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非急性期伏格特–小柳–原田综合征的眼底荧光造影特征分析

张娟，马银燕，黎铧，李娟娟

(云南省第二人民医院眼科，昆明 650021)

[摘　要]　**目的：**观察非急性期伏格特-小柳-原田综合征(Vogt-Koyanagi-Harada syndrome，VKH)的眼底荧光血管造影(fundus fluorescein angiography，FFA)特征。**方法：**本研究为回顾性病例研究。收集2016年1月至2019年8月诊断为非急性期VKH的40例(80眼)患者纳入研究，总结分析其眼底影像特征。**结果：**40例患者中12例(24眼)出现不同程度的色素上皮损伤改变；10例(20眼)出现不同程度的脉络膜毛细血管损伤；18例(36眼)患者眼底彩色照片可见已视盘为中心视网膜脉络膜皱褶形成的放射状条纹样改变。24例(48眼)非急性期VKH患者眼底荧光造影呈现不典型的荧光素渗漏。其中10例(20眼)FFA表现为早期后极部可见部分高荧光点，至造影晚期均未见高荧光点的扩大、渗漏及荧光积存现象；14例(28眼)可见后极部大量强荧光点，观察至晚期均强荧光点轻度扩大渗漏，呈弥漫的点状高荧光区。6例(12眼)造影均无明显脉络膜视网膜荧光素渗漏，但光相干断层扫描(optical coherence tomography，OCT)提示仍有不同程度神经上皮层脱离，伴视网膜色素上皮(retinal pigment epithelium，RPE)层波浪状改变。4例(8眼)病程较长患者其眼底表现为后极部灰白色视网膜下条状、片状纤维瘢痕。40例患者中有37例视盘于FFA晚期呈不同程度荧光素着染强荧光，3例伴少许荧光素渗漏。**结论：**非急性期VKH眼底改变可以是多种表现，而眼底影像表现提示病变不同恢复程度及进展情况，有助于更为深入、细致、动态地了解该病的组织病理改变、发展转归，从而指导临床诊断和治疗。

[关键词]　眼底荧光造影检查；光相干断层扫描；视网膜色素上皮；伏格特-小柳-原田综合征；葡萄膜炎

Fundus fluorescence angiography of the non-acute Vogt-Koyanagi-Harada

ZHANG Juan, MA Yinyan, LI Hua, LI Juanjuan

(Department of Ophthalmology, Second People's Hospital of Yunnan Province, Kunming 650021, China)

Abstract　**Objective:** To observe the fundus fluorescein angiography (FFA) features of non-acute Vogt-Koyanagi-Harada syndrome (VKH). **Methods:** In this retrospective case study, 40 patients (80 eyes) who were diagnosed with non-acute VKH admitted to our hospital from January 2016 to August 2019 were enrolled, and their fundus

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通信作者 (Corresponding author)：李娟娟，Email: ljj800502@163.com
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imaging features were summarized. **Results:** Twelve of 40 patients (24 eyes) developed varying degrees of pigment epithelial damage. Ten patients (20 eyes) presented with varying degrees of choroidal capillary damage. Color fundus images of 18 patients (36 eyes) showed a radial streak-like change in the retinal choroid folds. FFA showed atypical fluorescein leakage in 24 patients (48 eyes) with chronic VKH. Among them, FFA showed high fluorescence in the early posterior pole, and no enlargement, leakage and fluorescence accumulation in the late angiography of 10 cases (20 eyes); 14 cases (28 eyes) showed a large quantity of high fluorescence in the posterior pole. In the late stage, high fluorescence was slightly enlarged with leakage, showing a diffuse point-like high fluorescence area. No evident choroidal fluorescein leakage was observed in 6 cases (12 eyes), but optical coherence tomography (OCT) detected different degrees of neuroepithelial detachment with undulating changes in the retinal pigment epithelium (RPE) layer. In 4 cases (8 eyes), fundus images showed a gray-white subretinal strip and a flaky fibrous scar in the posterior pole. Thirty-seven cases showed strong fluorescence in optic disk to different degrees in the late FFA, 3 cases with slight leakage of fluorescein. **Conclusion:** The fundus changes are diverse in non-acute VKH. Fundus image shows different degrees of progression and recovery of the disease, which enables us to deepen the understanding of the histopathological changes, development and prognosis, and eventually provides guidance to clinical diagnosis and treatment of non-acute VKH.

