四川大学学报（医学版） 2024，55（6）：1364－1370
J Sichuan Univ（Med Sci） doi: 10.12182/20241160201

在线全文

·医学影像学论坛·

‖热点述评‖

阿尔茨海默病淀粉样蛋白相关影像学异常的影像识别与评估*

杨曦玥[1]，李婉婷[1]，杨兴隆[2]，陈　芹[3]，李红霞[1]，吕　粟[1△]，胡　娜[1△]

1. 四川大学华西医院 放射科（成都 610041）；2. 昆明医科大学第一附属医院 神经内科（昆明 650032）；
3. 四川大学华西医院 神经内科（成都 610041）

【摘要】 淀粉样蛋白相关影像学异常（amyloid-related imaging abnormalities, ARIA）为磁共振成像（magnetic resonance imaging, MRI）观察到的颅内信号异常，是阿尔茨海默病（Alzheimer's disease, AD）抗β淀粉样蛋白（amyloid-β, Aβ）单克隆抗体治疗的主要不良事件之一，严重者可危及患者生命。随着首个抗Aβ单克隆抗体在中国获批使用，临床科室在真实世界中面对ARIA的可能性将增加。ARIA在用药前的风险评估、用药期间的及时识别与严重程度判断对临床决策具有重要意义。对ARIA的识别评估可以从影像和临床症状两方面进行，本文聚焦于前者，对ARIA的病理生理学机制、流行病学及临床特点、影像检查方案及影像评估进行综述。本文最后指出，目前ARIA相关研究数据多来自高加索人种的药物临床试验，缺乏中国人真实世界应用抗Aβ单克隆抗体的治疗经验，未来的用药前风险评估仍有许多尚待探讨的问题。此外，是否存在其他帮助预判药物风险的临床因素和影像指标，使用不同的成像条件是否给真实世界的患者管理带来差异，都需要进一步探索。

【关键词】 淀粉样蛋白相关影像学异常　阿尔茨海默病　抗Aβ单克隆抗体　抗Aβ免疫治疗　磁共振成像　综述

Radiological Identification and Evaluation of Amyloid-Related Imaging Abnormalities in Alzheimer's Disease

YANG Xiyue[1], *LI Wanting*[1], *YANG Xinglong*[2], *CHEN Qin*[3], *LI Hongxia*[1], *LYU Su*[1△], *HU Na*[1△]. 1. *Department of Radiology, West China Hospital, Sichuan University*, Chengdu 610041, China; 2. *Department of Neurology, The First Affliliated Hospital of Kunming Medical University*, Kunming 650032, China; 3. *Department of Neurology, West China Hospital, Sichuan University*, Chengdu 610041, China

△ Corresponding author, LYU Su, E-mail: lusuwcums@hotmail.com; HU Na, E-mail: nahu_wch@163.com

【**Abstract**】 Amyloid-related imaging abnormalities (ARIA), intracranial signal abnormalities observed in magnetic resonance imaging (MRI), represent one of the main adverse events associated with treating Alzheimer's disease (AD) with anti-amyloid-β (anti-Aβ) monoclonal antibodies. In severe cases, patients' lives may be threatened. As the first anti-Aβ antibody was approved for use in China, clinical departments are now confronted with an increased likelihood of encountering ARIA in real-world scenarios. Accurate pre-treatment risk assessment, timely identification during medication, and severity evaluation of ARIA are of great significance in guiding clinical decisions. The identification and assessment of ARIA can be conducted from two perspectives—imaging and clinical symptoms. This article focuses on imaging. We reviewed the pathophysiological mechanisms, epidemiological and clinical characteristics, and imaging protocols and assessment of ARIA. We also stated at the end of the review that most current research data on ARIA came from clinical drug trials involving Caucasian populations, and that there was a lack of treatment experience in the real-world application of anti-Aβ monoclonal antibodies in Chinese populations. Many issues concerning pre-treatment risk assessment still need to be explored. Additionally, whether there are other clinical factors and imaging indicators that can help predict drug risks, and whether using different imaging protocols can help make a difference in patient management in the real world all require further investigation.

【**Key words**】 Amyloid-related imaging abnormalities　Alzheimer's disease　Anti-amyloid-β monoclonal antibodies　Anti-amyloid-β immunotherapies　Magnetic resonance imaging　Review

阿尔茨海默病（Alzheimer's disease, AD）在中国产生的社会经济负担正随着人口老龄化加快而日益加剧，预计到2050年中国AD的年治疗费用将高达1.8万亿美元[1]。AD的传统药物治疗主要以控制症状为主，长期以来缺乏特异性的有效手段来延缓或者逆转疾病进程。β淀粉样蛋白（amyloid-β, Aβ）级联假说是AD的经典致病假说之一，也是AD药物研发的主要治疗靶点。全球已在近年开展了抗Aβ单克隆抗体治疗AD的多项临床药物试验，部分已证实能有效清除Aβ异常沉积，减缓疾病进程[2-5]，给AD治疗带来了突破性进展。抗Aβ单克隆抗体的主要药

