·临床研究·

*SCN4A*基因R672G位点突变致低钾性周期性瘫痪伴肌萎缩一家系分析并文献复习

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【摘要】 **目的** 报道*SCN4A*基因R672G位点突变致低钾性周期性瘫痪伴肌萎缩一家系，结合文献总结其临床表现、骨骼肌病理学和MRI特点。**方法与结果** 男性先证者，27岁，7岁时以反复发作性四肢肌无力为首发表现，后发作频率增加，并逐渐出现下肢肌无力、肌萎缩；其母有类似发作史。发作时血清钾水平降低。长程肌电图提示0～45分钟尺神经复合肌肉动作电位波幅逐渐降低，长时间运动后小指展肌复合肌肉动作电位波幅下降75.8%，波幅下面积降低67.4%。骨骼肌MRI显示双侧股外侧肌、股内侧肌、腓肠肌、比目鱼肌等水肿。骨骼肌病理学可见肌纤维膜下团块状沉积物，透射电子显微镜可见肌纤维膜下沉积物为排列紊乱的原始肌丝团。基因检测显示，先证者及其母均存在*SCN4A*基因外显子12 c.2014C＞G(Arg672Gly)杂合突变。最终明确诊断为低钾性周期性瘫痪，该家系诊断为*SCN4A*基因Arg672Gly突变致低钾性周期性瘫痪家系。**结论** *SCN4A*基因R672G位点突变致周期性瘫痪可出现肌萎缩和肌纤维膜下肌原纤维沉积的病理表现，肌纤维膜下沉积物的本质尚待进一步研究。

【关键词】 低钾性周期性瘫痪(非*MeSH*词)； 肌萎缩； 钠通道； 基因； 突变； 系谱

The clinical and pathological characteristics of a hypokalemic periodic paralysis family with muscle atrophy due to *SCN4A* R672G mutation and review of literatures

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【Abstract】 **Objective** To report a family of hypokalaemic periodic paralysis (HypoPP) with muscle atrophy due to *SCN4A* gene R672G mutation. The clinical, pathological and MRI characteristics of HypoPP were summarized combining literatures review. **Methods and Results** The proband was a 27-year-old male patient who firstly presented periodic muscle weakness from 7 years old. The episode frequency increased with age, and gradually accompanied with muscle atrophy and permanent weakness. His mother has the similar episode but lower frequency. Serum potassium level decreased at the episode. The long-term EMG showed the compound muscle action potential (CMAP) on ulnar nerve gradually decreased from 0–45 min. The CMAP in abductor digiti minimi was decreased by 75.8% after long-time exercise test. Muscle MRI showed edema in vastus lateralis, vastus medialis, gastrocnemius lateralis, gastrocnemius medialis, soleus, et al. Muscle pathology showed eosinophilic light-stained sediment under the sarcolemma. Transmission electron microscopy (TEM) showed the sediment under the sarcolemma were primitive myofilaments with disordered arrangement. Gene test showed heterozygous mutation on exon 12 c.2014C＞G (Arg672Gly) in *SCN4A* gene in proband and his mother. Finally, the proband was diagnosed HypoPP, and the family was confirmed HypoPP due to *SCN4A* gene R672G mutation. **Conclusions** HypoPP due to *SCN4A* gene R672G mutation can have pathological feature of muscle atrophy and sediment of primitive

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myofilament. The nature of the sediment needs further study.

【Key words】 Hypokalemic periodic paralysis (not in *MeSH*); Muscular atrophy; Sodium channels; Genes; Mutation; Pedigree

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低钾性周期性瘫痪(HypoPP)是一类表现为周期性发作的弛缓性肌无力,且发作期血清钾水平降低(<3.50 mmol/L)的遗传性神经肌肉病[1]。遗传性低钾性周期性瘫痪的病理生理学机制为电压门控性钙离子通道(VGCC)或电压门控性钠离子通道(VGSC)功能异常,导致离子通道异常开放,血清钾水平降低。低钾性周期性瘫痪呈常染色体显性遗传,分为HypoPP1型和HypoPP2型,其主要致病基因分别为*CACNA1S*和*SCN4A*,其中*CACNA1S*基因变异致HypoPP1型占40%~60%、*SCN4A*基因变异致HypoPP2型仅占7%~14%[2-3]。本文报道1例*SCN4A*基因R672G位点突变致低钾性周期性瘫痪伴肌萎缩患者的临床、病理学和影像学特点,并复习相关文献,探究低钾性周期性瘫痪的发病机制、骨骼肌病理学和MRI特点。

