

肥大性下橄榄核变性

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摘要 肥大性下橄榄核变性,又称为肥大性橄榄核变性(HOD),是一种特殊的跨突触变性,头部磁共振图像呈特征性下橄榄核T₂WI高信号影。本文结合相关文献,对HOD的病因和病理学机制、临床特征、影像学特点和诊治等方面进行简要介绍,以期临床提供参考。

关键词 肥大性下橄榄核变性;垂直眼震;旁正中神经束

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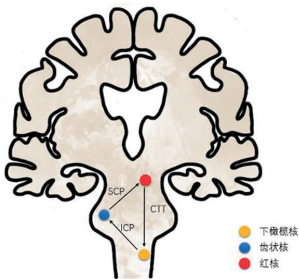
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肥大性下橄榄核变性(hypertrophic inferior olivary degeneration, HOD)是一种少见的涉及齿状核-红核-橄榄核环路的特殊跨神经突触变性。临床上通常表现为腭肌阵挛和共济失调;影像学改变为延髓下橄榄核增大,在磁共振图像(magnetic resonance imaging, MRI)上可见T₂WI的异常高信号影。以垂直眼震为突出表现的HOD误诊及漏诊率较高。本文对HOD的病因和病理学机制、临床特征、影像学特点和诊治进行综述,初步探讨了HOD垂直眼震的解剖学机制,以期HOD的临床诊治提供帮助。

1 病因及病理学表现

HOD又称下橄榄核肥大,是小脑齿状核、中脑红核和延髓下橄榄核神经元之间的联系发生病变导致的一种特殊的跨神经突触变性^[1]。1931年Guillain和Mollaret^[2]首次描述了齿状核-红核-下橄榄核环路并将其与HOD联系起来,故此环路也称为Guillain-Mollaret解剖三角。起源于齿状核的神经纤维在小脑上脚交叉,投射到对侧中脑红核,下行至脑桥中央被盖束,进入延髓下橄榄核。后经由小脑下脚投射到对侧齿状核,完成此三角环路^[3],见图1。Guillain-Mollaret解剖三角结构损伤的原因包括脑血管病^[4]、创伤性头部损伤^[5]、肿瘤^[6]、退行性神经病变^[7]和手术^[8]等。



注:CTT- central tegmental tract(中央被盖束); SCP- superior cerebellar peduncle(小脑上脚); ICP-inferior cerebellar peduncle(小脑下脚)

图1 Guillain-Mollaret解剖三角结构示意图

HOD的发病机制尚未十分清楚,主流观点认为其与下橄榄核去抑制有关。有学者发现其与基

因突变也有密切关系,如POLG基因和SURF1基因。发生于中脑、脑桥被盖、小脑上脚及小脑等部位病变均可造成上述环路破坏,导致远隔原发灶的延髓下橄榄核发生空泡样变性,影像学上表现为下橄榄核肥大^[2]。齿状核-红核-下橄榄核环路联系的破坏,使经此环路传递的抑制性神经冲动减少,下橄榄核发生失神经性超敏反应,最终导致肥大和变性^[2]。HOD病理分期主要分为6个发展期^[9]:①24 h内下橄榄核无变化;②2~7 d下橄榄核变性;③3周后下橄榄核肥大,下橄榄核神经细胞胞质肿胀,空泡逐渐形成;④8.5个月下橄榄核体积增至最大;⑤发病9.5个月下橄榄核假性肥大;⑥发病几年后下橄榄核萎缩,神经元细胞崩解、萎缩。