Keywords Fundus fluorescence angiography; optical coherence tomography; retinal pigment epithelium; Vogt-Koyanagi-Harada syndrome; uveitis

伏格特-小柳-原田综合征(Vogt-Koyanagi-Harada syndrome，VKH)是一类急性起病的双侧性肉芽肿性葡萄膜炎，常伴有脑膜刺激征、听觉障碍、毛发及皮肤异常等症状的一种自身免疫性疾病[1]。根据其病程特点，目前将其分为前驱期、急性葡萄膜炎期、慢性期(恢复期)、慢性复发期4个阶段[1]。在VKH发病的急性葡萄膜炎期，眼底影像检查具有较为显著的特点，例如眼底荧光血管造影(fundus fluorescein angiography，FFA)表现为典型的多点状强荧光、造影后期荧光渗漏呈多湖样荧光素积存的特征性表现；光相干断层扫描(optical coherence tomography，OCT)中视网膜色素上皮(retinal pigment epithelium，RPE)波浪样改变及视网膜神经上皮层内的隔膜样结构等均是诊断VKH的主要影像学手段，目前已为广大眼底病医生熟知和运用[2]。但VKH具有反复发作、慢性化的特点，且部分VKH患者由于激素治疗不规范，导致炎症迁延。因此非急性期患者就诊时常表现为较缓和的非肉芽肿性炎症，已无急性期时造影中荧光素渗漏积存及OCT上的典型影像特征，易导致临床的误诊误治。为增强对非急性期VKH眼底特征的认识，避免临床的误诊误治，本研究分析非急性葡萄膜炎期VKH患者眼底影像特征，现总结如下。

1 对象与方法

1.1 对象

本研究属回顾性病例观察研究，收集2016年1月至2019年8月在云南省第二人民医院(以下简称我院)诊断为非急性期VKH的40例(80眼)患者纳入研究：男18例，女22例，均为双眼发病；年龄29~54(35.5±4.3)岁；视力0.01~0.6。其中4例患者伴头晕、头昏等症状，6例患者伴耳鸣，30例患者无全身并发症。纳入标准[2]：提供我院及外院葡萄膜炎期的影像检查确诊为VKH，荧光造影早期为典型多点状荧光素渗漏，晚期形成“多湖样”荧光积存。所有患者中3例未接受任何治疗；37例行口服激素治疗，其中17例给予标准规范治疗，20例由于患者随访不及时未行规范治疗。所有患者确诊后持续观察8周~6个月后，眼底出现不同程度脱色素及OCT显示色素上皮层损伤等VKH慢性期眼底改变。排除标准：患者全身性、系统性、免疫性、遗传疾病史；既往内、外眼相关手术史及眼外伤史；患者屈光介质混浊或合并其他眼底疾病。

1.2 方法

所有患者行最佳矫正视力(best corrected visual acuity，BCVA)、裂隙灯显微镜、散瞳后间接检眼镜及眼底彩色照相及眼底自发荧光(fundus autofluorescence，FAF)、FFA及OCT检查。眼底彩色照相采用TOPCON眼底照相机(TRC-5EX)进行。FAF及FFA检查采用德国海德堡HRA眼底血管造影仪进行，患者散瞳后首先拍摄后极部眼底照相，随后行488 nm激光波长进行FAF扫描，调节敏感度旋钮，连续采集3~5张图像，使用Herdelberg Eye Explore软件处理，得到FAF影像。随后给予患者静脉注射10%荧光素钠2.5 mL快速推注入肘静脉内，8~10 s后加滤光片进行各个象限拍摄，起初为连续拍摄，后改为间歇拍摄，获取FFA图像。OCT检查采用海德堡Spectralis HRA OCT进行，扫描参数为：扫描深度2 mm，扫描部位为以病变部位为中心进行水平扫描，最后选择图像质量与位置较佳的图像进行标记保存。

2 结果

2.1 RPE 损伤

40例患者中12例(24眼)出现不同程度的色素上皮损伤改变。眼底彩色照相可见视网膜脱色素及色素沉着共存的病变，从而呈现色素紊乱的斑驳样眼底改变(图1A)。相应的FFA表现为色素上皮细胞不同程度损伤，脱色素造成造影早期透见荧光，造影晚期呈模糊强荧光，未见明显荧光渗漏。色素沉着区域呈现遮蔽荧光，视盘荧光着染并或不并荧光素渗漏(图1B，1C)。