病例资料

先证者 男性,27岁。因反复发作性四肢肌无力20年、加重伴肌萎缩7年,于2019年6月25日入院。患者20年前(7岁时)上呼吸道感染后出现肢体乏力,表现为突发四肢无法活动、无法翻身,仅可转头,每次持续4~5小时,每年发作1~2次,休息后自行缓解,外院疑诊为低钾性周期性瘫痪,间断性服用氯化钾0.50 g/次、2次/d,病情有所控制;17年前(10岁时)肌无力发作次数增多(每月1~2次),每次发作多有诱因,如上呼吸道感染、剧烈运动、腹泻、饱餐、进食油腻食物等,发作时肌力稍差(3~4级),可行走,但无法完成跑步、爬楼梯等剧烈运动,伴血清钾降低,最低2 mmol/L,外院诊断为低钾性周期性麻痹,予氯化钾0.50 g/次、2次/d长期规律口服,但病情仍进行性加重;7年前(20岁时)发作更加频繁(每2~3天发作1次),严重时伴吞咽困难、言语不清,发作间期亦有小发作,主要集中在每日下午,表现为肢体乏力、无法站立,1~2小时后自行缓解,并逐渐出现大腿肌肉萎缩,四肢近端抬起困难。近1年来发作更加频繁(每天下午发作1次、每次持续1~2小时),发作时需卧床无法动弹,发作间期肌力无法恢复正常,至我院就诊。患者自发病以来,精神尚可,饮食正常,大小便正常,近期体重未见明显改变。既往史和个人史无特殊。其母50岁,32年前(17岁时)开始出现类似发作,劳累和受凉为主要诱因,每年春季发作1~2次,发作时四肢肌无力,须卧床,休息12小时至2天后自行好转,未予诊治,40岁后未再发作;其姐30岁,身体健康;其父及其余家族成员均无类似表现。

入院后体格检查 神志清楚,语言流利,双侧眼动自如,双侧鼻唇沟对称,伸舌居中,无舌肌震颤和萎缩,颈部柔软,双上肢近端肌力3级、远端4级,双下肢近端肌力2级、远端4级,四肢肌张力均降低,深感觉和浅感觉正常,肱二头肌、肱三头肌、膝反射和踝反射减弱,双侧病理征未引出。

辅助检查 实验室检查:血清钾2.04 mmol/L(3.50~5.50 mmol/L),丙氨酸转氨酶(ALT)328 U/L(0~40 U/L),天冬氨酸转氨酶(AST)为62 U/L(15~40 U/L),乙型肝炎表面抗原(HBsAg)呈阳性,其余各项指标均于正常值范围。肌电图检查:长程肌电图提示右侧肢体部分受检肌肉插入电位减少,未见明显纤颤电位和正锐波,轻收缩时部分运动单位电位(MUP)波幅较低或未引出,重收缩募集减少;0~45分钟尺神经复合肌肉动作电位(CMAP)波幅逐渐降低,长时间运动(45分钟间断运动)后小指展肌复合肌肉动作电位波幅下降75.8%,波幅下面积较运动前降低67.4%(图1)。影像学检查:双下肢骨骼肌MRI显示,左侧大腿股内侧肌、股外侧肌、股直肌、股中间肌、大收肌、长收肌均可见水肿,右侧大腿股外侧肌、股直肌、大收肌、长收肌轻度水肿;双侧小腿腓内侧肌、腓外侧肌、比目鱼肌轻度水肿(图2)。取左侧肱二头肌组织行病理学检查,HE染色显示,肌纤维大小不等,核内移明显增多,部分肌纤维膜下可见均质性嗜伊红淡染物质沉积(图3a);还原型辅

