

·临床研究·

中脑梗死继发双侧肥大性橄榄核变性

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摘要:肥大性橄榄核变性(HOD)是一种罕见且特殊的跨突触变性,发病率低,易被忽略。主要继发于脑干和小脑的破坏性病变。临床典型表现为腭肌震颤和共济失调,影像学特征为T2WI高信号。现总结分析1例继发于中脑梗死的典型双侧HOD病例,以期提高临床工作中对该病的认识。

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关键词:中脑梗死;肥大性橄榄核变性;腭肌震颤;共济失调

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Bilateral hypertrophic olivary degeneration secondary to midbrain infarction: a case reportQIN Xue-Jiao^{1,2}, XIAO Yi-Ning², ZHANG Qiang^{1,2}, DONG Yan-Hong²

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Abstract: Hypertrophic olivary degeneration (HOD) is a rare and special transsynaptic disease with low incidence and tends to be overlooked. It is secondary to destructive lesions in the brainstem and cerebellum. Typical clinical manifestations include palatal tremor and ataxia, and the imaging is characterized by high T2WI signal. A typical case of bilateral HOD secondary to midbrain infarction is summarized and analyzed here to improve the understanding of the disease in clinical practice.

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Keywords: midbrain infarction; hypertrophic olivary degeneration; palatal tremor; ataxia**1 临床资料**

患者,女,62岁,主因“头晕较前加重20余天”入院。本次发病前8个月余曾患有中脑梗死,于外院对症治疗(具体诊疗经过不详),遗留有头晕。20余天前头晕较前加重,活动时明显,伴视物旋转,站立不稳、行走困难,伴右上肢不自主抖动,自觉肢体力量较前无明显变化。

既往高血压病史10年余,中脑梗死8个月余。

查体可见眼肌阵挛,双眼球漂浮不定,双眼可见垂直旋转性眼震;双侧腭弓对称,可见腭肌震颤;右上肢不自主抖动,存在意向性震颤,震颤频率较低;双侧共济试验均欠稳准,Romberg征阳性。余神经查体未见异常。

实验室生化检查示同型半胱氨酸12.6 μmol/L;甘油

三酯1.87 μmol/L。颈部血管超声示颈动脉粥样硬化伴斑块形成。余检查无明显异常。

追问病史既往患有中脑梗死急性期头颅弥散加权成像(diffusion weighted imaging, DWI)示中脑高信号影(图1)。本次入院后头部磁共振(magnetic resonance imaging, MRI)示延髓稍显饱满,其内可见对称性异常信号,磁共振增强无强化信号影(图2)。

综合患者临床症状、影像学表现以及既往患有中脑梗死的病史,诊断为双侧下橄榄核肥大变性。

给予止晕、营养脑神经、改善脑循环、改善脑代谢、活血等治疗后,症状好转出院。

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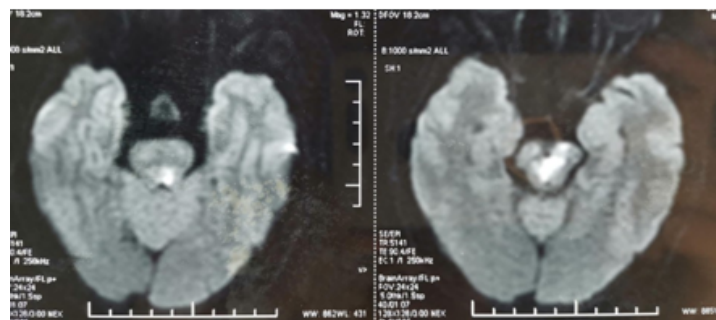