2.2 脉络膜毛细血管损伤

40例患者中10例(20眼)出现不同程度的脉络膜毛细血管损伤。眼底彩色照相见视网膜部分区域脱色素样改变(图2A)。眼底荧光造影可见脉络膜灌注不良或无灌注，呈现脉络膜背景荧光中的片状低荧光区。随着造影过程的进行，灌注不良的区域缓慢充盈，而无灌注区始终呈现荧光素的充盈缺损，提示该区域脉络膜毛细血管闭塞，视盘轻度荧光着染(图2B，2C)。

2.3 视盘周围脉络膜皱褶

18例(36眼)患者眼底彩色照片可见以视盘为中心视网膜脉络膜皱褶形成的放射状条纹样改变。相应的眼底荧光造影中可见以视盘为中心向四周呈放射状条纹低荧光，条纹周边可见脱色素形成的斑块状透见高荧光，从而呈现一种特殊的眼底“豹斑”样改变，视盘轻度荧光着染(图3)。

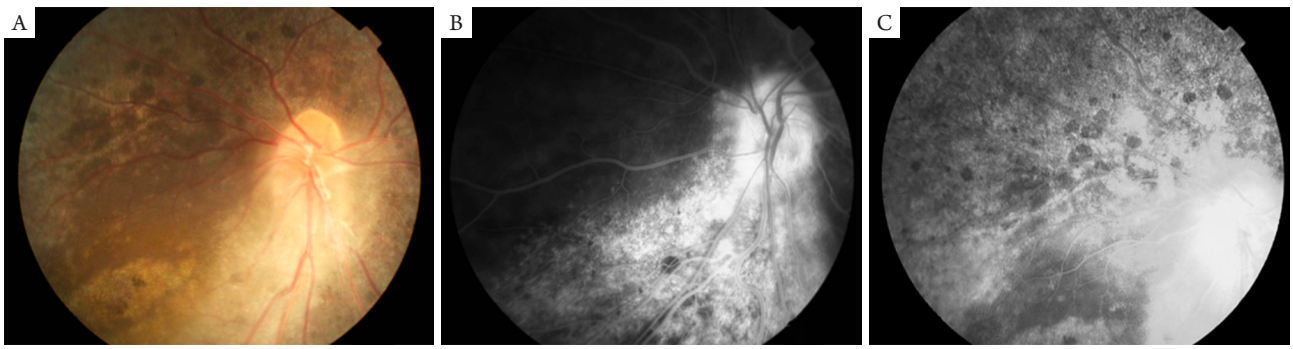

图1 VKH非急性期患者RPE损伤眼底影像特征

Figure 1 Fundus imaging features of RPE injury in patients with non-acute VKH

(A)眼底彩照。视网膜脱色素及色素沉着混杂区域；(B，C)图1A患者早、晚期眼底荧光造影表现。彩照对应脱色素区域呈现透见荧光，色素沉着区呈遮蔽荧光，网膜血管迂曲改变，视盘荧光着染，伴少许荧光素渗漏，边界不清。

(A) Color fundus images. Retinal depigmentation and mixed areas of pigmentation; (B, C) Figure 1A patient's early and late fundus fluorescein imaging findings. Color photographs correspond to depigmented areas with transparent fluorescence, pigmented areas with obscured fluorescence, tortuous changes in omental blood vessels, fluorescein staining of the optic disc, with light fluorescein leakage, and unclear borders.