* 科技部重点研发计划（No. 2022YFC2009901、No. 2022YF2009990）资助

△ 通信作者，吕粟，E-mail：lusuwcums@hotmail.com；胡娜，E-mail：nahu_wch@163.com

出版日期：2024-11-20

物不良反应为淀粉样蛋白相关影像学异常(amyloid-related imaging abnormalities, ARIA)[6-8], 为磁共振成像(magnetic resonance imaging, MRI)观察到的颅内信号异常, 部分可出现临床症状, 甚至危及生命。AD患者发生ARIA后, 其治疗和随访方案的调整也高度依赖于MRI反映的疾病严重程度。随着中国首个抗Aβ单克隆抗体药物——仑卡奈单抗(Lecanemab)于2024年1月获批使用, 临床科室在真实世界中面对ARIA的可能性将增加[9]。ARIA的影像识别和评估将成为我国AD患者安全用药的管理重点, 因此在以神经内科和放射科为代表的临床科室中普及ARIA的影像检查技术与诊断将势在必行。

1　ARIA的病理生理学机制

ARIA分为水肿/积液(edema/effusion, ARIA-E)和出血(microhemorrhages/superficial siderosis, ARIA-H)两类, 前者指脑实质血管源性水肿或脑沟积液, 后者指脑实质微出血和表面铁沉积[2, 10]。研发中及已获批的各种抗Aβ单克隆抗体的靶点为单个或多个阶段的Aβ异常沉积, 如仑卡奈单抗针对可溶性Aβ聚集体(原纤维)及不溶性的Aβ聚集体(纤维), 通过介导免疫反应来分解和清除脑实质的Aβ沉积[2, 4, 11]。目前认为ARIA的病理生理机制可能与AD患者脑血管壁完整性破坏及血管周围清除能力减弱相关[10, 12]。病理学研究显示AD患者大脑皮层中含Aβ42的血管数量在免疫治疗组明显高于对照组[13], 提示抗Aβ抗体引起Aβ沉积的分解产物可能经血管排出。由于血管周围清除障碍, 血管免疫反应随之启动, 进而导致AD患者脑血管通透性增加或脑血管壁破坏加重, 引起ARIA[6, 14]。ARIA-H常在ARIA-E发生后短期内出现, 并且受累脑区重叠, 二者时序和空间的关联也提示病理生理学机制存在重叠[10]。具体而言, 脑实质血管源性水肿被认为与血管内皮细胞对血浆蛋白的通透性增加有关, 导致脑内细胞外液增加; 脑沟积液则可能反映了脑膜血管的蛋白质液漏出到脑沟和/或柔脑膜间隙; 微出血和表面铁沉积则提示了血管内血红蛋白外渗后分别聚集在脑实质和软脑膜[2, 6, 10]。

AD与脑淀粉样血管病(cerebral amyloid angiopathy, CAA)在病理生理机制上存在重叠, 但前者Aβ异常沉积常见于脑实质, 后者则主要位于血管壁。CAA导致的神经血管单位损伤可能增加了AD的风险[13-15], 因此AD患者血管壁也可能存在Aβ异常沉积, 进而在抗Aβ免疫治疗中引起血管周围炎症, 最终导致ARIA。此外, AD患者脑实质及血管壁的Aβ异常沉积也有较低的概率引起自发性ARIA[16-17]。

2　流行病学及临床特点

目前已报道的抗Aβ免疫治疗临床试验患者多为高加索人, ARIA-E和ARIA-H的发病率范围差异较大, 分别为0.9% ~ 40.6%、0.5% ~ 28.4%[4, 18], 这与抗Aβ抗体结合位点的不同及其靶点亲和力的差异等因素有关。根据仑卡奈单抗Ⅲ期临床研究报道, 治疗组ARIA-E和ARIA-H的发病率分别为12.6%和17.3%, 试验组患者约有0.6%出现直径> 10 mm的出血灶[4]。目前已发现的ARIA危险因素包括高剂量使用抗Aβ单克隆抗体、既往存在脑微出血或卒中、合并脑淀粉样血管病、携带ApoE ε4等位基因、老龄、抗血栓/抗凝治疗等[10-11, 19-21]。目前暂无证据表明Aβ负荷是ARIA-E的危险因素[22]。仑卡奈单抗用药组中, ARIA-E和ARIA-H在ApoE ε4纯合子患者的发生率分别为32.6%和39.0%, 杂合子为10.9%和14.0%, 非携带者为5.4%和11.9%[4]。用药前需全面评估已知危险因素及其他可能导致ARIA风险增加的情况, 其中影像学评估的作用突出, 可辅助判断脑出血风险, 例如脑多发微出血、脑表面铁沉积、既往脑出血、血管畸形等。

ARIA多发生于治疗启动后前3个月内, 原因可能是治疗早期血管壁通透性及完整性受损较重, 此后随着淀粉样蛋白清除及血管壁修复, ARIA发生的风险逐渐降低, 约30% ~ 40%的患者无临床症状[23], 仅在常规MRI随访中发现脑部异常, 少部分可出现恶心、头晕、癫痫发作等症状, 甚至死亡[4, 10]。仑卡奈单抗Ⅲ期临床研究报告, 仅有2.8%和0.7%的治疗组患者出现症状性ARIA-E和症状性ARIA-H(不伴ARIA-E)[4]。ARIA与单抗用药剂量相关[4, 11, 19-20, 24], 例如巴匹珠单抗(bapineuzumab)Ⅱ期临床研究报道, 高剂量组出现ARIA的概率明显高于低剂量组[19]。当出现ARIA时, 需根据严重程度来决定是否维持用药、药物减量、暂停用药或终止治疗, 此后数周至十余周后可观察到ARIA消退[4, 20]。ARIA临床和影像表现易与多种神经急症相混淆, 例如急性缺血性卒中、蛛网膜下腔出血、脑淀粉样血管病相关炎症(cerebral amyloid angiopathy-related inflammation, CAA-ri)、可逆性后部脑病综合征(posterior reversible encephalopathy syndrome, PRES)等, 在临床实践中存在漏诊误诊的风险, 从而干扰治疗决策并可能造成严重后果[2, 10]。

