

(BCVA), slit-lamp microscopic examination, fundus photography, and full-field ERG were recorded in all cases. The full-field ERG recordings were performed according to standards and criteria set forth by the International Society for the Clinical Electrophysiology of Vision (ISCEV), using Nicolet Viking select master software V7.1 (Nicolet Biomedical Incorporated, Pleasanton, CA, USA) with skin electrodes (Ag/AgCl).

The BCVA was converted to a logarithm of the minimum angle of resolution (logMAR) equivalent. Statistical data were calculated by using Statistical Package for the Social Sciences software, version 23.0 (SPSS Inc., Chicago, Illinois). Demographic data were shown as mean with standard deviation.

Results

Sixty-seven charts of patients diagnosed with fleck retina syndrome were reviewed. Nineteen charts were excluded due to incomplete data, then 48 cases

were analyzed. The demographic data and fundus findings in specified subgroups are shown in Tables 1 and 2. The patients with night blindness tend to present earlier due to visual disturbance. The Stargardt's disease also presents early because the central vision had deteriorated.

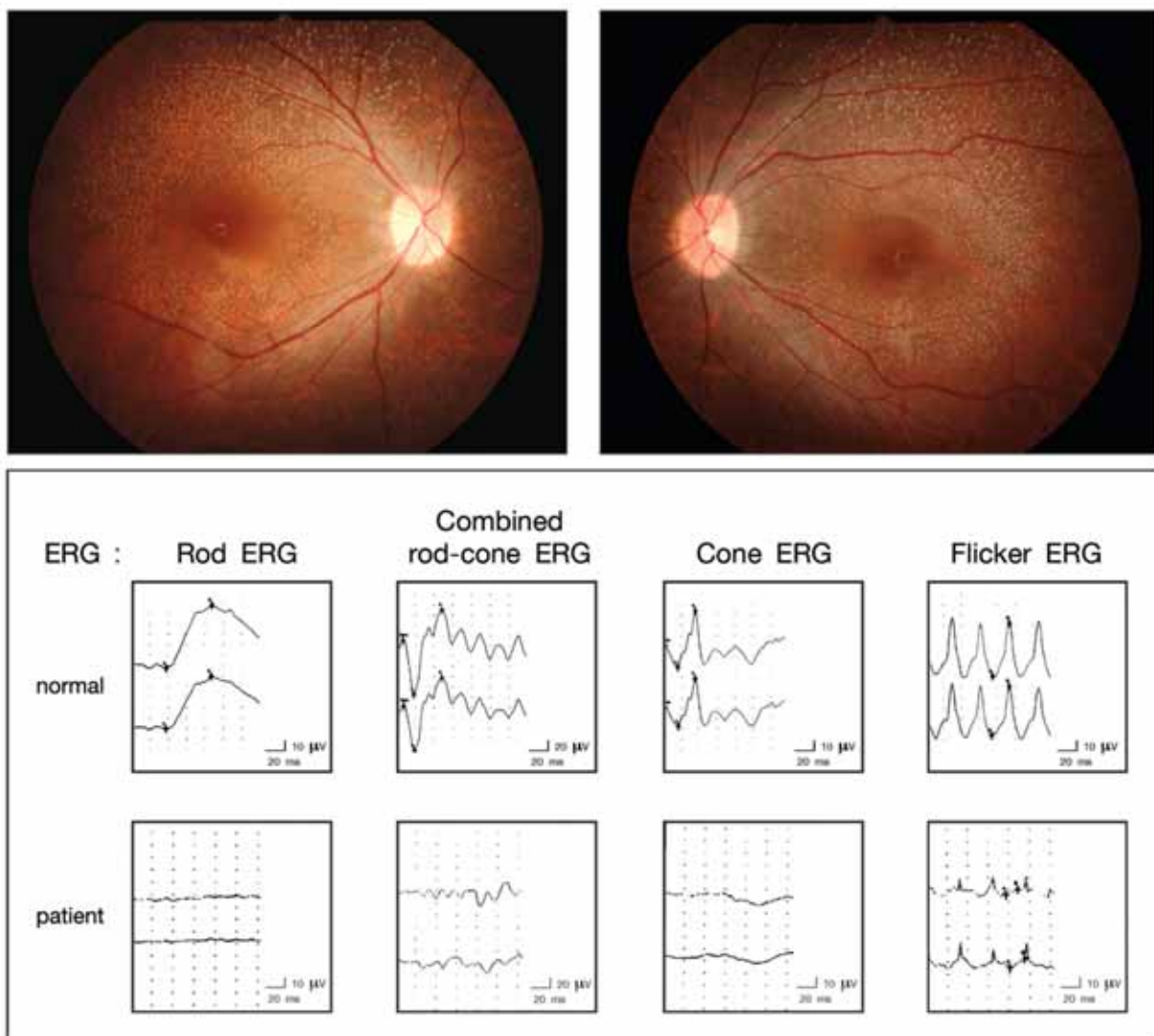
Twelve patients (25%) presented with fleck retina and nyctalopia, of which 11 patients (22.9%) demonstrated nonrecordable ERG that can be diagnosed as retinitis punctata albescens (Figure 1). The other patient (2.1%) showed abnormal rod ERG and normal flicker and cone ERG. After prolonged dark adaptation time for 2-3 hours, abnormal rod ERG could attain to nearly normal range, these characteristic findings were compatible with fundus albipunctatus (Figure 2). There were 36 patients (75%) of fleck retina presented without nyctalopia, 25 patients (52%) were diagnosed with Stargardt's disease by flecks with macular atrophy and mild decreased flicker and