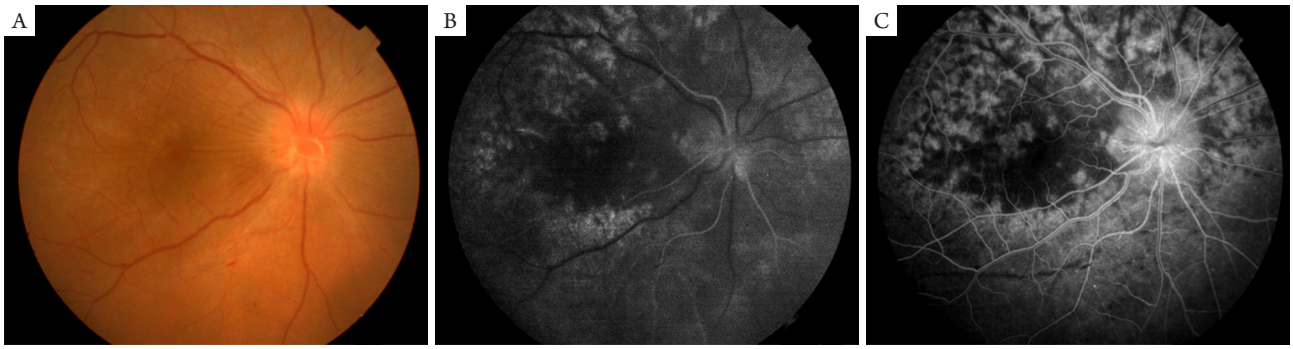

图2 VKH非急性期患者脉络膜毛细血管损伤眼底影像特征

Figure 2 Fundus imaging features of choroidal capillary injury in patients with non-acute VKH

(A)眼底彩照。视盘充血边界模糊，黄斑颞侧见片状视网膜相对苍白区域；(B，C)图2A患者早、晚期眼底荧光造影表现。造影早期后极部脉络膜血管充盈迟缓，晚期部分区域充盈缺损，伴RPE损伤的透见荧光，视盘轻度荧光着染

(A) Color fundus images. The congestion of the optic disc has blurred borders, and a relatively pale area of the retina can be seen on the temporal side of the macula; (B, C) The early and late fundus fluorescein imaging findings of the patient of Figure 2A. In the early stage of angiography, the choroidal blood vessels in the posterior pole are filled with delay, and some areas are filled with defects in the late stage, with RPE injury, and the optic disc is slightly stained with fluorescence.

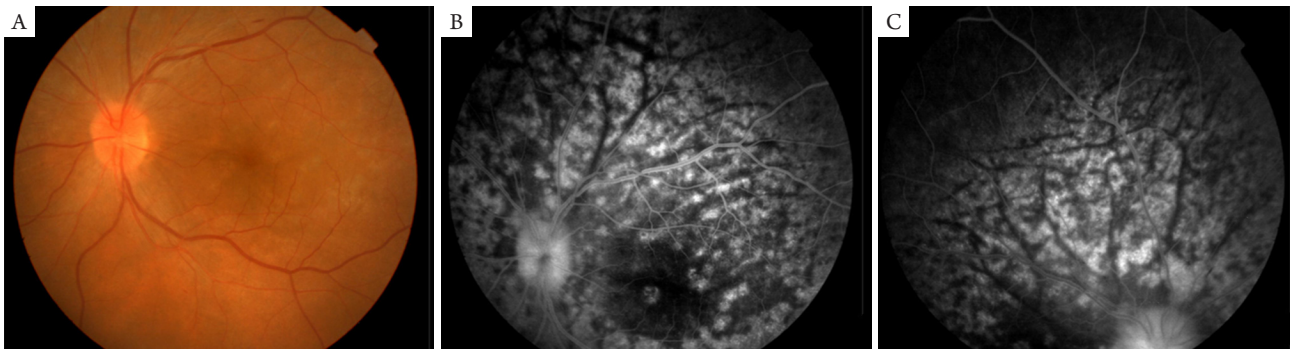

图3 VKH非急性期眼底脉络膜皱褶眼底影像

Figure 3 VKH non-acute fundus choroidal fold image

(A)眼底彩照。视盘周围可见放射状脉络膜皱褶，并可见后极部网膜散在斑块状脱色素；(B，C)图3A患者FFA中期影像。以视盘为中心呈放射状条纹低荧光，条纹周边可见脱色素形成的斑块状透见高荧光，视盘荧光轻度着染。

(A) Color fundus images. Radial choroidal folds can be seen around the optic disc, and plaque-like depigmentation can be seen in the posterior retina; (B, C) Mid-term FFA images of the patient of Figure 3A. With the optic disc as the center, there are radial stripes with low fluorescence, and plaques formed by depigmentation can be seen around the stripes, and high fluorescence is seen, and the optic disc fluorescence is slightly stained.

