· 临床研究 ·

KCNV2 相关视锥细胞营养不良患者基因及临床特征

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【摘要】　目的　分析 *KCNV2* 相关视锥细胞营养不良患者的基因及临床特征。　**方法**　纳入 2017 年 8 月至 2019 年 12 月在北京协和医院确诊的 3 个 *KCNV2* 基因相关视锥细胞营养不良家系。采集病史及眼科检查结果，包括视力、色觉、彩色眼底照相、眼底自发荧光（FAF）、光相干断层扫描（OCT）、视野和视网膜电图（ERG）。采集患者及其父母外周血 5 ml 并提取 DNA。利用二代测序（NGS）靶向捕获技术，确诊 *KCNV2* 基因变异相关视锥细胞营养不良患者，并进行 Sanger 验证及家系共分离检测。　**结果**　本研究中共确定 3 例来自不同家系的中国汉族 *KCNV2* 基因相关视锥细胞营养不良患者，其中 2 例患者携带复合杂合变异，1 例近亲患者携带纯合变异。共确定 5 种新发致病变异包括 p.T121M、p.R244C、p.C199Y、p.M250R 和 p.L171Pfs＊201。3 例患者均为男性，年龄分别为 25 岁、16 岁和 2 岁，均有双眼视力低下和畏光症状，2 例患者存在色觉障碍和眼球震颤，呈牛眼征、金箔样反光等特征性眼底表现。FAF 显示黄斑区低荧光伴或不伴周围高荧光环，OCT 示黄斑区视网膜变薄，感光细胞层萎缩，年龄较大的患者萎缩范围相对较宽，视野显示中心暗点伴或不伴周边视野缺损，ERG 显示视锥系统严重受累，表现为明适应反应振幅严重降低，峰时延长，视杆系统受累情况各异，但均可见暗适应特征性 a 波基底宽大。　**结论**　*KCNV2* 相关视锥细胞营养不良患者具有特征性 ERG 表现。中国患者 ERG 表现及基因型与国外患者不同。

【关键词】　*KCNV2* 基因；视锥细胞营养不良；基因突变；二代测序；视网膜电图

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Clinical and genetic characteristics of patients with *KCNV2*-associated cone dystrophy

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[**Abstract**]　**Objective**　To access the genetic defects and clinical characteristics of patients with *KCNV2*-associated cone dystrophy.　**Methods**　Three pedigrees with *KCNV2*-associated cone dystrophy were recruited in Peking Union Medical College Hospital from August 2017 to December 2019. Peripheral blood from each patient and their parents was collected, and genomic DNA was extracted. Targeted exome capture plus next-generation sequencing (NGS) was used to detect the candidate variants. Suspected causative variants were validated by Sanger sequencing and segregation analysis. Comprehensive ocular examinations were performed, including vision acuity, colour vision, fundus photography, fundus autofluorescence (FAF), optical coherence tomography (OCT), visual field and electroretinogram (ERG). This study was approved by the Institutional Review Board of Peking Union Medical College Hospital and adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from each patient prior to any medical examination.　**Results**　Three probands from three unrelated Chinese families were confirmed carrying biallelic *KCNV2* disease-causing variants. Two patients harbored compound heterozygous variants and one patient with history of consanguinity was identified carrying homozygous variant. Five novel variants in the *KCNV2* gene were identified, including p.T121M, p.R244C, p.C199Y, p.M250R and p.L171Pfs＊201. All patients

enrolled in this study were male with age of 25, 16 and 2 years old, respectively. Three affected individuals complained of vision loss and photophobia and two patients demonstrated reduced color perception and nystagmus. Macular discoloration (bull´s eye maculopathy or gold foil macular reflex) was observed in fundus photographs. Macular hypofluorescence was illustrated in FAF imaging, which accompanying a broad hyperfluorescent ring surrounding the central atrophy or not. Macular thinning with loss of the inner segment ellipsoid zone was noted in OCT images, and the disruption was more profound in older patients. Central scotoma with or without peripheral visual field defects was observed in perimetry. Severe cone function loss and variable scotopic rod impairment were demonstrated in ERG, whereas a broad a-wave trough response to scotopic bright flash stimulation was noted. **Conclusions** Patients with *KCNV2*-associated cone dystrophy show a characteristic ERG manifestation. ERG results and *KCNV2* variants in Chinese patients differ from those in foreigners.