Table 1. Demographic data

		Stargardt's Disease	Fundus Flavimaculatus	Dominant Familial Drusen	Retinitis Punctata Albescens	Fundus Albipunctatus
Patients	(Total N=48)	25	5	6	11	1
Age	(Mean±SD)	32.04±19.20	36.20±24.53	58.67±12.59	28.18±11.19	38
Gender	Female	14	4	5	5	1
	Male	11	1	1	6	-
BCVA	RE (mean±SD)	1.00±0.54	0.26±0.43	0.21±0.30	0.86±0.79	0.1
	LE (mean±SD)	1.00±0.53	0.25±0.32	0.28±0.36	0.96±0.98	0.1
Symptoms	Blur vision	25	2	4	5	1
	Night Blindness	0	0	0	6	0
	No symptoms	0	3	2	0	0
Family history	Positive	4	0	3	2	0
	Negative	21	5	3	9	1

Table 2. Fundus findings of patients in specified subgroups

	Fundus findings (case)			
	Regular fleck, mid periphery	Irregular fleck, mid periphery	Irregular fleck, macular involvement	Macula atrophy/ Beaten bronze appearance
Stargardt's disease	-	-	19	6
Fundus Flavimaculatus	-	5	-	-
Dominant Familial Drusen	6	-	-	-
Retinitis Punctata Albescens	-	9	2	-
Fundus Albipinctatus	1	-	-	-