图1 外院头颅DWI示患者中脑梗死急性期中脑被盖部、大脑脚、小脑上脚高信号影

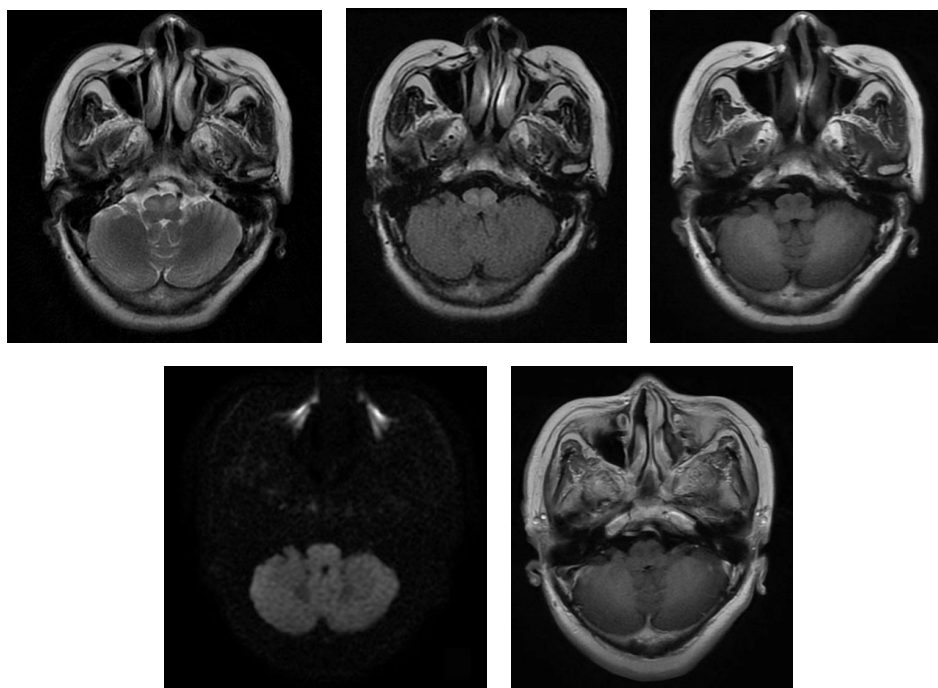


图2 本院头颅磁共振示延髓稍显饱满,其内可见对称性T1WI稍低、T2WI及FLAIR高信号,DWI呈等信号;增强核磁示延髓可见片状无强化低信号影

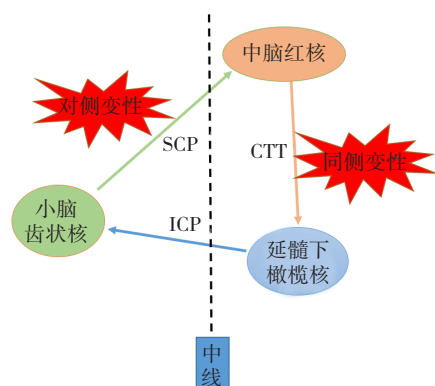
2 讨论

肥大性橄榄核变性(hypertrophic olivary degeneration, HOD)是由于齿状核(dentate nucleus, DN)—红核(red nucleus, RN)—下橄榄核(inferior olivary nucleus, ION)神经元环路(dentato-rubro-olivary pathway, DROP)病变引起的跨突触变性^[1]。DROP亦称为格莫三角(Guillain-Mollaret triangle, GMT)(图3),起源于DN的传入纤维经小脑上脚(superior cerebellar peduncle, SCP)穿过中线到达对侧RN,然后从RN传出的纤维通过中央被盖束(central tegmental tract, CTT)下行至同侧ION,最后经小脑下脚(inferior cerebellar peduncle, ICP)与对侧DN联系^[2]。因此,当CTT通路受损引起同侧HOD,SCP或ICP受损则引起对侧HOD,双侧HOD多见于双侧病变,亦有报道^[3]单侧小脑病变引起双侧HOD的罕见病例。1项专门针对HOD患者头部MRI的回顾性队列研究^[4]发现,双侧HOD发生率约

76%大于单侧发生率,此研究还发现其中约55%的HOD患者在DROP内发现明确病灶。亦有病例报道^[5]发现,延髓梗死损伤DN-ION通路但并未引起HOD。

本病例患者既往有中脑梗死病史,梗死急性期MRI示中脑被盖部、大脑脚、小脑上脚DWI高信号影,梗死病灶损伤DROP内CTT和SCP两条离子通路,GMT通路中断导致ION失神经病变造成跨神经元变性。HOD的独特之处在于变性导致细胞核增大而非萎缩,组织病理学上表现为神经元空泡化、纤维胶质增生、星形胶质细胞数量和体积增生以及脱髓鞘变性^[6]。GMT涉及脑干和小脑之间相关的神经纤维,临床上HOD主要是继发于脑干和小脑破坏性病变数周或数月后,Dogan等^[7]报道1例海绵状瘤致脑干出血9个月后继发单侧HOD病例。Yang等^[8]报道1例继发于脑桥海绵状瘤术后HOD病例。Özdemir等^[9]报道1例脑梗死2年后继发单侧HOD病例。本病例

双侧HOD继发于中脑梗死后8个月余。



SCP(小脑上脚)将齿状核连接到红核;CTT(中央被盖束)将红核连接到下橄榄核;ICP(小脑下脚)将下橄榄核连接到齿状核。当CTT病变时引起同侧HOD病变,当SCP病变时引起对侧HOD病变,当同时累及CTT和SCP时则引起双侧HOD。

图3 格莫三角示意图(自绘)

HOD的MRI表现为T2WI、FLAIR序列特征性的非增强型高信号和ION体积增大。ION高信号最早在病变后约1个月出现并持续存在,而ION肥大约6个月后才出现,并在3~4年后消失^[10]。HOD的MRI表现与肿瘤、感染、脱髓鞘病变相似,信号缺乏对比增强是其一大诊断特征。本病例MRI表现十分典型,延髓下橄榄核T1WI低、T2WI高、FLAIR高信号、DWI等信号、增强无强化信号影,结合中脑梗死病史8月余,诊断双侧HOD。

HOD最典型的临床症状是腭肌震颤和共济失调, Samuel等^[11]通过回顾性研究进行性共济失调和腭肌震颤综合征病例,发现几乎所有病例均显示与双侧HOD有关。近年也有同样病例报道^[10, 12]。HOD患者的震颤发生率约为33%^[1, 4],其机制可能与小脑橄榄核通路损伤有关。小脑橄榄核环路通常是抑制脑干网络异常或潜在的节律性,失神经支配的ION放大并发展为持续的同步振荡信号,小脑放大了这种信号导致低频率的振荡^[10, 13-14],眼球震颤同样与此机制相关。而HOD另一典型症状共济失调的机制同样与ION变性影响小脑功能相关,ION变性导致爬行纤维减少,浦肯野细胞进行性退化,逐渐释放小脑深核细胞的抑制作用。本病例患者临床症状较为典型,故DROP区病变后延迟出现的眼球震颤、腭肌震颤及共济失调对HOD诊断有提示意义。

HOD是一种自限性疾病,在疾病发展后期橄榄核逐渐萎缩,症状可逐步缓解^[15]。目前缺乏对HOD的特效治疗,有报道指出加巴喷丁^[10]、地西洋、氯硝西泮^[15]及乙拉西坦亦可减少震颤,震颤严重者亦可进行深部电刺激^[16]治疗。本病例曾应用氯硝西泮治疗效果尚可,电话随访患者,目前症状较前缓解且生活自理。

在临床上当GMT病变后延迟出现的腭肌震颤、共济

失调等症状,且MRI示ION区T2WI高信号,这种情况下应高度怀疑HOD。

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