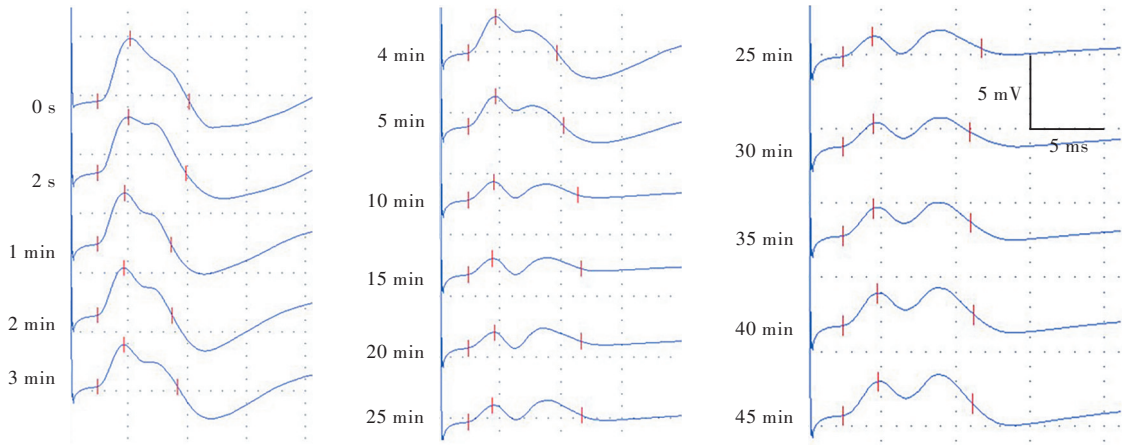

图1　长程肌电图显示，0～45分钟右侧尺神经复合肌肉动作电位逐渐降低，长时间运动后小指展肌复合肌肉动作电位波幅下降75.8%，波幅下面积降低67.4%

Figure 1　Long-term EMG showed decreasing CMAP on the right ulnar nerve during 0-45 min. After long-time exercise, the CMAP on abductor digiti minimi decreased by 75.8%, and the areas decreased by 67.4%.

酶Ⅰ四氮唑还原酶（NADH-TR）染色显示，肌纤维膜下和胞质内沉积物还原型烟酰胺腺嘌呤二核苷酸（NADH）活性异常增高（图3b）；改良Gomori三色（MGT）染色显示，部分肌纤维膜下沉积物呈紫红色，符合管聚集病理改变（图3c）；透射电子显微镜下可见肌纤维膜下沉积物为排列紊乱的原始肌丝团，未见双层膜结构的管聚集表现（图3d）。

基因检测　征得先证者及其父母知情同意后，采集肘静脉血各5 ml，送检上海金域医学检验所行全外显子组测序（WES），结果显示，先证者存在*SCN4A*基因（NM_000334.4）外显子12 c.2014C > G（Arg672Gly）杂合突变；Sanger测序验证先证者之母携带*SCN4A*基因c.2014C > G（Arg672Gly）杂合突变，先证者之父未见该位点突变（图4）。根据美国医学遗传学和基因组学会（ACMG）标准判断为致病性变异。最终先证者明确诊断为低钾性周期性瘫痪，该家系诊断为*SCN4A*基因Arg672Gly突变致低钾性周期性瘫痪家系（图5）。

治疗与预后　入院后即服用氯化钾0.50 mg/次（2次/d）对症治疗、辅酶Q10 30 mg/次（3次/d）营养肌肉、乙酰唑胺0.25 mg/次（2次/d）减少钾离子内流、甘草酸二铵肠溶胶囊150 mg/次（3次/天）保肝治疗，病情趋于平稳（每天发作1次），严重程度有所减轻。患者共住院10天，出院时血清钾正常。出院后服用乙酰唑胺和辅酶Q10（剂量同前）。随访2年，病情稳定，发作频率和严重程度均略有减轻，目前生活自理，可从事非体力型工作。

讨　论

原发性周期性瘫痪系骨骼肌离子通道病导致的神经肌肉病，根据发作时血清钾水平分为高钾性、低钾性和正常血钾性周期性瘫痪[2]。本文先证者7岁开始出现典型的周期性瘫痪发作和特征性诱发因素，发作期血清钾 < 2 mmol/L，且其母有类似症状；长程肌电图提示小指展肌复合肌肉动作电位波幅下降75.8%，面积下降67.4%，依据Weber和Lehmann-Horn[1]提出的低钾性周期性瘫痪诊断标准，要求长时程运动试验复合肌肉动作电位波幅和面积至少降低30%，故该例患者低钾性周期性瘫痪诊断明确。