**Figure 1.** Fundus and electroretinographic findings in retinitis punctata albescens.

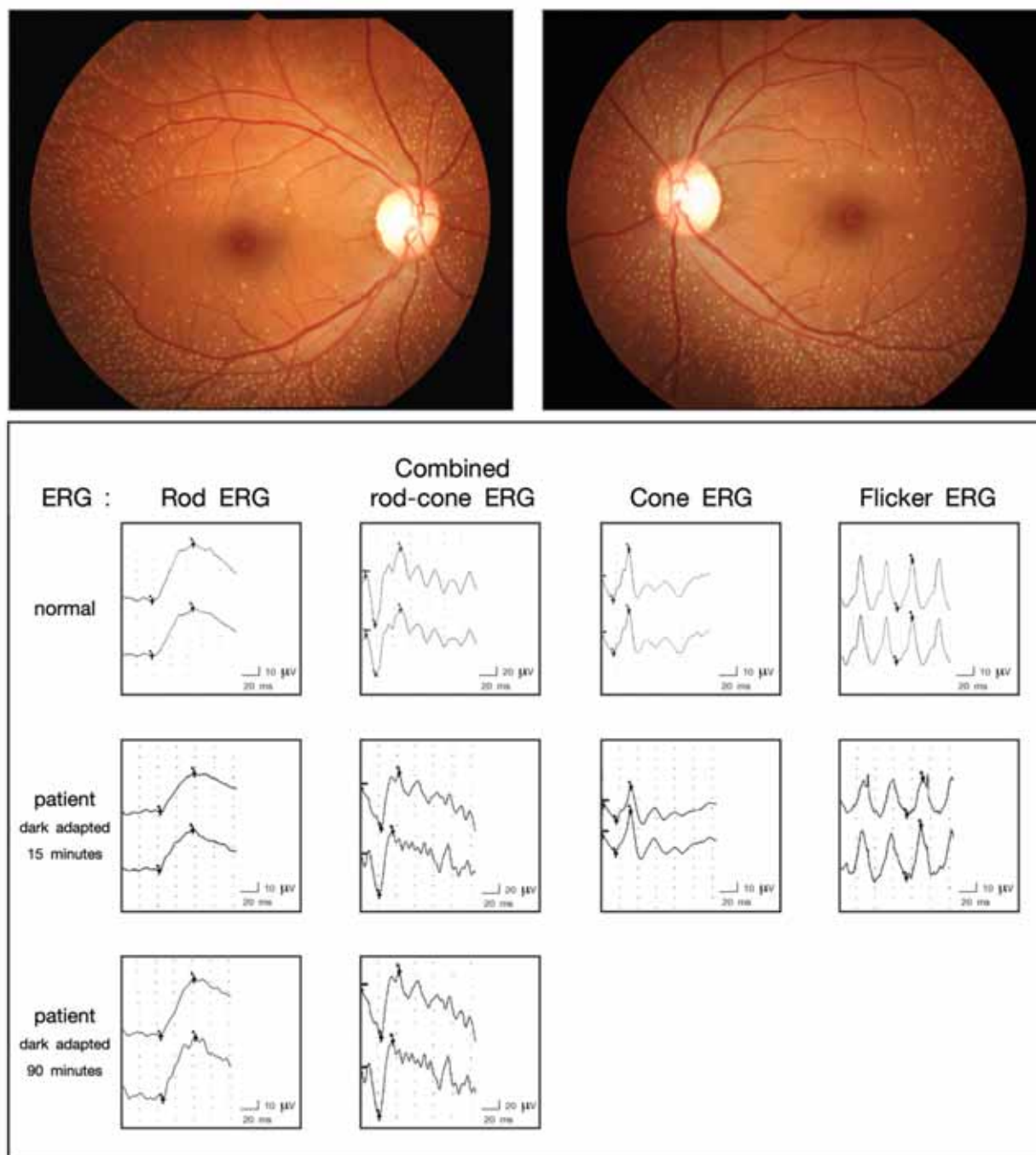


Figure 2. Fundus and electroretinographic findings in fundus albipunctatus.

cone ERG (Figure 3). Five patients (10.4%) were diagnosed with fundus flavimaculatus by showing irregular or pisciform flecks throughout the mid-peripheral retina (Figure 4), and 6 patients (12.5%) were

diagnosed with familial drusen by numerous flecks, round and of varying size extending beyond the vascular arcades (Figure 5), both of these subgroups had minimal change of ERG.