3　影像检查方案

为提高ARIA的检出率, MRI设备场强以选择3.0T为宜; 对于设备条件有限的地区及医院, 可改用1.5T MRI成像仪扫描。MRI扫描方案应至少包括如下3种序列[6, 8]: ①T_2加权液体衰减反转恢复(T_2-weighted fluid-attenuated

inversion recovery, T_2-FLAIR)序列, ②T_2^*梯度回波(T_2^* gradient echo, T_2^* GRE)序列或磁敏感加权成像(susceptibility weighted imaging, SWI), ③弥散加权成像(diffusion weighted imaging, DWI)。

3.1 T_2-FLAIR序列

用于检测ARIA-E的脑水肿和脑沟渗出。三维采集的高分辨率T_2-FLAIR序列与二维序列相比, 能提高ARIA-E的显示度并减轻脑脊液伪影[25]。然而, 三维序列对MRI设备要求较高, 可获取性差, 容易受到患者运动伪影的干扰[26], 采集时间更长[25], 这可能降低患者常规随访的依从性。多项抗Aβ免疫治疗的临床试验已证实, 二维T_2-FLAIR已能满足ARIA-E检测和管理的需要[27]。

3.2 T_2^* GRE或SWI

用于检出ARIA-H的微出血及表面铁沉积等顺磁性物质, 评估治疗后引起颅内出血的风险。这些物质在计算机断层扫描(computed tomography, CT)或常规T_1加权成像(T_1 weighted imaging, T_1WI)或T_2加权成像(T_2 weighted imaging, T_2WI)上常常难以识别。T_2^* GRE与传统的T_2加权自旋回波序列相比, 增强了微出血引起的局部磁场变化和自旋去相位效应, 放大了磁敏感相关的信号丢失程度, 呈现出易于观察的晕染效应[28]。二维T_2^*GRE已被多项临床试验用于评估ARIA-H[27], 相应产生的试验数据已成为当前药物调整策略的依据。然而, SWI使用了三维采集的高分辨率序列, 不仅检出ARIA-H更敏感、更可靠[29-30], 还能有效区分微出血(顺磁性)和微钙化(反磁性)[31]。T_2^* GRE和SWI对抗Aβ免疫治疗的临床管理是否产生不同的临床结局, 目前尚缺乏足够的对比研究证据, 但须强调在诊疗全过程需要坚持使用同一种序列。为提高微出血的检出能力, MRI设备通常使用更高场强(3.0T), 参数设置使用更长的回波时间(echo time≥20 ms)、更小的扫描层厚≤5 mm和更低的读出带宽[31]。

3.3 DWI

用于鉴别ARIA-E引起的血管源性水肿和其他疾病引起的细胞毒性水肿(例如急性或亚急性缺血性脑卒中)。当患者出现疑似急性卒中症状或随访T_2-FLAIR发现脑内新增高信号病变时, 基于影像的鉴别诊断与评估将成为后续治疗决策的关键依据。

患者用药前的基线影像检查应在治疗前1年内完成, 并且尽可能接近治疗启动时间, 其影像结果用于评估ARIA风险并作为随访ARIA严重程度的基准[21]。为保证多扫描时点图像的可比性, 在基线和后续随访监测中应尽可能使用相同的MRI成像设备、场强、序列方案和扫描参数, 这对于规范化监测ARIA-H极其重要。由于ARIA多发生于治疗早期, 影像随访监测在治疗前期较为频繁。以仑卡奈单抗为例, 无ARIA相关症状时, 在第5、7、14次用药前进行扫描; 若出现可疑症状, 需及时进行影像复查[21]。抗Aβ单克隆抗体治疗中的AD患者出现脑卒中症状时, 应紧急使用MRI而非CT进行评估。CT既无法发现脑微出血和表面铁沉积, 也无法鉴别ARIA-E和急性或亚急性脑梗死。如将脑部影像改变误判为阴性或脑梗死, 使用静脉溶栓治疗可能引发脑出血, 危及患者生命。

4 影像诊断与评估

ARIA的影像征象与多种神经急症存在相似, 其漏诊误诊可能影响临床决策并造成严重后果[2, 10]。放射科医生应熟练掌握ARIA的影像学诊断及严重程度评估要点。下文中使用的患者影像资料除特别声明外, 均经过四川大学华西医院生物医学伦理审查委员会批准, 批准号: 2021年审(1967)号。

4.1 ARIA的影像诊断

ARIA-E: 血管源性水肿在T_2-FLAIR表现为脑实质高信号[6](图1A), 边缘模糊; 病变范围大小不一, 信号强度各异, 严重时可合并局部脑实质肿胀或占位效应。脑沟渗出在T_2-FLAIR表现为脑沟高信号(图1B)[6], 这与含蛋白物