[**Key words**] *KCNV2* gene; Cone dystrophy; Mutation; Next-generation sequencing; Electroretinogram

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KCNV2 (potassium channel, voltage-gated, subfamily V, member 2; MIM # 607604) 基因位于染色体 9p24.2, 包含 2 个外显子, 编码的蛋白 Kv8.2 是跨膜蛋白电压门控钾离子通道亚家族的成员, 包含 545 个氨基酸, 由 N 端 A 和 B 盒、6 个跨膜区域 (S1～S6) 和 1 个孔环路构成[1]。Kv8.2 蛋白主要表达于视锥视杆细胞内段, 与 Kv2 亚基组装成异源四聚体改变 I_{kx} 电流从而影响感光细胞膜电位[2-5]。Gouras 等[6] 首次报道, *KCNV2* 基因变异可导致常染色体隐性遗传视锥细胞营养不良, 多伴 ERG 视杆反应超高波形 (cone dystrophy with a supernormal rod response, CDSRR), 是一种特殊类型的视锥细胞营养不良。目前已报道 96 种 *KCNV2* 基因变异位点 (http://www.hgmd.cf.ac.uk/ac/index.php), 93 种与视锥细胞营养不良相关, 其中 71 种与 CDSRR 相关, 中国迄今报道 8 种 *KCNV2* 基因变异位点, 均为大样本基因检测下的变异报道或个案报道, 并未详细总结其临床特征[7-11]。本研究中应用二代测序技术确诊 3 例 *KCNV2* 基因相关视锥细胞营养不良中国家系, 分析其基因和临床特征。

1　资料与方法

1.1　一般资料

纳入 2017 年 8 月至 2019 年 12 月在北京协和医院眼科确诊的 3 个 *KCNV2* 基因相关视椎细胞营养不良家系。本研究通过中国医学科学院北京协和医院伦理委员会审核批准 (伦审号: JS-2059), 遵循赫尔辛基宣言。所有患者或其监护人均自愿参加并签署知情同意书。

1.2　方法

1.2.1　临床检查　采集患者眼部病史、家族史和患者父母婚育史。对患者进行视力、色觉、裂隙灯显微镜前节检查、扩瞳后眼底检查、彩色眼底照相 (美国 Topcon 公司)、眼底自发荧光 (fundus autofluorescence, FAF) (德国 Heidelberg 公司)、光相干断层扫描 (optical coherence tomography, OCT) (德国 Heidelberg 公司, 德国 Carl Zeiss 公司)、视野 (Octopus 101 型全自动视野计 Dynamic 策略 60° 视野, Zeiss humphery 30-2 程序 SITA 标准策略 30° 视野) (德国 Roland Cousult 公司); 视网膜电图 (electroretinography, ERG) (美国 Diagnosys 公司) 检查。ERG 采用国际临床视觉电生理协会 (International Society for Clinical Electrophysiology of Vision, ISCEV) 的标准进行检查和分析, 3 例患者均使用 ERG-Jet 角膜接触镜电极, 患者 3 于镇静条件下进行检查。

1.2.2　分子遗传学检测　采集患者及其父母的外周静血 5 ml, 利用 QIAamp DNA Blood Midi 试剂盒法提取全基因组 DNA。采用 Illumina 二代测序技术对 256 个与视网膜疾病相关的基因编码区进行测序, 测序数据与 UCSC 人类基因组参考序列 hg19 (Feb. 2009)、1000 Genomes、人类基因突变数据库 (Human Gene Mutation Database, HGMD)、ExAC、ClinVar 及内部 1 个 30 万人的对照数据库进行比对, 判断是否为单核苷酸多态性 (single nucleotide polymorphism, SNP) 或已报道变异; 应用 SIFT、Polyphen2 和 Mutation Taster 等多个软件对新发现的错义变异进行致病性预测; 根据美国医学遗传学和基因组学 (American College of Medical Genetics and Genomics, ACMG) 推荐指南进行致病性评估[12]。对可疑致病变异进行 Sanger 测序及父母亲共分离验证。