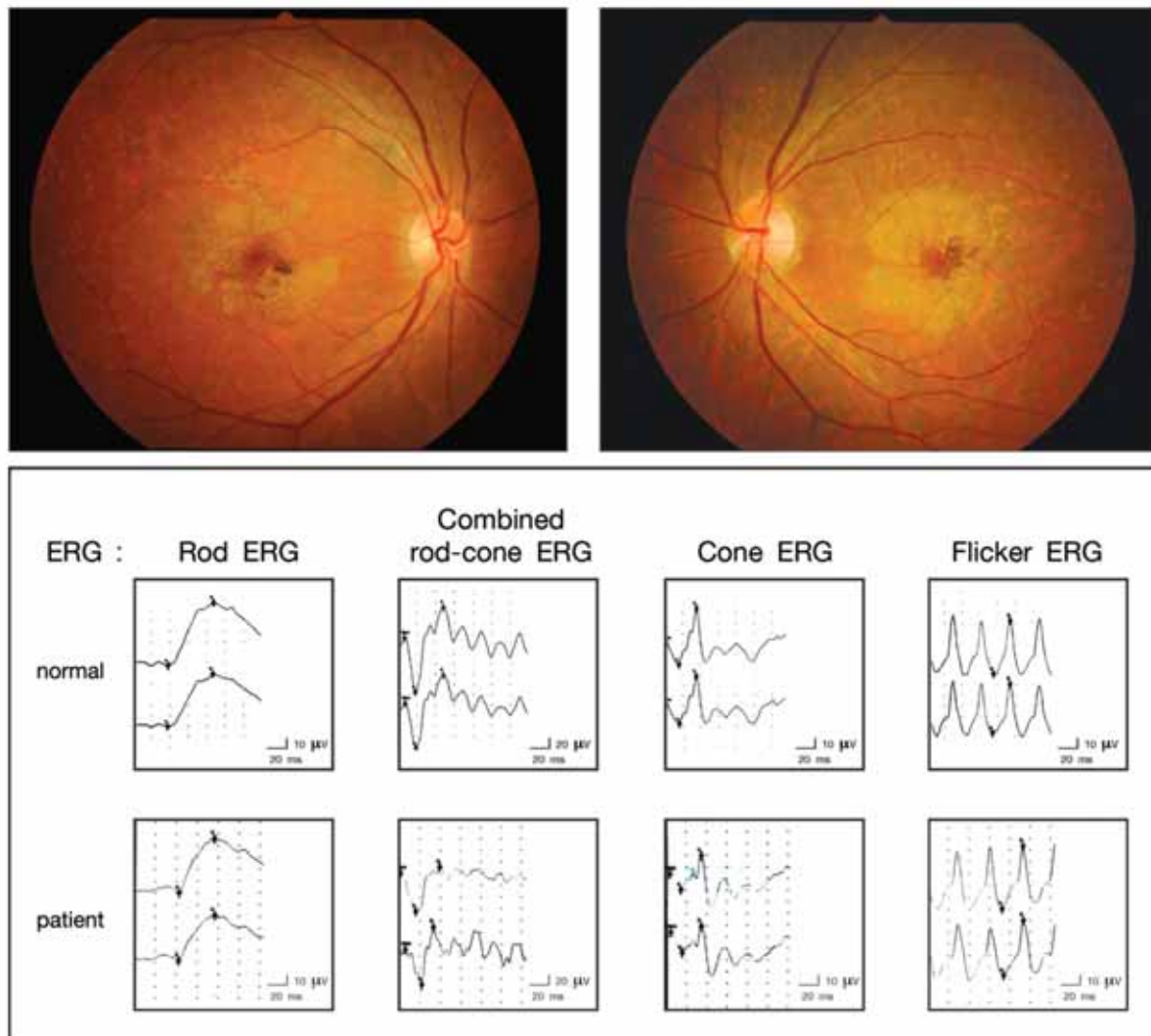


Figure 3. Fundus and electroretinographic findings in Stargardt disease.

Discussion

Fleck retina syndrome can present with various clinical courses from asymptomatic that was found incidentally during routine ophthalmologic examination, mild to severe visual deterioration, or nyctalopia. The diagnosis of this group of disease can be obtained by a meticulous historical review of the presence of poor vision in dim light, blurriness either in general only in the central visual field, diminished color perception, photophobia, the medications recently used, and the exploration of family members who suffered the same symptom or had been

diagnosed with retina disease. The careful ophthalmological examination of anterior and posterior segments to rule out other diseases and to seek for sign of white or yellow spots distributed in the deep layer of the retina should be performed.

Fleck retina syndrome can be approached with the presence or absence of nyctalopia (Diagram 1). In the group of fleck retina with nyctalopia, it can be subdivided by clinical course whether the night blindness was progressive or stationary. Electroretinography is the specific test to diagnose the subgroup of fleck retina syndrome and confirm true