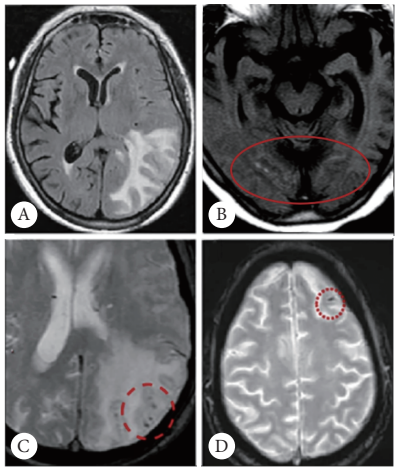

图 1 ARIA-E及ARIA-H的影像学表现

Fig 1 Imaging findings of ARIA-E and ARIA-H

ARIA: amyloid-associated imaging abnormalities; E: edema/effusion; H: microhemorrhages/superficial siderosis; T_2-FLAIR: T_2-weighted fluid-attenuated inversion recovery; T_2^* GRE: T_2^* gradient echo. A, T_2-FLAIR shows vasogenic edema (ARIA-E) in the left parieto-occipital lobe, characterized by hyperintensity predominantly involving the white matter, with local gyral swelling; B, T_2-FLAIR reveals focal effusion in the bilateral occipital lobes, and the sulci are filled with punctate and linear hyperintensities (red solid circle); C, T_2^* GRE shows multiple microbleeds (ARIA-H) within the area of vasogenic edema (ARIA-E) in the left temporo-occipital lobe (red dashed circle); D, T_2^* GRE shows superficial siderosis (ARIA-H) in the left frontal lobe (red dotted circle), characterized by short linear hypointensity distributed along the brain surface. Figure A, C, and D[27] have been reproduced with permission (Rightslink® by Copyright Clearance Center. This is an open access article distributed under the terms of the Creative Commons CC BY license).

质缩短T_1时间有关。脑水肿和脑沟渗出可单独或同时存在, 以脑后部多见, 最常见于枕叶, 其次是顶、额和颞叶, 少见于幕下[28]。

ARIA-H: 微出血在T_2^* GRE或SWI表现为脑实质内的点状或圆形低信号灶, 直径多为2 ~ 5 mm, 一般< 10 mm, 边界清楚(图1C), 可分布于皮层、皮层下和/或脑深部区域。SWI序列结合相位图及幅度图可用于鉴别微出血及微钙化灶。脑表面铁沉积在T_2^* GRE序列或SWI上表现为沿脑回表面分布的线状或曲线状低信号(图1D)。若脑沟两侧的脑表面均存在铁沉积, 低信号则呈“双轨征”。此外, 极少数患者可能出现脑叶出血, 这可能与潜在合并CAA有关, 常表现为直径> 10 mm的血肿, MRI信号特点在常规T_1WI或T_2WI图像上因出血时间的长短而异。

4.2　ARIA的影像鉴别诊断

4.2.1　急性缺血性卒中

AD患者多为老年人群, 常合并高血压、糖尿病、高脂血症等急性缺血性卒中的危险因素, 但ARIA与急性缺血性卒中治疗方向截然不同。急性缺血性卒中引起的细胞毒性水肿与ARIA-E的血管源性水肿在常规T_1WI、T_2WI及T_2-FLAIR序列的表现类似, 表现为T_1WI稍低-低信号、T_2WI及T_2-FLAIR高信号(图2A)。DWI可用于鉴别二者: 急性缺血性卒中的病灶呈弥散受限改变(图2B ~ 2C), 表现为DWI高信号、表观弥散系数(apparent diffusion coefficient, ADC)图低信号; 而ARIA-E导致的血管源性脑水肿则弥散不受限, DWI可呈高信号, 但ADC图为正常或呈稍高信号。此外, 急性大血管闭塞性脑卒中的脑部病变分布常符合动脉供血区域, 并同时累及皮层和白质; 而血管源性脑水肿以白质受累为主, 可不累及皮层。值得注意的是, 当急性卒中进入亚急性期时, 脑梗死区呈弥散不受限改变。因此如在亚急性卒中期间进行MRI监测则可能误诊为ARIA-E, 此时需结合患者的基础疾病、急性期影像学资料和近期是否存在局灶性神经功能缺失症状来综合判断。

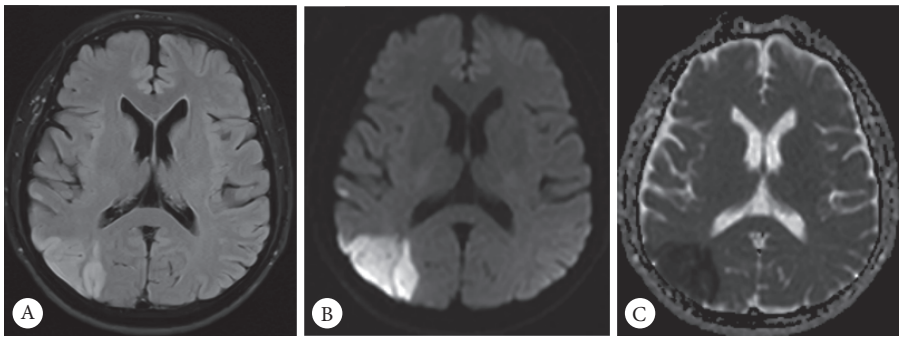

图 2　急性缺血性卒中的影像学表现

Fig 2　Imaging findings of acute ischemic stroke

T_2-FLAIR: T_2-weighted fluid-attenuated inversion recovery; DWI: diffusion weighted imaging; ADC: apparent diffusion coefficient. A, T_2-FLAIR shows patchy hyperintensity in the right parietotemporal area, involving both the cortex and white matter, with local gyral swelling; the lesion presents as hyperintensity on DWI (B) and hypointensity on ADC map (C), indicating restricted diffusion.