2　结果

2.1　*KCNV2* 相关视锥细胞营养不良家系的临床特征

本研究纳入 3 个家系的 3 例患者，各家系成员均为中国汉族人，家系遗传特点符合常染色体隐性遗传方式（图 1，表 1）。

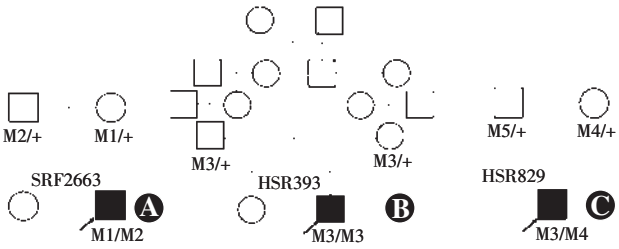

图 1　*KCNV2* 相关视锥细胞营养不良家系图及基因变异携带情况　A：1 号家系　B：2 号家系　C：3 号家系　M1～M5 分别代表 5 种不同的 *KCNV2* 基因变异；□：正常男性；○：正常女性；■：男性患者；/：已故；↗：先证者；+：野生型

Figure 1　Pedigrees of families with *KCNV2*-associated cone dystrophy　A: Pedigrees of family 1　B: Pedigrees of family 2　C: Pedigrees of family 3　□: normal male; ○: normal female; ■: male patient; /: dead; ↗: proband; +: wild type

表 1　*KCNV2* 相关视锥细胞营养不良患者分子遗传学结果及致病性预测

Table 1　Molecular genetic results and pathogenicity prediction of *KCNV2*-associated cone dystrophy patients

先证者	外显子	核苷酸改变	氨基酸改变	杂合性	SIFT	Polyphen 2	Mutation Taster
家系 1	1	c.362C>T	p.T121M	杂合	致病	可疑致病	致病
	1	c.730C>T	p.R244C	杂合	致病	可疑致病	临床意义不明
家系 2	1	c.596G>A	p.C199Y	纯合	致病	可疑致病	致病
家系 3	1	c.749T>G	p.M250R	杂合	致病	可疑致病	致病
	1	c.511dupC	p.L171Pfs*201	杂合	-	-	-

注：SIFT、Polyphen 2、Mutation Taster 均为变异有害性预测软件　-：未检测

Note: SIFT: Sorting Intolerant from Tolerant; Polyphen 2: Polymorphism Phenotyping v2; Mutation Taster. In silico variants pathogenicity prediction software　-: undetected

家系 1 先证者，25 岁，男，自幼畏光，视力差，矫正不提高，检查视力右眼 0.10，左眼 0.12。色觉检查显示色盲本识别小部分。眼底检查可见黄斑区反光异常；FAF 示黄斑区不规则样低荧光伴周围高荧光环；OCT 示视网膜外层变薄，椭圆体带严重萎缩伴少量残留；视野示中心暗点。ERG 示暗适应 0.01 b 波振幅轻度下降；双混合及增强反应 a 波振幅正常，基底宽大，b 波振幅降低，b/a 值缩小（右眼 1.17，左眼 1.15），呈负波形；OPS 反应波数目正常，振幅中度降低，明适应及闪烁光反应 a、b 波振幅重度降低（图 2～4，表 2）。

家系 2 先证者，16 岁，男，父母系近亲，自幼视力差，夜盲，畏光。色觉检查示仅识别色盲本示教图，最佳矫正视力右眼 0.25，屈光度为+1.75DS/+2.27DC*70°，左眼 0.15，屈光度为+1.75 DS/+2.00 DC*100°。患者注视时双眼眼球震颤。眼底可见黄斑区金箔样反光；FAF 示中央椭圆形低荧光；OCT 检查示视网膜外层变薄，椭圆体带消失，视网膜色素上皮（retinal pigment epithelium，RPE）萎缩；视野示中心暗点伴周边不规则缺损。ERG 示视锥、视杆系统均受累，即暗适应 0.01 b 波记录不到；双眼混合及增强反应示 a、b 波振幅严重降低，峰时延长；明适应及闪烁光反应振幅严重降低（图 2～4，表 2）。

家系 3 先证者，2 岁，男，监护人发现患儿双眼眼球震颤，光线强烈时眯眼。眼底检查可见黄斑区牛眼征；OCT 示中心凹处椭圆体带不连续；ERG 检查可见暗适应反应重度下降，明适应反应记录不到（图 2～4，表 2）。

2.2　*KCNV2* 相关视锥细胞营养不良家系的分子遗传学表现

3 个家系共确定 5 种不同的新发变异，均位于 1 号外显子。家系 1 先证者携带复合杂合变异 c.362C>T（p.T121M）和 c.730C>T（p.R244C），分别来自于父