2.4 非典型的荧光素渗漏

24例(48眼)非急性期VKH患者眼底荧光造影呈现荧光素不同程度着染和不典型的荧光素渗漏。其中10例(20眼)FFA表现为早期后极部可见部分高荧光点，至造影晚期均未见高荧光点的扩大、渗漏及荧光积存现象，视盘轻度荧光着染(图4)。14例(28眼)可见后极部大量强荧光点，观察至晚期强荧光点均轻度扩大渗漏，呈弥漫的点状高荧光区，未见明显荧光素渗漏而呈现“多湖状”荧光积存，视盘荧光素渗漏(图5)。

2.5 OCT 中 RPE 波浪状及神经上皮层积液

3例(6眼)FFA提示早、中、晚期均无明显脉络膜视网膜荧光素渗漏，仅有视盘荧光着染强荧光，但OCT提示仍有不同程度神经上皮层脱离，伴RPE层波浪状改变(图6)。

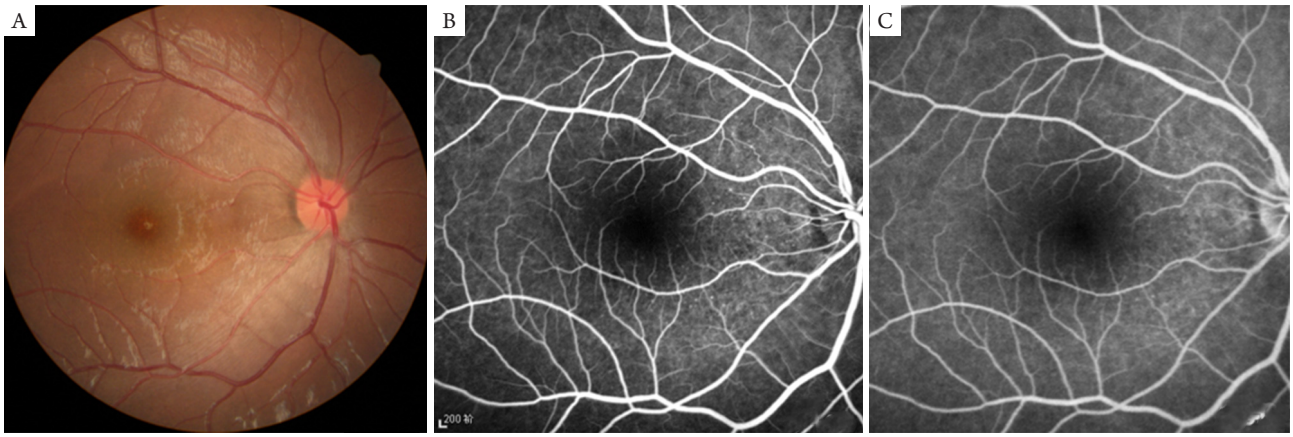

图 4VKH非急性期患者眼底影像

Figure 4 Fundus images of patients in the non-acute VKH

(A)眼底彩照。视盘轻度充血，后极部未见明显神经上皮脱离；(B，C)图4A患者FFA中期、晚期影像。视盘颞侧与黄斑区之间可见点状强荧光，至造影晚期未见强荧光点明显扩大，视盘轻度荧光着染。

(A) Color fundus images. The optic disc was slightly congested, and no obvious neuroepithelial detachment was seen in the posterior pole; (B, C) The mid-term and late-stage FFA images of the patient of Figure 4A. Spot-like strong fluorescence can be seen between the temporal side of the optic disc and the macular area, and there is no significant expansion of the strong fluorescent spot until the late stage of the angiography, and the optic disc is slightly stained with fluorescence.