周期性瘫痪的病理生理学机制研究近年来取得较多进展，常见的致病基因主要有编码VGCC CaV1.1的*CACNA1S*和编码VGSC NaV1.4的*SCN4A*，但上述2种基因变异不仅导致相似的临床症状，而且其致病机制也与同一结构域有关[3]：即VGCC CaV1.1蛋白和VGSC NaV1.4蛋白均有1个电压传感器（VSD）区域，位于该区域第4个跨膜段（-S4段）带正电的精氨酸残基替换为不带电的其他氨基酸，导致电压门控性离子通道离子失衡，产生异常的离子电流，称为门控漏电流（gating pore currents），该电流的持续存在使骨骼肌胞膜静息电位稳态改变，导致在血清钾降低的情况下出现肌无力发作，上述机制已经多个离体和在体研究证实[3-5]。然而最近，Kubota等[6]在5例*CACNA1S*基因或*SCN4A*基因变

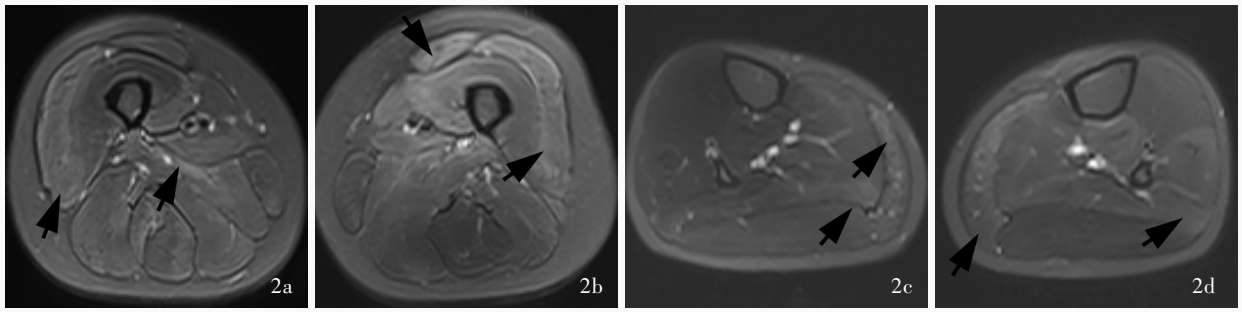

图2 双下肢横断面T_2WI STIR序列所见 2a 右侧大腿股外侧肌、股直肌、大收肌、长收肌水肿(箭头所示) 2b 左侧大腿股内侧肌、股外侧肌、股直肌、股中间肌、大收肌、长收肌水肿(箭头所示) 2c,2d 双侧小腿腓内侧肌、腓外侧肌、比目鱼肌轻度水肿(箭头所示)

Figure 2 Axial T_2WI STIR findings of the bilateral lower limb Edema in the vastus lateralis, rectus femoris, magniductor, adductor longus of right thigh (arrows indicate, Panel 2a). Edema in the vastus medialis, rectus femoris, vastus lateralis, vastus intermedius, magniductor, adductor longus of left thigh (arrows indicate, Panel 2b). Mild edema in gastrocnemius and musculi soleus of both lower legs (arrows indicate; Panel 2c, 2d).