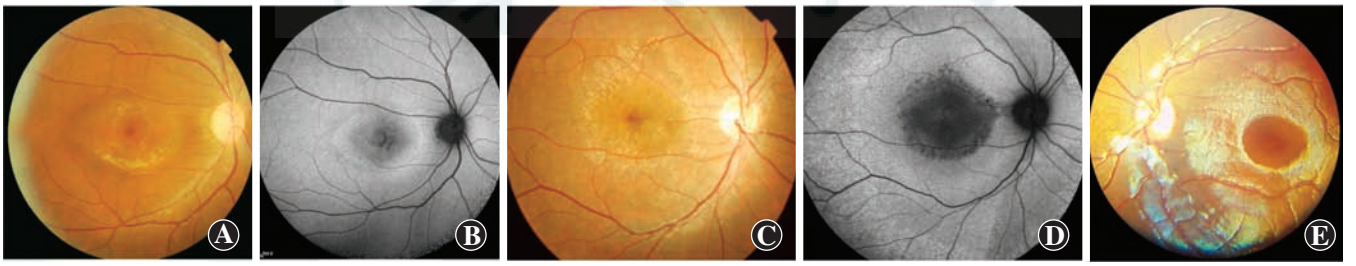

图 2　*KCNV2* 相关视锥细胞营养不良患者彩色眼底照相和 FAF 表现　A：家系 1 先证者右眼彩色眼底照片示黄斑区反光异常　B：家系 1 先证者右眼 FAF 示黄斑中心凹不规则低荧光伴周围高荧光环　C：家系 2 先证者右眼彩色眼底照片示黄斑区金箔样反光　D：家系 2 先证者右眼 FAF 示中央椭圆形低荧光团　E：患者 3 左眼彩色眼底照片示牛眼征

Figure 2　Colored fundus photographs and FAF images in patients with *KCNV2*-associated cone dystrophy　A: Right eye of proband 1 displayed macular discoloration by colored fundus photograph　B: Right eye of proband 1 showed foveal reduced autofluorescence surround with ring of increased autofluorescence by FAF　C: Right eye of proband 2 revealed gold foil macular reflex by colored fundus photograph　D: Right eye of proband 2 showed an oval shaped area of reduced autofluorescence corresponding to the maculopathy by FAF　E: Left eye of proband 3 displayed a bull's eye maculopathy by by colored fundus photograph

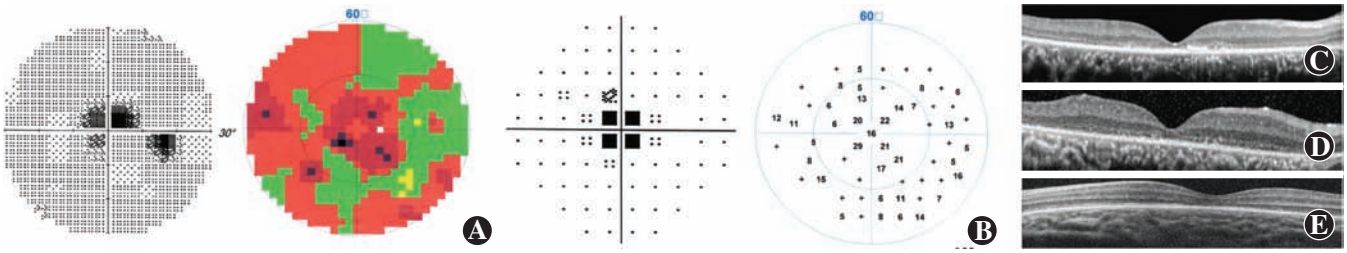

图 3　*KCNV2* 相关视锥细胞营养不良患者视野和 OCT 表现　A：家系 1 先证者右眼 30°视野显示中心暗点　B：家系 2 先证者右眼 60°视野显示中心暗点伴周边不规则缺损　C：家系 1 先证者右眼 OCT 示视网膜外层变薄，椭圆体带消失伴少量残留　D：家系 2 先证者右眼 OCT 示视网膜外层变薄，椭圆体带消失，RPE 萎缩　E：家系 3 先证者左眼 OCT 示中心凹处椭圆体带不连续