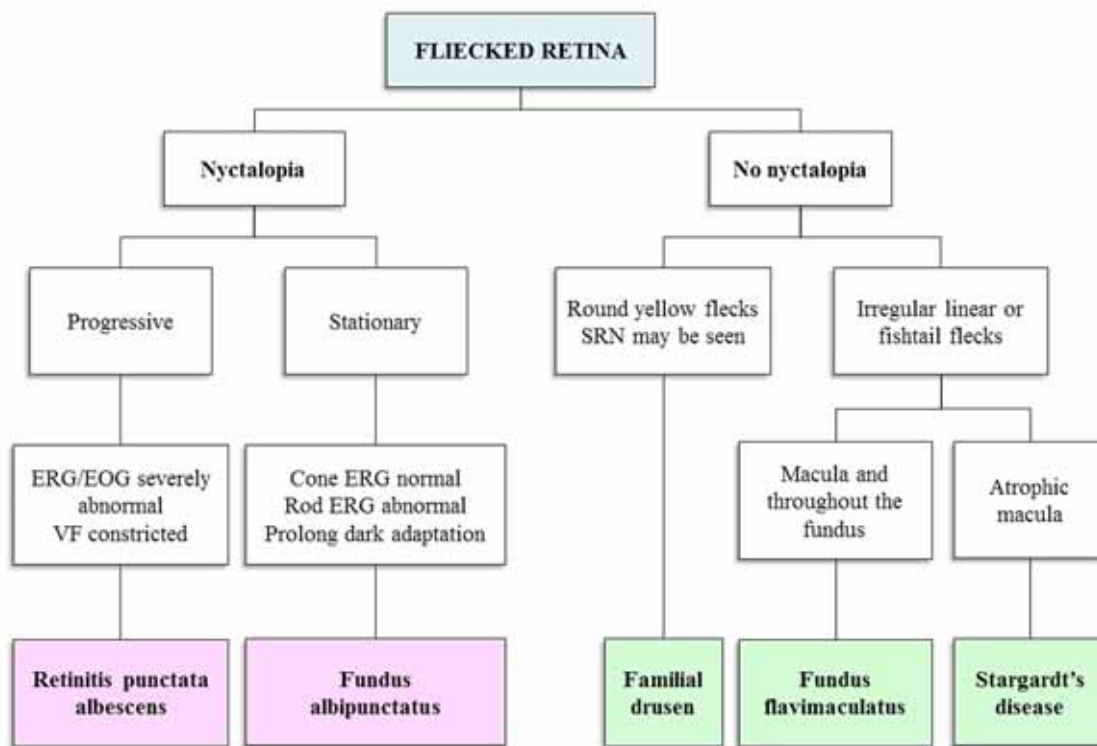


Diagram 1. Subgroups in fleck retina syndrome

night vision impairment. Retinitis punctate albescens has a progressive retinal degeneration with night blindness and peripheral visual field loss, ERG demonstrates a nonrecordable pattern the same as in retinitis pigmentosa.⁴ Mode of inheritance can be either autosomal recessive, dominant form or x-linked recessive. Fundus albipunctatus is an autosomal recessive disorder which is characterized by non-progressive poor night vision and the presence of numerous round flecks scattered throughout the retina, with the exception of the macula. There is no evidence of peripheral retinal pigment clumping, the optic disc and retinal vessels are normal. ERG reveals abnormal rod function which would progress to nearly normal after prolonged dark adaptation time for 2-3 hours.^{4,5} This disorder results from a prolonged rod visual pigment regeneration.⁶

Flecks without nyctalopia can be categorized by characteristic features into round flecks and irregular or fishtail flecks. Fundus flavimaculatus has been differentiated from other fleck retina diseases by characteristic deep yellow, pisciform-shaped or fishtail flecks deposited within the pigmented epithelium and limited to the posterior equatorial regions. Stargardt disease is specified by a juvenile-onset foveal atrophy surrounded by discrete yellowish pisciform flecks. A patient may present with central visual loss and any combination of the clinical triad of macular atrophy, flecks and dark choroid.⁷ The majority of fundus flavimaculatus and Stargardt disease are autosomal recessive, but some dominant pedigrees have been reported. ERG findings in fundus flavimaculatus are usually normal or mildly decreased in all stimuli, while in Stargardt disease