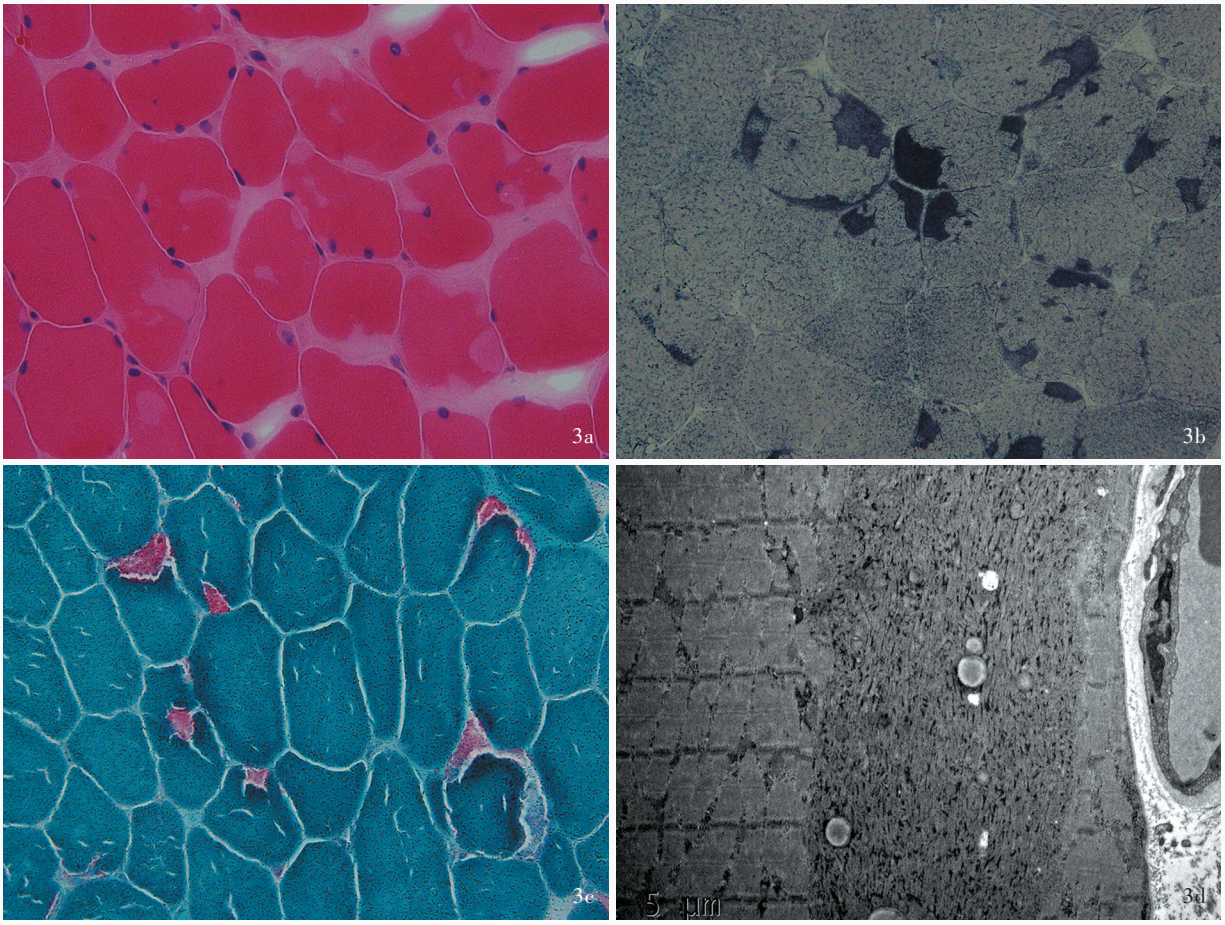

图3 骨骼肌病理学检查所见 3a 肌纤维大小不等,核内移明显增多,部分肌纤维膜下可见均质性嗜伊红淡染物质沉积 HE染色 ×400 3b 肌纤维膜下及胞质内沉积物NADH活性异常增高 NADH染色 ×400 3c 部分肌纤维膜下沉积物呈紫红色,类似管聚集病理改变 MGT染色 ×400 3d 透射电子显微镜观察可见肌纤维膜下沉积物为排列紊乱的原始肌丝团 锇酸染色 ×10 000

Figure 3 Pathological findings of skeletal muscle The muscle fibers size was different, the nuclear migration was significantly increased, and homogeneous eosinophilic light-stained material was deposited under the membrane of some muscle fibers (Panel 3a). HE staining ×400 The activity of NADH in myofiber submembrane and cytoplasmic sediments increased abnormally (Panel 3b). NADH staining ×400 Some of the subfibromal deposits were purplish red, similar to the pathological changes of tubular aggregation (Panel 3c). MGT staining ×400 Transmission electron microscopy showed that the sediments under the sarcolembrane were primitive myofilaments with disordered arrangement (Panel 3d). Osmic anhydride staining ×10 000