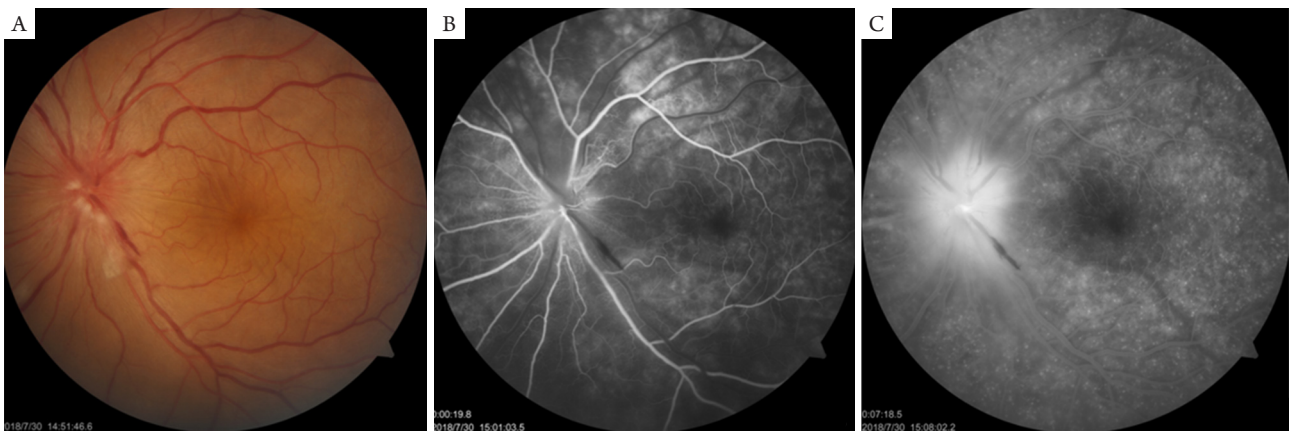

图5 VKH非急性期患者眼底影像

Figure 5 Fundus images of patients in the non-acute VKH

(A)眼底彩照。视盘充血水肿，放射状脉络膜褶皱可见；(B，C)图5A患者FFA中期、晚期影像。造影早期后极部可见强荧光点，至造影晚期强荧光点轻度扩大渗漏，但未形成“多湖样”荧光素积存现象，视盘荧光渗漏。

(A) Color fundus images. Optic disc congestion and edema, radial choroidal folds are visible; (B, C) FFA intermediate and late images of the patient of Figure 5A. In the early stage of angiography, strong fluorescent spots were seen at the posterior pole, and to the late stage of angiography, the strong fluorescent spots slightly enlarged and leaked, but there was no “multi-lake-like” fluorescein accumulation phenomenon, and the optic disc fluorescence leakage.

2.6 视网膜下纤维瘢痕形成

4例(8眼)病程较长患者其眼底表现为后极部灰白色视网膜下条状、片状纤维瘢痕；FFA表现为早期纤维瘢痕区呈遮蔽荧光，周围网膜可见脱色素形成的透见荧光，晚期瘢痕区不同程度荧光着染，视盘荧光着染，部分伴色素沉着遮蔽荧光(图7)。