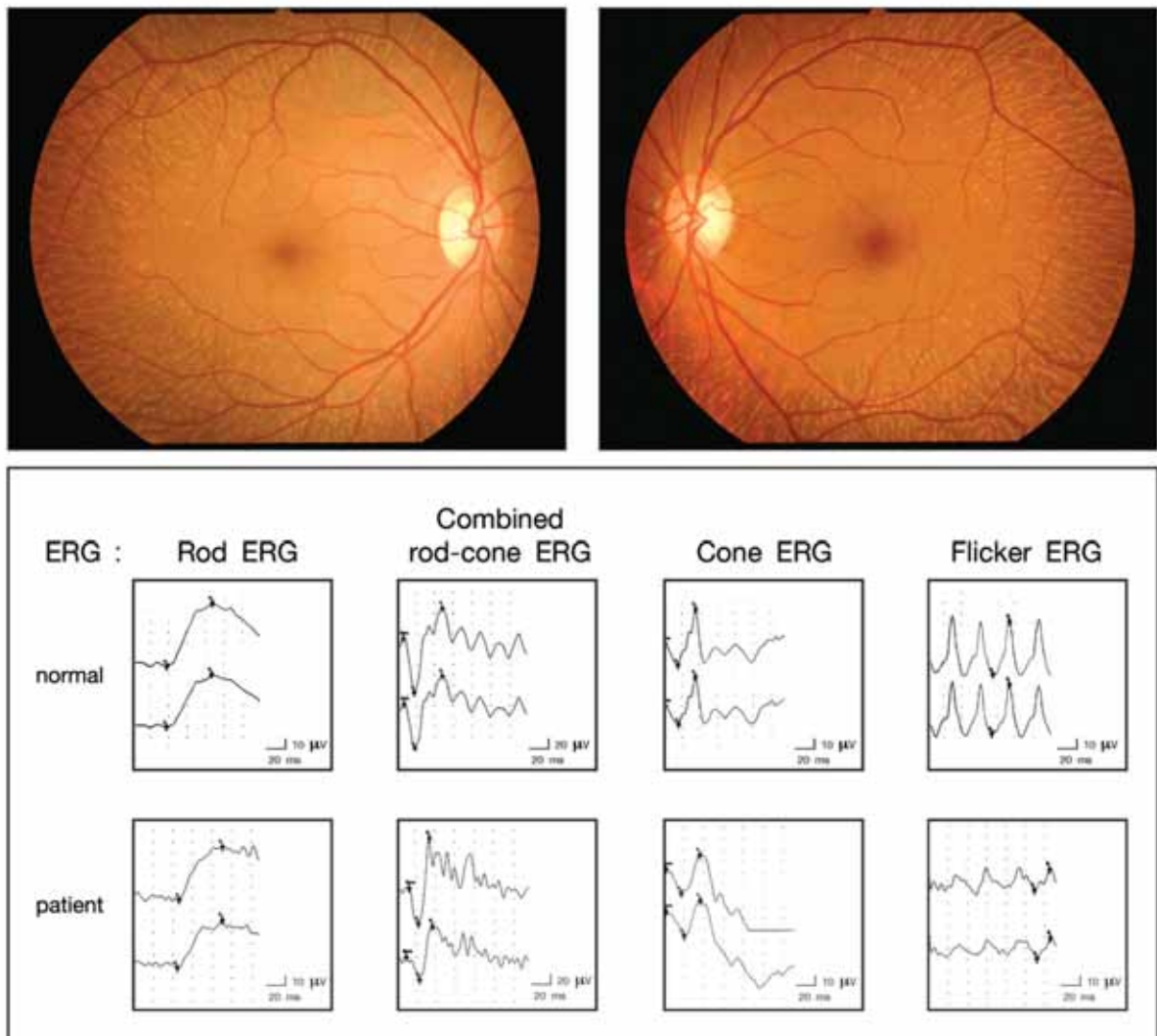


Figure 4. Fundus and electroretinographic findings in fundus flavimaculatus.

there is abnormal flicker or cone ERG.⁸ Drusen, defined as small, round, discrete yellowish lesions in the posterior fundus, are common in older eyes and are thought to develop as a part of the aging process.⁹ The terms inherited drusen, autosomal dominant or familial drusen, are used to refer to discrete drusen present in younger eyes that do not show stigmata of aged-related macular degeneration. Changes in ERG are uncommon but may be occasionally found in eyes with extensive disease, usually in proportion to the degree of damage to the retinal pigment epithelium (RPE). Apparently, the pathological

changes that cause the development of the drusen do not significantly alter the electrical properties of the RPE cells.¹⁰

This study demonstrated that the most prevalent form of fleck retina syndrome in Thailand was Stargardt disease, the second one was retinitis punctata albescens, then followed by familial drusen, fundus flavimaculatus and fundus albipunctatus, respectively. ERG is a very important and special tool for definite diagnosis in subgroups of fleck retina syndrome.¹¹