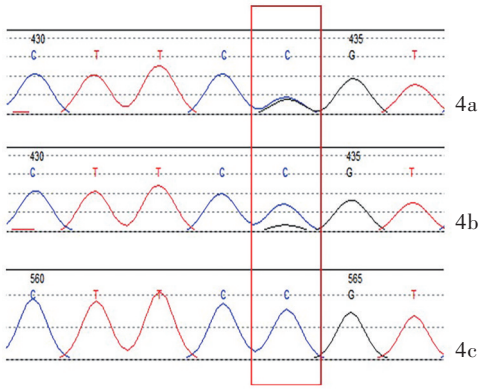

图4 全外显子组测序和Sanger测序所见 4a 先证者存在*SCN4A*基因外显子12 c.2014C>G(Arg672Gly)杂合突变(矩形区域所示) 4b 先证者之母携带*SCN4A*基因c.2014C>G(Arg672Gly)杂合突变 4c 先证者之父未见该位点突变(矩形区域所示)

Figure 4 WES and Sanger sequencing WES showed a heterozygous mutation on c.2014C>G (Arg672Gly) in *SCN4A* gene in the proband (rectangle area indicates, Panel 4a). Sanger sequencing showed the patient's mother had a heterozygous the c.2014C>G mutation, while the patient's father did not have this mutation (rectangle area indicates; Panel 4b, 4c).

异导致的低钾性周期性瘫痪患者中发现,精氨酸替换为保留电荷的氨基酸后并未见较强的门控漏电流,提示除门控漏电流外,还可能有其他机制参与疾病的发生。

虽然周期性瘫痪为发作性疾病,发作间期表现正常,但多次发作后部分患者可出现持久性肌无力和肌萎缩。本文先证者20岁开始即出现发作间期肌无力和肌萎缩。Holm-Yildiz等[7]总结55例*CACNA1S*基因变异导致的低钾性周期性瘫痪患者,发现有4种临床表现形式:31例表现为经典型周期性发作,17例在周期性发作基础上出现持久性肌无力症状(主要发生在40岁后),3例单纯持久性肌无力(无发作性麻痹),4例无症状;并且在35例未出现持久性肌无力的患者骨骼肌MRI也发现肌肉脂肪变性,提示周期性瘫痪患者发生永久性肌肉病变的普遍性。

周期性瘫痪的永久性肌肉损害在骨骼肌病理中也有所反应:可表现为肌纤维大小不等、核内移、脂肪浸润、靶样纤维、空泡变性和管聚集[8-9],其中管聚集和空泡变性较有特征性。Sternberg等[8]共总结37例低钾性周期性瘫痪患者的骨骼肌病理学表现,发现23例出现空泡变性,9例可见管聚集;国内学者也发现低钾性周期性瘫痪患者出现MGT染色呈紫

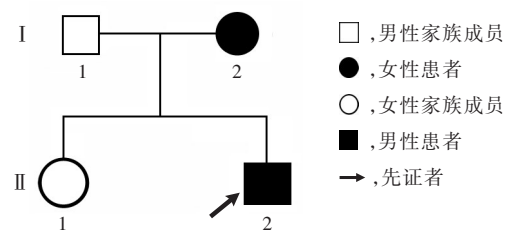

图5 低钾性周期性瘫痪家系图

Figure 5 The HypoPP pedigree of the patient's family.

红色的管聚集样沉积物,透射电子显微镜下可见肌原纤维排列紊乱和微管样结构[10-11]。高钾性和低钾性周期性瘫痪的病理表现差异不甚明显,*SCN4A*基因T704M位点突变导致的高钾性周期性瘫痪患者多表现为管聚集和空泡变性[9,12];*SCN4A*基因变异致低钾性周期性瘫痪患者除空泡变性和管聚集外,还表现为Arg672His突变导致的烟酰胺腺嘌呤二核苷酸磷酸(NADPH)染色微小轴空样改变[13];R675Q位点突变致正常血钾性周期性瘫痪表现为NADPH染色靶样纤维[14];甚至在*SCN4A*基因Arg1142Gln和Cys375Arg复合杂合突变患者中可观察到核内移围绕沉积物呈"花环"样结构,沉积物结蛋白呈阳性,证实肌纤维膜下沉积物本质上可能是排列紊乱的肌原纤维[15]。本文先证者光学显微镜下也观察到MGT染色呈紫红色的管聚集样改变,而透射电子显微镜未观察到典型的双层膜结构管聚集[16],但可见排列紊乱的肌原纤维团,与Gonorazky等[15]的报告相一致。