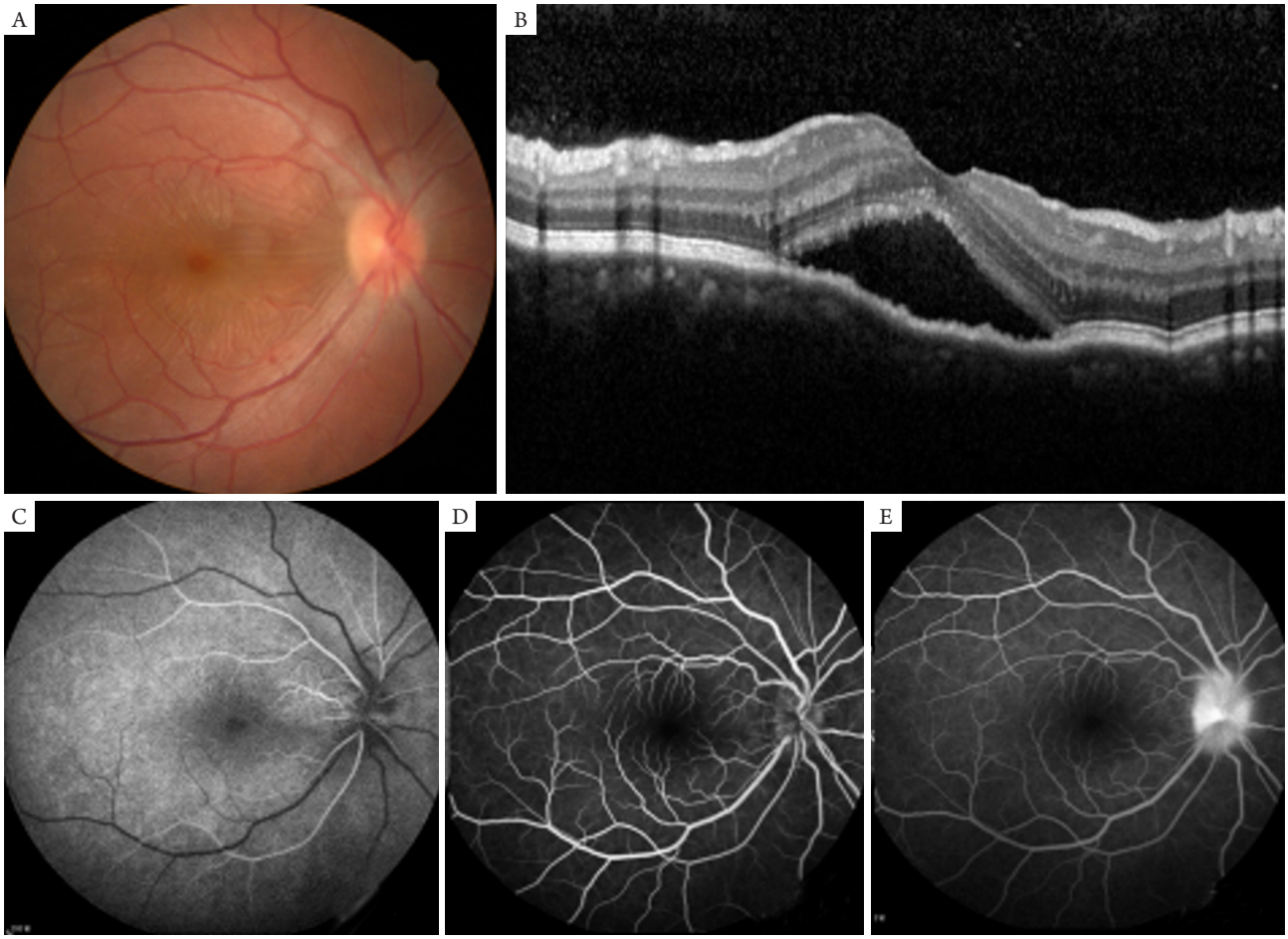

图6 VKH非急性期患者眼底影像

Figure 6 Fundus images of patients with non-acute VKH

(A)眼底彩色照相。视盘轻度充血，后极部放射状脉络膜皱褶；(B)黄斑区OCT图像。黄斑区神经上皮层脱离区RPE层可见颗粒状高反射，RPE层呈现“波浪样”改变；(C~E)眼底FFA图像。FFA早、中、晚期整个造影过程视网膜及脉络膜均未见明显荧光素渗漏，仅在造影晚期视盘呈现荧光着染强荧光，伴少许荧光素渗漏。

(A) Fundus color photography. The optic disc is mildly hyperemic, with radial choroidal folds at the posterior pole; (B) OCT image of the macula. The neuroepithelial layer in the macular area detached from the RPE layer in the detachment area, and granular high reflections were seen in the RPE layer, and the RPE layer showed “wave-like” changes; (C–E) Fundus FFA images. There was no obvious fluorescein leakage in the retina and choroid during the early, middle, and late stages of FFA. Only in the late stage of the contrast, the optic disc showed strong fluorescence with a little fluorescein leakage.

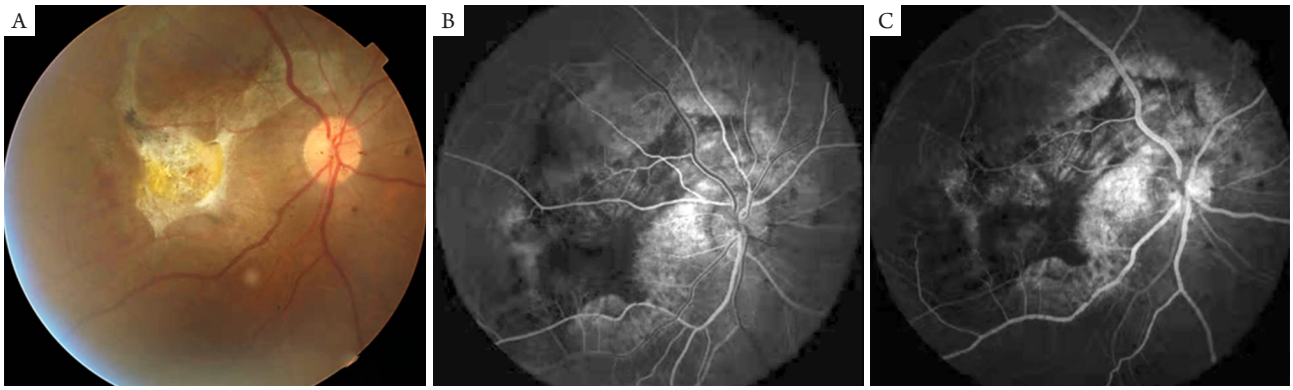

图7 VKH非急性期视网膜下纤维瘢痕患者眼底影像

Figure 7 Fundus images of patients with subretinal fibrous scars in non-acute VKH