Impairment in mesopic vision can compromise

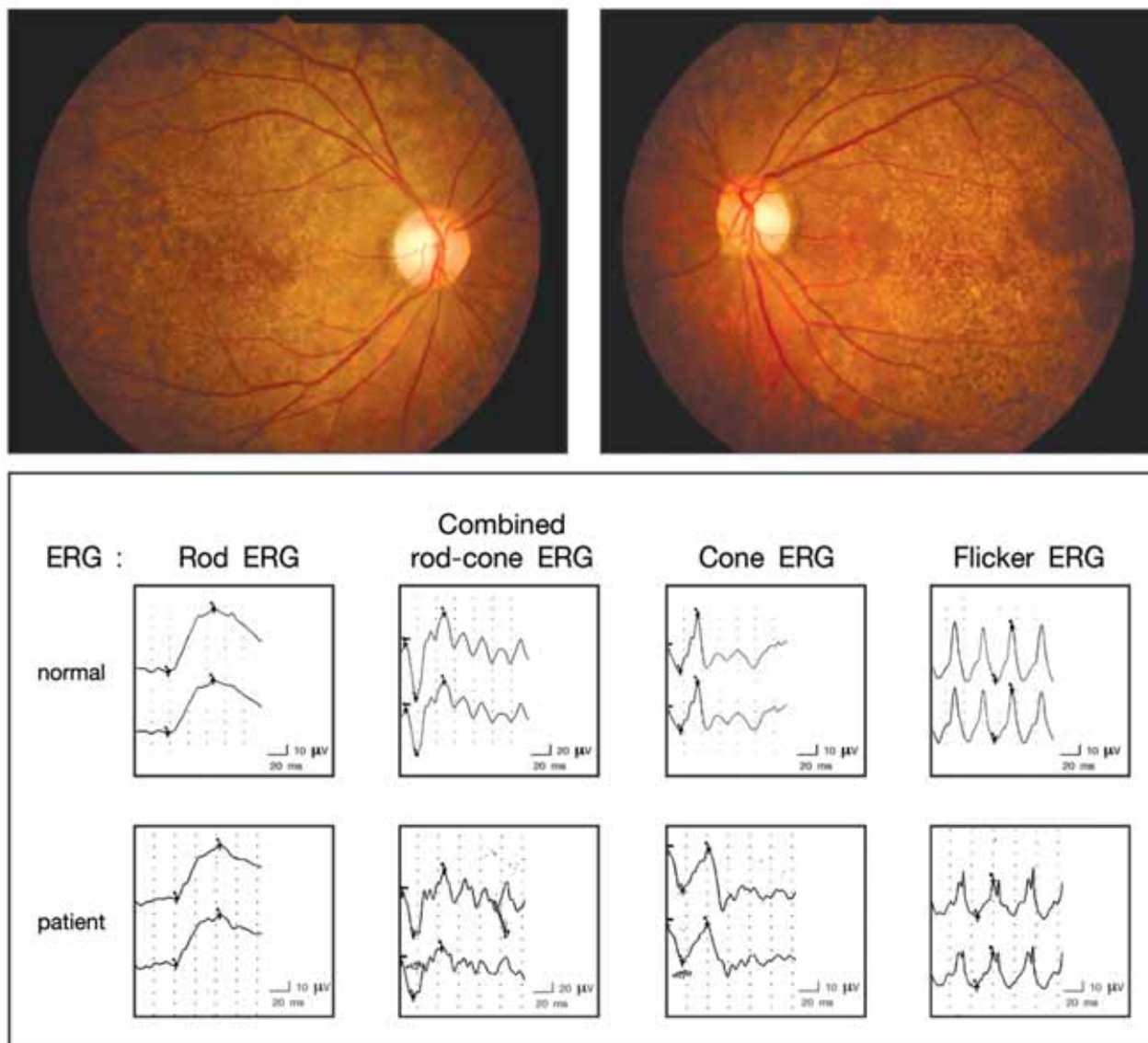


Figure 5. Fundus and electroretinographic findings in familial drusen.

activities in daily life particularly driving at night. Specification of each subgroup helps the clinicians to better understand each entity and can provide appropriate data of disease progression for patients and relatives. Finally, the patients should be referred for visual rehabilitation where they can be helped

to improve their vision and daily activities via using spectacles with best refraction, walking cane, magnifier for reading, visual field enhancer devices, systematic scanning technique, and cataract surgery when needed. These would aid the better course of living in this group with visual deterioration.

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