4.2.2　蛛网膜下出血

由脑底部和脑表面的血管破裂后, 血液流入蛛网膜下腔引起。脑沟内积血在T_2-FLAIR可呈高信号, 与ARIA-E的脑沟积液类似(图3)。但在SWI可因血液产物的顺磁性而呈现低信号, 在DWI亦可能产生一定程度的磁敏感伪影。CT平扫图像也可辅助鉴别, 急性蛛网膜下腔出血在CT表现为脑沟、脑池的密度增高或消失, 而脑沟积液则常呈低密度。

4.2.3　CAA-ri

由沉积在脑皮质或软脑膜的Aβ所引起的炎性反应, 属于CAA的少见类型, 对糖皮质激素或免疫抑制治疗有效[32], 可出现ARIA-H及ARIA-E的类似影像表现。因其病理生理学机制的相似及重叠性, 单从影像学上难以鉴别二者[15], 如图4, 需结合患者的抗Aβ抗体免疫治疗史来判

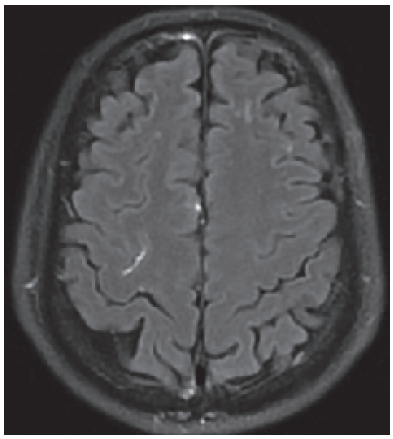

图 3　蛛网膜下腔出血的影像学表现

Fig 3　Imaging findings of subarachnoid hemorrhage

T_2-weighted fluid-attenuated inversion recovery (T_2-FLAIR) shows linear hyperintensity in the right frontal sulcus, similar to effusion seen with ARIA-E.

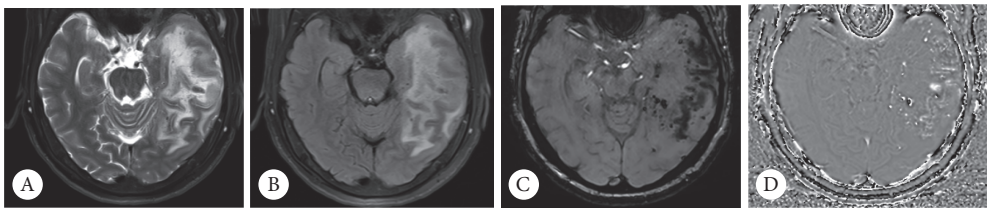

图 4 CAA-ri的影像学表现

Fig 4 Imaging findings of CAA-ri

CAA-ri: cerebral amyloid angiopathy-related inflammation; T_2WI: T_2 weighted imaging; T_2-FLAIR: T_2-weighted fluid-attenuated inversion recovery; SWI: susceptibility weighted imaging. A, T_2WI shows large-scale patchy hyperintensity in the left temporal lobe with local brain parenchyma swelling; B, T_2-FLAIR also shows hyperintense signal of the lesion; SWI sequence amplitude map (C) and phase map (D) show multiple microhemorrhages (punctate) within the lesion and superficial siderosis (distributed along the brain surface).

断是否为ARIA。

4.2.4 PRES

机制尚不明确,可能与灌注异常、内皮细胞损伤有关,多见于高血压、妊娠产褥期疾病、器官移植后应用免疫抑制药物、细胞毒性药物、化疗药物的患者。病变多累及后循环供血区的皮层下白质,也可累及皮质,为血管源性水肿病灶,在T_2-FLAIR呈高信号,弥散不受限,如图5。PRES病灶的信号特点与ARIE-E类似,但通常呈双侧对称、多灶性分布,还常伴随更严重的神经系统症状,如癫痫发作、意识障碍、认知障碍等。需综合患者的基础疾病、用药情况、临床症状及病灶分布特点进行鉴别。

4.3 ARIA影像严重程度分级

依据ARIA病灶的数量及大小,ARIA-E及ARIA-H可分别分为轻、中、重度。既往研究中使用过不同的分级标准[27, 33],鉴于仑卡奈单抗为国内获批的首款抗Aβ单克隆抗体药物,本文参考该药的美国食品药物管理局(Food and Drug Administration, FDA)文件进行分级[34],如表1。基于用药安全,早期研究中一旦发现ARIA就会停药[5, 35],随着证据增加,不同的临床症状及ARIA分级的试验组患者可以分别采取继续用药同时严密观察、药物减量、暂停用药、停药等不同的临床治疗决策[3-4]。依据FDA推荐,对出现ARIA-E或者ARIA-H的患者,影像学评估为轻度