(A)眼底彩照 表现为后极部灰白色视网膜下条状、片状纤维瘢痕，其间散在色素沉着，瘢痕区周边可见脱色素改变；(B，C)图7A患者FFA早、晚期图像。早期纤维瘢痕区呈遮蔽荧光，周围网膜可见脱色素形成的透见荧光，晚期瘢痕区荧光轻度着染，伴色素沉着遮蔽荧光，视盘荧光着染。

(A) The color photo of the fundus images shows a gray-white subretinal strip and sheet-like fibrous scar at the posterior pole, with scattered pigmentation, and depigmentation changes can be seen around the scar area; (B, C) FFA early and late image early fiber of the patient in Figure 7A. The scar area showed obscured fluorescence, the surrounding omentum showed depigmented transparent fluorescence, the late scar area was slightly stained with pigmentation obscured fluorescence, and the optic disc was stained with fluorescence.

3 讨论

典型的急性期VKH患者具有多种较为典型的眼底影像特征，而急性期之后或药物治疗后的患者由于这些典型特征消失或变得不典型而容易被临床医生误诊误治。本组病例所观察到的各类非急性期VKH眼底影像改变可帮助临床医生更为全面和动态地认识、分析VKH的临床及病理变化。

在非急性期的VKH患者中，较有代表性的眼底改变，即脉络膜毛细血管及RPE复合体的损伤[3]。眼底表现为色素脱失及色素沉着，相应的荧光造影可见透见荧光及遮蔽荧光混合表现。从疾病发生的病理过程及机制分析，在疾病早期，由于脉络膜炎症造成的急性渗漏，眼底表现渗出液积聚在视网膜神经上皮层下而形成了典型的“多湖样”荧光积存[4]。随着疾病的缓解，渗出减少，但炎症刺激、渗出液中的嗜酸性物质损伤、加之脉络膜血管部分闭塞引发的缺血反应[5]，多种途径共同造成了RPE及脉络膜毛细血管层次的破坏。病理学检查也证实了RPE细胞空泡形成及包膜破裂，RPE附近可见淋巴细胞、巨噬细胞、类上皮细胞及RPE细胞本身增生聚集[6]。

本组病例所观察到的非急性期VKH患者的另一类眼底表现为视盘放射状皱褶所形成的条纹样改变[7]。这一征象并非慢性期患者所独有的眼底特征，急性期患者同样可见。但当其他影像特征不显著时，皱褶条纹可作为诊断VKH非急性期期的影像依据之一。放射状条纹是由于由RPE、Bruch膜和内层脉络膜皱褶形成，目前认为是由于脉络膜炎症所致充血、水肿、增厚，而致密的巩膜限制了脉络膜的延伸，导致脉络膜组织在有限的空间内皱褶[8]。而皱褶凹陷处的RPE层折叠，降低了脉络膜背景荧光的通透性，呈现出条纹状的低荧光。

眼底荧光造影中的荧光渗漏是诊断VKH的一项重要影像学依据[9]。在非急性期的患者中，这种造影的渗漏也呈现了相应的变化。本组病例中多个患者FFA造影示多点状高荧光，但观察至晚期未见明显荧光素渗漏。推测可能原因为脉络膜渗漏通道在此阶段已逐步修复，渗漏明显减少，不足以形成液体的积存，但原本的炎症导致渗漏点处的色素上皮层细胞损伤、凋亡，因此在造影中可见透见的高荧光[10]。同时在2例非急性期患者中观察到荧光造影已无渗漏，但OCT中仍有神经上皮层下的积液，推测这种现象是由于炎症的控制导致血管屏障功能的修复，因此荧光渗漏不明显，但由于RPE功能损伤，原有的液体未能完全吸收或吸收较慢，故有原先渗漏的液体仍少量积存。

而视网膜下的纤维条索形成已是大家较为熟

知的一类慢性VKH的眼底表现，本组病例中在病程较长的患者身上也观察到了这种表现。视网膜下的纤维组织是由于炎症反复发作导致RPE组织异常移行、增生后形成纤维增殖膜[11]。部分文献还报道有慢性期VKH患者脉络膜新生血管[12]形成及脉络膜与视网膜粘连的发生[13]。这两类较为少见的慢性期表现在本组病例中没有观察到。

因此，由于VKH疾病的慢性化或炎症的迁延，患者眼底或表现出与急性期完全不一样的眼底特征。从疾病发生发展的病理过程及机制结合眼底表现全面理解和分析，有助于临床更为全面而动态地认识VKH，减少误诊误治。

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