MRI对遗传性神经肌肉病的研究价值最早由Koltzenburg等[17]报告,在肌肉损害的评估中越来越受到重视。与低钾性周期性瘫痪的肌肉水肿不同,正常人运动后也存在肌肉水肿表现,但持续时间短暂[18-19]。Maggi等[20]对15例遗传性骨骼肌离子通道病患者的肌肉MRI进行研究发现,大部分患者存在大腿和(或)小腿肌肉MRI信号异常,表现为脂肪浸润、水肿和萎缩,最常受累肌群依次为小腿腓内侧肌、腓外侧肌、比目鱼肌,大腿大收肌、缝匠肌、股薄肌和半腱肌,而股直肌和胫骨前肌较少受累。Jeong等[21]随访7例*SCN4A* T704M位点突变致高钾性周期性瘫痪患者,肌肉病变累及小腿后群和大腿前群股外侧肌、股内侧肌、股中间肌和股直肌,30个月后逐渐累及大腿后群半腱肌、缝匠肌,原有脂肪化程度和范围逐渐增加。但上述MRI的肌群分布特点

在高钾性、低钾性和正常血钾性周期性瘫痪患者中均有类似表现，因此骨骼肌MRI对骨骼肌离子通道病基因型和临床表型的区分并无很大帮助[9,14]。但最近Holm-Yildiz等[7]报告55例*CACNA1S*基因变异致低钾性周期性瘫痪患者，发现受累最严重的肌肉是椎旁肌、腰大肌、髂肌、大腿和小腿后群肌肉，而股直肌和股薄肌无明显变化，提示应注意周期性瘫痪患者中轴肌的累及。

综上所述，*SCN4A*基因R672G位点突变致低钾性周期性瘫痪可出现肌萎缩和肌纤维膜下肌原纤维沉积的病理表现，肌纤维膜下沉积物的本质尚待进一步研究。

利益冲突 无

参 考 文 献

[1] Weber F, Lehmann-Horn F. Hypokalemic periodic paralysis[M]// Adam MP, Ardinger HH, Pagon RA, Wallace SE, Bean LJH, Gripp KW, Mirzaa GM, Amemiya A. Gene Reviews. Seattle (WA): University of Washington (Seattle), 1993-2022: 1-8.

[2] Fialho D, Griggs RC, Matthews E. Periodic paralysis[J]. Handb Clin Neurol, 2018, 148:505-520.

[3] Cannon SC. Channelopathies of skeletal muscle excitability[J]. Compr Physiol, 2015, 5:761-790.

[4] Cannon SC. Sodium channelopathies of skeletal muscle [J]. Handb Exp Pharmacol, 2018, 246:309-330.

[5] Pan X, Li Z, Zhou Q, Shen H, Wu K, Huang X, Chen J, Zhang J, Zhu X, Lei J, Xiong W, Gong H, Xiao B, Yan N. Structure of the human voltage-gated sodium channel Nav 1.4 in complex with β1[J]. Science, 2018, 362:eaau2486.

[6] Kubota T, Wu F, Vicart S, Nakaza M, Sternberg D, Watanabe D, Furuta M, Kokunai Y, Abe T, Kokubun N, Fontaine B, Cannon SC, Takahashi MP. Hypokalaemic periodic paralysis with a charge-retaining substitution in the voltage sensor[J]. Brain Commun, 2020, 2:fcaa103.

[7] Holm-Yildiz S, Witting N, Dahlqvist J, de Stricker Borch J, Solheim T, Fornander F, Eisum AS, Duno M, Soerensen T, Vissing J. Permanent muscle weakness in hypokalemic periodic paralysis[J]. Neurology, 2020, 95:e342-352.

[8] Sternberg D, Maisonobe T, Jurkat-Rott K, Nicole S, Launay E, Chauveau D, Tabti N, Lehmann-Horn F, Hainque B, Fontaine B. Hypokalaemic periodic paralysis type 2 caused by mutations at codon 672 in the muscle sodium channel gene SCN4A[J]. Brain, 2001, 124(Pt 6):1091-1099.

[9] Yoshimura K, Morihata H, Takeda K, Sakoda S, Yuan JH, Nakano S. A case of hyperkalemic periodic paralysis presenting progressive myopathy with tubular aggregates [J]. Rinsho Shinkeigaku, 2018, 58:663-667.