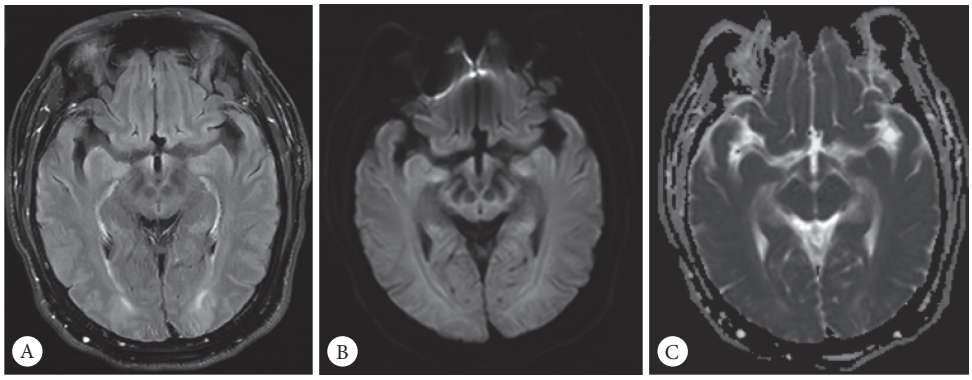

图 5 PRES的影像学表现

Fig 5 Imaging findings of PRES

PRES: posterior reversible encephalopathy syndrome; T_2-FLAIR: T_2-weighted fluid-attenuated inversion recovery; DWI: diffusion weighted imaging; ADC: apparent diffusion coefficient. A: T_2-FLAIR shows patchy hyperintense signals predominantly affecting the bilateral occipital white matter with mild local gyral swelling; lesions appear iso-/slightly hyperintense on DWI (B) and slightly hyperintense on ADC map (C), indicating unrestricted diffusion.

表 1 ARIA影像严重程度分级

Table 1 Radiological severity classification of ARIA

ARIA		Severity		
		Mild	Moderate	Severe
ARIA-E	Edema and effussion	1 location <5 cm	1 location 5-10 cm or >1 location (each <10 cm)	≥1 location (each >10 cm)
ARIA-H	Number of new microhemorrhages	≤4	5-9	≥10
	Superficial siderosis	1 focal area	2 focal areas	≥3 focal areas

ARIA: amyloid-associated imaging abnormalities; ARIA-E: amyloid-associated imaging abnormalities-edema/effusion; ARIA-H: amyloid-associated imaging abnormalities-microhemorrhages/superficial siderosis.

且无症状者可继续用药; 出现ARIA-E的患者, 影像学评估轻度且伴有轻度临床症状的可经过临床医生评估后继续用药; 其余患者应暂停用药。是否恢复用药需评估临床症状缓解情况, 并随访2 ~ 4个月的MRI表现, 由临床医生综合评估[34]。

5　建议与展望

抗Aβ单克隆抗体为治疗AD带来了里程碑式的改变, 用药前评估ARIA风险对判断患者用药的危险性及获益具有重要意义。然而, 目前ARIA相关研究数据多来自药物临床试验, 缺乏真实世界应用抗Aβ单克隆抗体的治疗经验, 未来的用药前风险评估仍有许多尚待探讨的问题, 例如: ARIA在中国真实世界的发生、转归和延长用药的后果如何? 除抗Aβ单克隆抗体的高剂量使用、携带ApoE ε4等位基因、老龄等危险因素之外, 是否存在其他帮助预判药物风险的临床因素和影像指标? 使用不同的成像条件是否给真实世界的患者管理带来差异? 临床研究对AD患者的纳入及排除标准较为严格, 仅有少部分AD患者能从中获益, 药物适应证的扩大也将是未来研究的重要议题。值得指出的是, 前期大量研究的纳入患者群体多为高加索人, 其流行病学特点、临床表现可能与中国人群存在差异。用药前, 应向患者和家属充分告知药物的获益及风险; 用药期间, 与之保持良好沟通, 应鼓励患者按医嘱坚持定期随访, 助其及时自评药物可能引起的不良反应。

*　　*　　*

作者贡献声明　杨曦玥负责论文构思、调查研究和初稿写作, 李婉婷和李红霞负责数据审编和调查研究, 杨兴隆负责数据审编和可视化, 陈芹负责论文构思、监督指导和审读与编辑写作, 吕粟和胡娜负责论文构思、提供资源、监督指导和审读与编辑写作。所有作者已经同意将文章提交给本刊, 且对将要发表的版本进行最终定稿, 并同意对工作的所有方面负责。

Author Contribution　YANG Xiyue is responsible for conceptualization, investigation, and writing--original draft. LI Wanting and LI Hongxia are responsible for data curation and investigation. YANG Xinglong is responsible for data curation and visualization. CHEN Qin is responsible for conceptualization, supervision, and writing--review and editing. LYU Su and HU Na are responsible for conceptualization, resources, supervision, and writing--review and editing. All authors consented to the submission of the article to the Journal. All authors approved the final version to be published and agreed to take responsibility for all aspects of the work.

利益冲突　本文作者吕粟是本刊编委会编委。该文在编辑评审过程中所有流程严格按照期刊政策进行, 且未经其本人经手处理。除此之外, 所有作者均声明不存在利益冲突。

Declaration of Conflicting Interests　LYU Su is a member of the Editorial Board of the journal. All processes involved in the editing and reviewing of this article were carried out in strict compliance with the journal's policies and there was no inappropriate personal involvement by the author. Other than this, all authors declare no competing interests.