Figure 3　perimetry and OCT results of patients with *KCNV2*-associated cone dystrophy　A: Right eye of proband 1 showed a preserved peripheral visual field and central scotoma by VF　B: Right eye of proband 2 showed central scotoma accompanying irregular peripheral defect by VF　C: Right eye of proband 1 showed thinning of the outer retina and loss of ellipsoid zone with small remaining island by OCT　D: Right eye of proband 2 showed thinning of the outer retina and loss of the ellipsoid zone with RPE atrophy by OCT　E: Left eye of proband 3 showed focal ellipsoid zone disruption by OCT

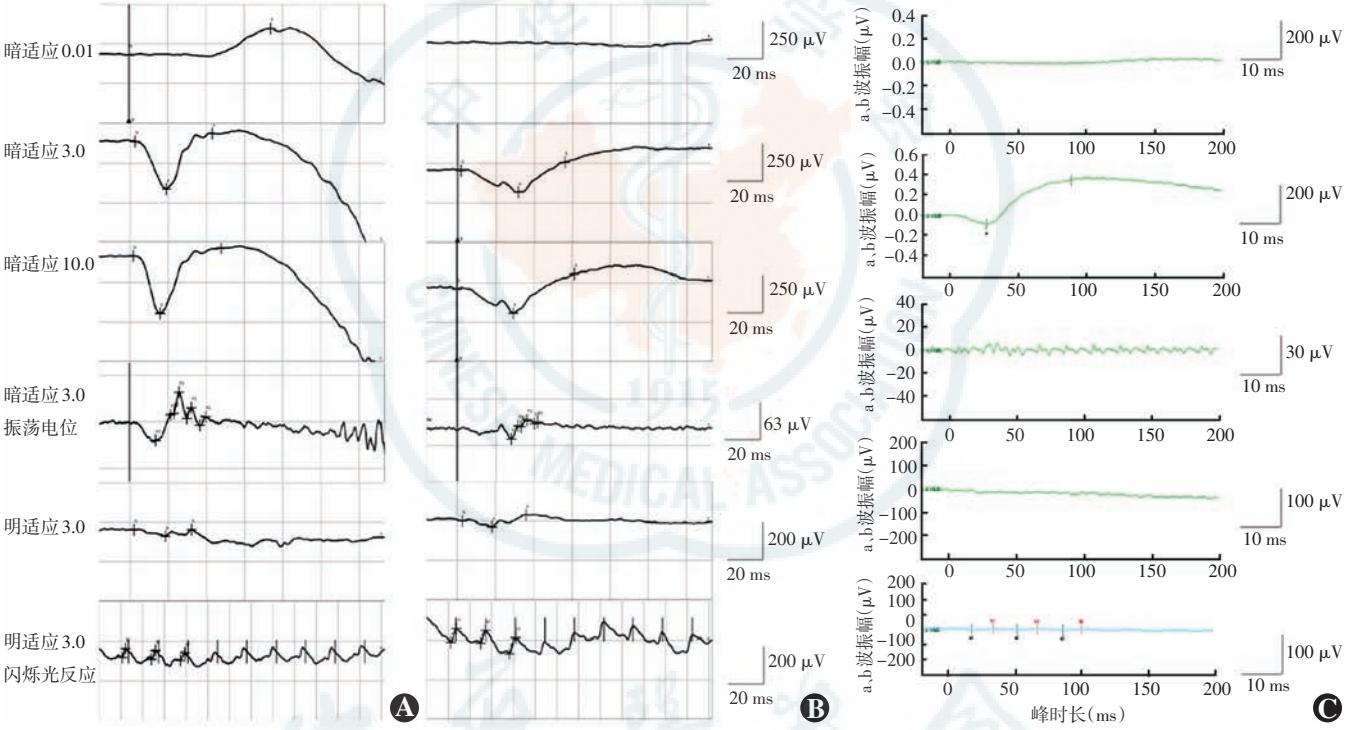

图 4　*KCNV2* 相关视锥细胞营养不良患者 ERG 表现　A：家系 1 先证者右眼视锥反应振幅降低，视杆反应 a 波基底宽大，呈负波形　B、C：家系 2 先证者右眼和家系 3 先证者左眼视杆反应振幅轻度降低，视锥反应振幅重度降低

Figure 4　ERG characteristics in patients with *KCNV2*-associated cone dystrophy　A: Right eye of proband 1 showed attenuated photopic responses, but normal scotopic b-wave with a broad rather than a tapered a-wave trough by ERG. The b-wave to a-wave was decreased which revealed a negative ERG　B、C: Right eye of the proband 2 and left eye of proband 3 showed slightly diminished rod responses and severely reduced cone responses by ERG