[10] Luan XH, Chen B, Liu Y, Zhen RL, Zhang W, Yuan Y. The autosomall dominant inheritance tubular aggregate myopathy with SCN4A gene mutation[J]. Zhongguo Shen Jing Jing Shen Ji Bing Za Zhi, 2008, 34:193-197.[栾兴华, 陈彬, 刘旸, 郑日亮, 张巍, 袁云. 常染色体显性遗传性微管聚集性肌病存在SCN4A基因突变(附1家系报告)[J]. 中国神经精神疾病杂志, 2008, 34:193-197.]

[11] Zhang WQ, Lü Q, Zhang YQ, Zhang H, Chen XT, Wang J, Shi J, Song DL. Clinical and pathological study on hypokalemic periodic paralysis[J]. Zhonghua Shen Jing Ke Za Zhi, 2004, 37:203-205.[张卫清, 吕强, 张英谦, 张宏, 陈雪涛, 王健, 石进, 宋东林. 低钾型周期性瘫痪的临床及病理研究[J]. 中华神经科杂志, 2004, 37:203-205.]

[12] Huang S, Zhang W, Chang X, Guo J. Overlap of periodic paralysis and paramyotonia congenita caused by SCN4A gene mutations two family reports and literature review[J]. Channels (Austin), 2019, 13:110-119.

[13] Chen JJ, Zou W, Tong XX, Zhang HO, Wu J. The clinical, pathological, and genetic features of a family with both hypokalemic and normokalemic periodic paraly - sis [J]. Zhongguo Shen Jing Mian Yi Xue He Shen Jing Bing Xue Za Zhi, 2014, 21:199-202.[陈涓涓, 邹文, 童晓欣, 张海鸥, 吴军. 低钾性和正常钾性周期性瘫痪共存一家系病例的临床、病理及遗传学特点[J]. 中国神经免疫学和神经病学杂志, 2014, 21:199-202.]

[14] Shi J, Qu Q, Liu H, Cui W, Zhang Y, Lv H, Lu Z. SCN4A p. R675Q mutation leading to normokalemic periodic paralysis: a family report and literature review[J]. Front Neurol, 2019, 10:1138.

[15] Gonorazky HD, Marshall CR, Al-Murshed M, Hazrati LN, Thor MG, Hanna MG, Männikkö R, Ray PN, Yoon G. Congenital myopathy with "corona" fibres, selective muscle atrophy, and craniosynostosis associated with novel recessive mutations in SCN4A[J]. Neuromuscul Disord, 2017, 27:574-580.

[16] Engel WK, Bishop DW, Cunningham GG. Tubular aggregates in type Ⅱ muscle fibers: ultrastructural and histochemical correlation[J]. J Ultrastruct Res, 1970, 31:507-525.

[17] Koltzenburg M, Yousry T. Magnetic resonance imaging of skeletal muscle[J]. Curr Opin Neurol, 2007, 20:595-599.

[18] Jia BX, Yang Q, Li SY, Wan M, Wang H, Huo LY, Zhao E, Ding YC, Ji XM, Guo XH. Muscle edema of the lower limb determined by MRI in Asian hypokalaemic periodic paralysis patients[J]. Neurol Res, 2015, 37:246-252.

[19] Jia BX, Yang Q, Wang H, Guo XH. The genetic and skeletal muscle imaging characteristics of hypokalaemic periodic paralysis patients [J]. Zhongguo Shen Jing Mian Yi Xue He Shen Jing Bing Xue Za Zhi, 2014, 21:36-40.[贾白雪, 杨旗, 王涵, 郭秀海. 原发性低钾型周期性麻痹患者的基因及影像学研究[J]. 中国神经免疫学和神经病学杂志, 2014, 21:36-40.]

[20] Maggi L, Brugnoni R, Canioni E, Maccagnano E, Bernasconi P, Morandi L. Imaging alterations in skeletal muscle channelopathies: a study in 15 patients[J]. Acta Myol, 2015, 34:109-115.

[21] Jeong HN, Yi JS, Lee YH, Lee JH, Shin HY, Choi YC, Kim SM. Lower-extremity magnetic resonance imaging in patients with hyperkalemic periodic paralysis carrying the SCN4A mutation T704M: 30-month follow-up of seven patients[J]. Neuromuscul Disord, 2018, 28:837-845.

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