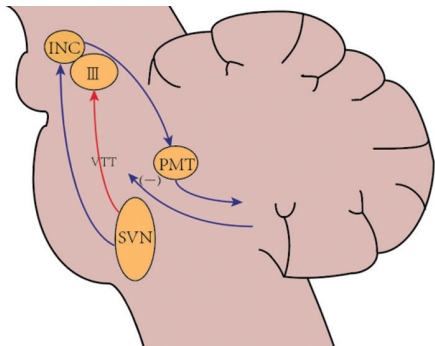
2 临床特征

HOD的典型表现为腭肌阵挛,其特征是腭肌以固定2~3 Hz的频率收缩^[10]。但腭肌阵挛并非HOD必需的临床表现。Wang等^[11]对151例HOD患者进行荟萃分析,发现明确报道有腭肌阵挛者仅占33.8%。Dogan等^[12]针对16例HOD患者的文献回顾中,仅有2例伴有腭肌阵挛。腭肌阵挛可引起构音障碍,其原因是腭肌阵挛致使言语发音肌群不协调^[13]。但有关其临床特点的报道极少。共济失调型构音障碍的特点为语速慢,元音辅音失真,发音含糊不清、不协调、震颤,爆发性、分节性发音,言语清晰度下降^[14]。HOD还可表现为小脑性共济失调和其他不自主运动^[15,16]。少见垂直眼震和四肢震颤^[12]。四肢震颤目前机制尚不明确,可能与齿状核-橄榄核通路的病变有关^[17]。

3 垂直眼震的解剖学机制

垂直眼震与中枢前庭系统结构异常和(或)功能障碍有关,表现为垂直方向上的快速眼震^[18]。垂直眼震的原因主要与腹侧被盖和(或)脑桥后基底部受损有关,有3种可能的相关解释:①兴奋性的上向前庭神经上核-腹侧被盖束的前庭眼动传导束受损,导致传导至动眼神经核内的上直肌和下斜肌运动神经元神经冲动减弱,进而导致下向的兴奋性

动眼神张力增高,从而引发上跳性垂直眼震^[19,20]。②与中脑上部Cajal中介核-旁正中束-小脑小叶和旁小叶通路的破坏有关。旁正中束细胞群是散布在脑桥和延髓中线内侧纵束上的神经元簇,其接受前庭神经上核经Cajal中介核等的传入,属于兴奋性神经元,进一步投射到同侧小脑绒球^[21,22]。上述通路的损伤会导致绒球的反馈通路中对前庭神经上核的抑制作用减弱,引起兴奋性前庭神经上核-腹侧被盖束前庭眼动通路失抑制,上向性动眼神张力增高,最终导致下跳性垂直眼震的发生^[23-26],见图2。③与兴奋性前庭神经内侧核-内侧纵束-动眼神核通路受损有关,此通路传递上下方向的前庭信号到动眼神核团,但下向的兴奋性信号更强一些,因此其受损表现出下跳性垂直眼震^[23,27]。



注:图示为脑干矢状切面,箭头所示为神经传导通路。①前庭神经上核的冲动经腹侧被盖束传入动眼神核(红色箭头);②Cajal中介核接受前庭神经上核纤维的传入,并投射到旁正中束细胞群所在的位置,进一步投射到小脑,对通路①产生抑制作用(蓝色箭头)。SVN- superior vestibular nucleus(前庭神经上核);INC- interstitial nucleus of Cajal(Cajal中介核);PMT-paramedian tract(旁正中束)。

图2 垂直性眼震相关涉及路径示意图

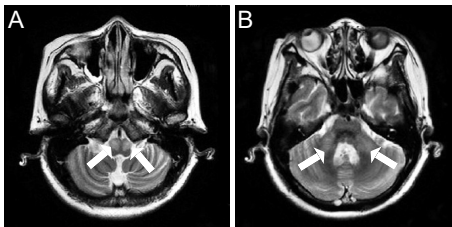
4 影像学特点

HOD的影像学检查首选MRI,其特征性表现为延髓下橄榄核体积增加或无明显改变,T₂WI呈异常高信号,T₂FLAIR呈稍高或高信号,T₁WI呈等或稍低信号,DWI呈等信号^[28],见图3、4。T₁WI、DWI像的信号表现有助于与延髓梗死相鉴别^[29]。DTI表现为早期轴向扩散率降低,后期轴向和径向扩散率增加,前者与轴突变性有关,后者则是脱髓鞘和星形胶质细胞肥大所致^[30]。当病变累及中央被盖束时可导致同侧HOD;当病变位于小脑,累及齿状核或小脑上脚时可导致对侧HOD;当病变同时累及中央被盖束和小脑上脚可导致双侧HOD^[11],见图5。