表 2　*KCNV2* 相关视锥细胞营养不良患者一般资料
Table 2　Clinical features of *KCNV2*-associated cone dystrophy patients

先证者	性别	父母近亲史	年龄（岁）	视力	色觉障碍	畏光	眼球震颤	夜盲	ERG	
									明适应	暗适应
家系 1	男	(-)	25	0.10/0.12	(+)	(+)	(-)	(-)	重度降低	“负波形”
家系 2	男	(+)	18	0.25/0.15	(+)	(+)	(+)	(+)	重度降低	重度降低
家系 3	男	(-)	2	NA	NA	(+)	(+)	(-)	平波	重度降低

注：ERG：视网膜电图；NA：未能配合检查
Note: ERG: electroretinogram; NA: not available

母；家系 2 先证者携带纯合变异 c.596G>A(p.C199Y)，父母杂合携带；家系 3 先证者携带复合杂合变异 c.749T>G(p.M250R)和 c.511dupC(p.L171Pfs*201)，分别来自于其父母(图 5)。4 个新发错义变异的致病性预测见，变异未在对照数据库中出现过，SIFT、Polyphen2 及 Mutation Taster 等多个软件预测结果表明为疑似致病变异。c.511dupC(p.L171Pfs*201)是一个新的移码变异，位于 chr9:2718249，未在对照数据库中出现。该变异改变了读码框，对蛋白功能造成影响。

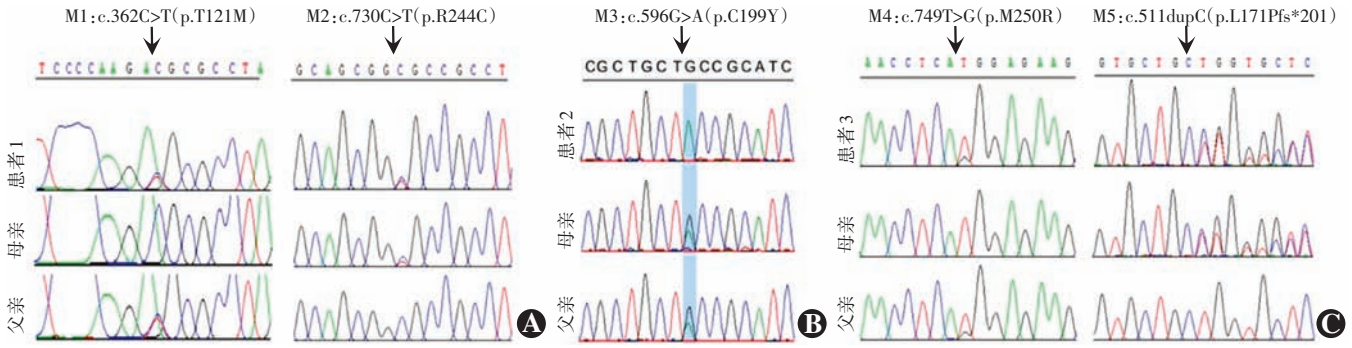

图 5　*KCNV2* 相关视锥细胞营养不良患者 Sanger 测序图　A：家系 1 先证者携带 *KCNV2* 基因复合杂合变异 M1 c. 362C>T(p. T121M)和 M2 c. 730C>T(p. R244C)，其父母杂合携带　B：家系 2 先证者纯合携带 M3 c. 596G>A(p. C199Y)，其父母杂合携带　C：家系 3 先证者携带复合杂合变异 M4 c. 749T>G(p. M250R)和 M5 c. 511dupC(p. L171Pfs * 201)，其父母杂合携带

Figure 5　Sequence chromatograms of patients with *KCNV2*-associated cone dystrophy　A: Proband 1 carried the compound heterozygous *KVNV2* variants (c. 362C>T, p. T121M and c. 730C>T, p. R244C), the unaffected patients only carried either p. T121M or p. R244C heterozygously　B: Proband 2 carried the homozygous *KVNV2* variants (c. 596G>A, p. C199Y), and the unaffected patients only carry p. C199Y heterozygously　C: Proband 3 carried the compound heterozygous *KVNV2* variants (c. 749T>G, p. M250R and c. 511dupC, p. L171Pfs * 201), and the unaffected patients only carried either p. M250R or c. 511dupC, p. L171Pfs * 201 heterozygously