参　考　文　献

[1] REN R, QI J, LIN S, *et al*. The China Alzheimer report 2022. Gen Psychiatr, 2022, 35(1): e100751. doi: 10.1136/gpsych-2022-100751.

[2] FILIPPI M, CECCHETTI G, SPINELLI E G, *et al*. Amyloid-related imaging abnormalities and β-amyloid-targeting antibodies: a systematic review. JAMA Neurol, 2022, 79(3): 291-304. doi: 10.1001/jamaneurol.2021.5205.

[3] SALLOWAY S, CHALKIAS S, BARKHOF F, *et al*. Amyloid-related imaging abnormalities in 2 phase 3 studies evaluating aducanumab in patients with early Alzheimer disease. JAMA Neurol, 2022, 79(1): 13-21. doi: 10.1001/jamaneurol.2021.4161.

[4] Van DYCK C H, SWANSON C J, AISEN P, *et al*. Lecanemab in early Alzheimer's disease. N Engl J Med, 2023, 388(1): 9-21. doi: 10.1056/NEJMoa2212948.

[5] DOODY R S, THOMAS R G, FARLOW M, *et al*. Phase 3 trials of solanezumab for mild-to-moderate Alzheimer's disease. N Engl J Med, 2014, 370(4): 311-321. doi: 10.1056/NEJMoa1312889.

[6] SPERLING R A, JACK C R, Jr, BLACK S E, *et al*. Amyloid-related imaging abnormalities in amyloid-modifying therapeutic trials: recommendations from the Alzheimer's Association Research Roundtable Workgroup. Alzheimers Dement, 2011, 7(4): 367-385. doi: 10.1016/j.jalz.2011.05.2351.

[7] SPERLING R, SALLOWAY S, BROOKS D J, *et al*. Amyloid-related imaging abnormalities in patients with Alzheimer's disease treated with bapineuzumab: a retrospective analysis. Lancet Neurol, 2012, 11(3): 241-249. doi: 10.1016/s1474-4422(12)70015-7.

[8] AGARWAL A, GUPTA V, BRAHMBHATT P, *et al*. Amyloid-related imaging abnormalities in Alzheimer disease treated with anti-amyloid-β therapy. Radiographics, 2023, 43(9): e230009. doi: 10.1148/rg.230009.

[9] 王刚, 李彬寅, 任汝静, 等. 关于抗Aβ单克隆抗体的临床应用建议(2024版). 中国现代神经疾病杂志, 2024, 24(3): 120–126. doi: 10.3969/j.issn.1672-6731.2024.03.002.
WANG G, LI B Y, REN R J, *et al*. Recommendations for the clinical use of anti-Aβ monoclonal antibody for Alzheimer's disease (2024) . Chin J Contemp Neurol Neurosurg, 2024, 24(3): 120–126. doi: 10.3969/j.issn.1672-6731.2024.03.002.

[10] HAMPEL H, ELHAGE A, CHO M, *et al*. Amyloid-related imaging abnormalities (ARIA): radiological, biological and clinical characteristics. Brain, 2023, 146(11): 4414-4424. doi: 10.1093/brain/awad188.

[11] CUMMINGS J L, COHEN S, Van DYCK C H, *et al*. ABBY: a phase 2 randomized trial of crenezumab in mild to moderate Alzheimer disease. Neurology, 2018, 90(21): e1889-e1897. doi: 10.1212/wnl.0000000000005550.

[12] BOCHE D, ZOTOVA E, WELLER R O, *et al*. Consequence of Abeta immunization on the vasculature of human Alzheimer's disease brain. Brain, 2008, 131(Pt 12): 3299–3310. doi: 10.1093/brain/awn261.

[13] THAL D R, GRIFFIN W S, De VOS R A, *et al*. Cerebral amyloid angiopathy and its relationship to Alzheimer's disease. Acta Neuropathol, 2008, 115(6): 599-609. doi: 10.1007/s00401-008-0366-2.

[14] GREENBERG S M, BACSKAI B J, HERNANDEZ-GUILLAMON M, *et al*. Cerebral amyloid angiopathy and Alzheimer disease--one peptide, two pathways. Nat Rev Neurol, 2020, 16(1): 30-42. doi: 10.1038/s41582-019-0281-2.

[15] ANTOLINI L, DIFRANCESCO J C, ZEDDE M, *et al*. Spontaneous ARIA-like events in cerebral amyloid angiopathy-related inflammation: a multicenter prospective longitudinal cohort study. Neurology, 2021, 97(18): e1809-e1822. doi: 10.1212/wnl.0000000000012778.

[16] RAMAN M R, WISTE H J, SENJEM M L, *et al*. Spontaneous amyloid-related imaging abnormalities in a cognitively normal adult. Neurology, 2014, 83(19): 1771-1772. doi: 10.1212/wnl.0000000000000957.

[17] CHEN Y, HE Y, HAN J, *et al*. Blood-brain barrier dysfunction and Alzheimer's disease: associations, pathogenic mechanisms, and therapeutic potential. Front Aging Neurosci, 2023, 15: 1258640. doi: 10.3389/fnagi.2023.1258640.

[18] DORAN S J, SAWYER R P. Risk factors in developing amyloid related imaging abnormalities (ARIA) and clinical implications. Front Neurosci, 2024, 18: 1326784. doi: 10.3389/fnins.2024.1326784.