5 HOD的诊断及治疗

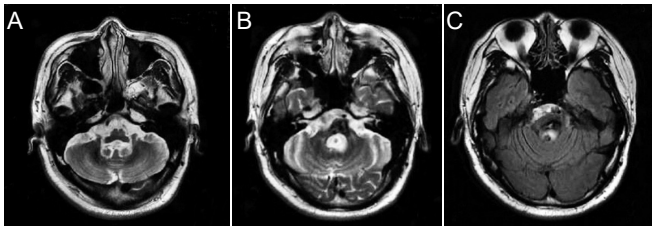
HOD的鉴别诊断需排除肿瘤、脑梗死^[31]、脱髓鞘^[32]、感染/炎症过程等,这些疾病也可能表现为延髓前部T₂WI信号的升高。HOD的诊断要点可以分为以下3个方面:①典型的临床表现;②Guillain-Mollaret解剖三角的损伤;③T₂WI高信号区定位于增大的下橄榄核上^[33]。

熟悉这种HOD的特征性临床和影像学表现有助于避免误诊和不必要的临床干预。HOD易与肿瘤复发相混淆,增强MRI



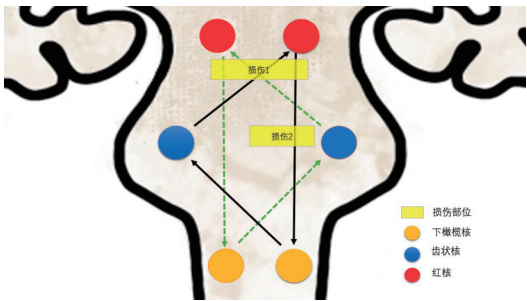
注:(A)双侧延髓下橄榄核增大,T₂WI可见异常高信号影;(B)双侧脑桥臂可见T₂WI异常高信号影,脑桥可见软化灶

图3 脑干出血3月后病例的颅脑MRI平扫影像



注:(A)左侧延髓下橄榄核体积稍增大,T₂WI信号稍增高;(B)T₂WI左侧脑桥臂局部高信号影;(C)脑桥软化灶位置偏左

图4 脑桥出血2年后病例的颅脑MRI平扫



注:当病变累及中央被盖束时可导致同侧HOD;当病变位于小脑,累及齿状核或小脑上脚时可导致对侧HOD;当病变同时累及中央被盖束和小脑上脚可导致双侧HOD

图5 损伤部位与HOD关系的示意图

扫描有助于鉴别。同时,外科医生在进行脑干手术时,应避免损伤Guillain-Mollaret解剖三角,防止患者术后并发HOD^[34,35]。HOD尚无特殊治疗方法。目前口服药物治疗仍有争议。Tilikete等^[36]的治疗试验表明加巴喷丁或美金刚对缓解眼球震颤有一定的作用。Gabriela B等^[37]发现左旋多巴和丘脑立体定向激光治疗可用于腭肌阵挛。卡马西平、氯硝西泮、左旋多巴、苯海索、硫必利等药物可用于治疗肢体震颤,但大多效果不佳^[38]。HOD较为罕见,故对于预后因素的研究目前相对较少。有学者认为,HOD预后不佳,但部分患者可在3~5年内自行缓解^[39],也有学者认为HOD患者症状无法得到实质性缓解^[40]。Konno等^[41]认为,单侧HOD有缓解的趋势,而双侧HOD则有可能恶化。

6 小结和展望

HOD是齿状核-红核-橄榄核环路病变引起的跨神经突触变性,可继发于脑桥出血、肿瘤,创伤和血管畸形。其典型的临床表现为腭肌阵挛和共济失调,罕见垂直眼震和四肢震颤。HOD的特征性MRI表现为延髓腹外侧下橄榄核区的T₂WI异常高信

号,T₂FLAIR呈稍高或高信号,T₁WI呈等或稍低信号,DWI呈等信号,伴或不伴有下橄榄核的体积增加。其中垂直眼震的发生可能与前庭神经上核-腹侧盖束、Cajal中介核-旁正中束-小脑小叶和旁小叶、前庭神经内侧核-内侧纵束中的某一种或几种通路的损伤有关。在临床工作过程中,若脑干病变的患者在恢复期或后遗症期出现肌阵挛、眼球震颤或四肢震颤,需高度警惕HOD的发生。颅脑MRI检查有助于诊断。目前对HOD的治疗尚无普遍共识,加巴喷丁、美金刚和左旋多巴等药物可能有效。

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