3　讨论

视锥系统受累表现为幼时视力低下，眼球震颤、畏光和色觉障碍。视锥细胞营养不良、全色盲和锥杆营养不良(cone-rod dystrophy, CORD)等均有上述表现。彩色眼底照相可见正常眼底或黄斑区反光异常，少数可出现中心凹处 RPE 萎缩；OCT 可见黄斑区视网膜外层变薄，椭圆体带不连续，全色盲患者可出现中心凹平坦样表现，提示发育不良；FAF 可见黄斑区低荧光伴或不伴周围高荧光环，呈牛眼征；视野显示中心暗点或旁中心暗点[13-18]。本研究中 3 例 *KCNV2* 相关视锥细胞营养不良患者均有自幼视力低下，矫正后不能提高，色觉障碍，其中 2 例年龄较小的患者(16 岁和 2 岁)存在眼球震颤，且家系 2 先证者(16 岁)仅在注视时可观察到眼球震颤，提示该症状随年龄增加逐渐好转或消失，这与 Wissinger[16]等、Khan 等[19]和 Kato 等[20]的研究相符。本研究中 3 例患者眼底、OCT 和视野结果均符合视锥系统受累表现。家系 3 先证者仅 2 岁，OCT 可见黄斑中心凹处椭圆体带消失，萎缩宽度明显小于其他 2 例患者，提示随年龄增长病变逐渐进展。此外 Kustuma 等[21]对 *KCNV2* 相关视锥细胞营养不良患者进行长达 15 年的随访显示该病变进展缓慢。

对于无法配合某些检查或视力低下而眼底并无特殊异常的患者，通常需要 ERG 检查以进一步辅助诊断。全色盲患者 ERG 表现为视锥系统功能丧失或严重降低而视杆反应正常或接近正常[22-23]。本研究中 3 例患者 ERG 均表现为视锥系统严重受累(明适应反应振幅降低、峰时延长)，视杆系统受累情况各异，但暗适应反应均可见特征性 a 波宽大基底，与国外报道 CDSRR 患者的 ERG 相符[15,17,24]，提示功能障碍发生在光传导后但在内层视网膜产生 b 波之前[15,25]。家系 3 先证者 ERG 明适应呈平波，可能与检查时服用镇静剂有关。国外报道的 *KCNV2* 相关 CDSRR 患者特征性 ERG 表现为暗适应下刺激强度依赖性反应即低闪光刺激，如 0.01 cd·s/m^2 b 波振幅严重降低，峰时延长，而高闪光刺激，如 3.0 cd·s/m^2 或 10.0 cd·s/m^2 b 波振幅正常或出现超高型，b/a 值升高[6]。Khan 等[19]和 Zelinger 等[26]研究发现，并非所有 *KCNV2* 相关视锥细胞营养不良患者暗适应高闪光刺激下 b 波均有超高波形，部分患者 b 波波幅在正常范围内。本研究中 2 例患者表现为暗适应下各刺激强度波幅均明显降低，1 例患者表现为低闪光刺激 b 波振幅降低，而高闪光刺激下 a 波正常而 b 波振幅降低，b/a 值降低，呈负波形，提示中国 *KCNV2* 相关视锥细胞营养不良患者 ERG 表现与国外患者不同。

视锥细胞营养不良的致病基因达 30 余种，需基因检测进一步明确病因以预测病程进展并指导相应治疗[9]。本研究中 3 例患者进行二代测序均发现 *KCNV2* 基因变异，经 Sanger 验证家系共分离结合临床表现确诊为 *KCNV2* 基因相关视锥细胞营养不良。该基因变异罕见，不同地区患病率各异。欧洲大样本视锥细胞营养不良或视锥视杆细胞营养不良患者的相关研究中，*KCNV2* 变异占 2.2%～4.3%[14,27]。一项关于阿拉伯联合酋长国小儿科遗传性视网膜变性的基因检测显示 *KCNV2* 患者占 11.3%[28]。5 个日本家系 6 例 *KCNV2* 患者表型与西方国家类似，均为 CDSRR[21,29-30]。2016 年 Huang 等[9]报道的 163 例中国视锥视杆细胞营养不良先证者中，*KCNV2* 基因变异占 0.6%。2015