[19] SALLOWAY S, SPERLING R, GILMAN S, *et al*. A phase 2 multiple ascending dose trial of bapineuzumab in mild to moderate Alzheimer disease. Neurology, 2009, 73(24): 2061-2070. doi: 10.1212/WNL.0b013e3181c67808.

[20] OSTROWITZKI S, LASSER R A, DORFLINGER E, *et al*. A phase Ⅲ randomized trial of gantenerumab in prodromal Alzheimer's disease. Alzheimers Res Ther, 2017, 9(1): 95. doi: 10.1186/s13195-017-0318-y.

[21] CUMMINGS J, APOSTOLOVA L, RABINOVICI G D, *et al*. Lecanemab: appropriate use recommendations. J Prev Alzheimers Dis, 2023, 10(3): 362-377. doi: 10.14283/jpad.2023.30.

[22] LIU E, WANG D, SPERLING R, *et al*. Biomarker pattern of ARIA-E participants in phase 3 randomized clinical trials with bapineuzumab. Neurology, 2018, 90(10): e877-e886. doi: 10.1212/wnl.0000000000005060.

[23] COGSWELL P M, BARAKOS J A, BARKHOF F, *et al*. Amyloid-related imaging abnormalities with emerging Alzheimer disease therapeutics: detection and reporting recommendations for clinical practice. AJNR Am J Neuroradiol, 2022, 43(9): e19-e35. doi: 10.3174/ajnr.A7586.

[24] SWANSON C J, ZHANG Y, DHADDA S, *et al*. A randomized, double-blind, phase 2b proof-of-concept clinical trial in early Alzheimer's disease with lecanemab, an anti-Aβ protofibril antibody. Alzheimer Res Therapy, 2021, 13(1): 80. doi: 10.1186/s13195-021-00813-8.

[25] CHAGLA G H, BUSSE R F, SYDNOR R, *et al*. Three-dimensional fluid attenuated inversion recovery imaging with isotropic resolution and nonselective adiabatic inversion provides improved three-dimensional visualization and cerebrospinal fluid suppression compared to two-dimensional flair at 3 Tesla. Invest Radiol, 2008, 43(8): 547-551. doi: 10.1097/RLI.0b013e3181814d28.

[26] VOS S B, MICALLEF C, BARKHOF F, *et al*. Evaluation of prospective motion correction of high-resolution 3D-T2-FLAIR acquisitions in epilepsy patients. J Neuroradiol, 2018, 45(6): 368-373. doi: 10.1016/j.neurad.2018.02.007.

[27] BARAKOS J, PURCELL D, SUHY J, *et al*. Detection and management of amyloid-related imaging abnormalities in patients with Alzheimer's disease treated with anti-amyloid beta therapy. J Prev Alzheimers Dis, 2022, 9(2): 211-220. doi: 10.14283/jpad.2022.21.

[28] ROYTMAN M, MASHRIQI F, Al-TAWIL K, *et al*. Amyloid-related imaging abnormalities: an update. AJR Am J Roentgenol, 2023, 220(4): 562-574. doi: 10.2214/ajr.22.28461.

[29] CHENG A L, BATOOL S, MCCREARY C R, *et al*. Susceptibility-weighted imaging is more reliable than T2*-weighted gradient-recalled echo MRI for detecting microbleeds. Stroke, 2013, 44(10): 2782-2786. doi: 10.1161/strokeaha.113.002267.

[30] ASSIS LOPES P, RAPOSO N, CHARIDIMOU A, *et al*. SWI versus GRE-T2*: assessing cortical superficial siderosis in advanced cerebral amyloid angiopathy. Rev Neurol (Paris), 2024, 180(6): 532-538. doi: 10.1016/j.neurol.2023.10.008.

[31] HALLER S, HAACKE E M, THURNHER M M, *et al*. Susceptibility-weighted imaging: technical essentials and clinical neurologic applications. Radiology, 2021, 299(1): 3-26. doi: 10.1148/radiol.2021203071.

[32] 孟强. 重视脑淀粉样血管病相关炎症的诊治. 中华神经科杂志, 2022, 55(10): 1065-1070. doi: 10.3760/cma.j.cn113694-20220516-00392.
MENG Q. Pay attention to the diagnosis and treatment of cerebral amyloid angiopathy-related inflammation. Chin J Neurol, 2022, 55(10): 1065-1070. doi: 10.3760/cma.j.cn113694-20220516-00392.

[33] BARKHOF F, DAAMS M, SCHELTENS P, *et al*. An MRI rating scale for amyloid-related imaging abnormalities with edema or effusion. AJNR Am J Neuroradiol, 2013, 34(8): 1550-1555. doi: 10.3174/ajnr.A3475.

[34] LEQEMBI® (lecanemab-irmb) injection, for intravenous use prescribing information. 2023[2024-09-01]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761269Orig1s001lbl.pdf.

[35] VANDENBERGHE R, RINNE J O, BOADA M, *et al*. Bapineuzumab for mild to moderate Alzheimer's disease in two global, randomized, phase 3 trials. Alzheimers Res Ther, 2016, 8(1): 18. doi: 10.1186/s13195-016-0189-7.

（2024－09－30收稿，2024－10－30修回）

编辑 吕 熙