年 Huang 等[10]利用靶向捕获二代测序技术对 179 例中国遗传性视网膜变性患者进行基因检测，发现 1 例 *KCNV2* 相关视锥视杆营养不良患者。目前，HGMD 已报道的 96 种 *KCNV2* 基因变异中，错义/无义变异 65 种，占 67.7%；微缺失/微重复 20 种，占 20.8%；大片段缺失/重复/重排 10 种，占 10.4%；调控区域变异 1 种。本研究中共确定 5 种新发致病变异，包括 4 种错义变异和 1 种移码变异，均位于 1 号外显子。迄今，中国共报道 13 种 *KCNV2* 基因变异位点，均为新发变异，提示中国 *KCNV2* 相关视锥细胞营养不良患者具有独特的基因型[7-11]。本研究中家系 2 先证者的临床表现明显比患者 1 严重，而年龄却比患者 1 小，可能与基因型不同有关。本研究中纳入的病例数较少，并不能明确基因型与表型之间的关系。

目前，*KCNV2* 相关视锥细胞营养不良尚无有效治疗方法。近年基因治疗进展迅速，如针对 *CNGA3*、*CNGB3* 基因变异导致的 ACHM，已开展相关基因治疗临床试验，为将来治疗 *KCNV2* 相关视锥细胞营养不良提供了思路[13]。此外，可对 *KCNV2* 相关视锥细胞营养不良进行对症治疗：畏光患者应避免阳光直射，伴屈光不正者可验光配镜。

综上所述，本研究中首次对中国汉族 *KCNV2* 相关视锥细胞营养不良患者的临床特征及基因型进行总结研究。*KCNV2* 基因变异患者具有特征性 ERG 表现，且中国患者 ERG 表型及基因型与国外患者相比差异较大。本研究拓展了 *KCNV2* 基因变异谱，揭示了中国 *KCNV2* 相关视锥细胞营养不良患者的独特表型。

利益冲突　所有作者均声明不存在任何利益冲突

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· 病例报告 ·

首发和伴发结膜炎的新型冠状病毒肺炎二例

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【摘要】 作为新型冠状病毒肺炎（COVID-19）疫情暴发中心的一线医护人员，自 2019 年 12 月起，我们在接诊过程中发现多例无呼吸道症状而以结膜炎为首发或发病时伴有结膜炎的 COVID-19 患者。本文中报道的例 1 患者与确诊的 COVID-19 患者密切接触后发生双眼结膜炎而首诊眼科，结膜炎经 1 周的抗病毒药物治疗眼部症状消失后发生 COVID-19，患者鼻咽拭子 2019-nCoV 核酸检测结果阳性，但双眼结膜囊拭子 2019-nCoV 核酸检测结果阴性。例 2 有流行病史的患者同时发生 COVID-19 和双眼结膜炎，鼻咽拭子 2019-nCoV 核酸检测和双眼结膜囊拭子 2019-nCoV 核酸检测结果阳性，实验室相关检查支持 COVID-19 诊断，但胸部 CT 检查正常。双眼经 1 周的抗病毒药物局部治疗眼部症状消失。

【关键词】 新型冠状病毒肺炎；结膜炎；新型冠状病毒；感染性疾病；传播；病例报告

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Novel coronavirus disease with conjunctivitis and conjunctivitis as first symptom: Two cases report

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[Abstract] As the frontline health care workers at the center of the novel coronavirus disease (COVID-19) outbreak, we have encountered many asymptomatic COVID-19 patients or patients with mild symptoms since December 2019. A number of COVID-19 cases with conjunctivitis or conjunctivitis as the first symptom have been observed in our clinical work. This paper reports the diagnosis and treatment of one COVID-19 patient with conjunctivitis as the first symptom and one COVID-19 patient with conjunctivitis. In case one conjunctivitis occurred at the third day after patient came in close contact with determined COVID-19 patient and visited an eye doctor, and the symptom of conjunctivitis following the topical administration of anti-viral eyedrops for 1 week, followed by COVID-19. Her 2019-nCoV RNA detection of nasopharynx swab was positive but that of conjunctival sac swab was a negative result. Case two had a positive epidemiological history and simultaneous onset of COVID-19 and conjunctivitis. She presented positive results of 2019-nCoV RNA detection in both nasopharynx and conjunctival sac swabs, and other lab results