·专论·

儿童脑动静脉畸形治疗策略

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【摘要】 目前儿童脑动静脉畸形的主要治疗方式包括显微外科手术、血管内介入治疗及立体定向放射外科治疗，由于无法通过其中某一项治疗使所有病例达到最佳治疗效果，建议在了解不同治疗方式适应证与优势的前提下，结合患儿临床特点和病灶特征，根据不同治疗时机制定个体化治疗策略。本文对儿童脑动静脉畸形的不同治疗方式及整体治疗现状进行概述，为规范治疗提供思路及依据。

【关键词】 脑动静脉畸形；　显微外科手术；　脑血管造影术；　儿童

Treatment of pediatric cerebral arteriovenous malformation

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【**Abstract**】 The mainstream treatment strategies for pediatric cerebral arteriovenous malformation (CAVM) include microsurgery, interventional surgery and stereotactic radiosurgery (SRS). The best prognosis of a patient cannot be achieved by any single treatment strategy. The treatment indication and advantages of different strategy should be fully acquainted, and the clinical characteristics and features of the lesion should also be taken into consideration when making clinical decision for pediatric CAVM cases at different stages of management. This article introduces different treatment strategies and the current status of management for pediatric CAVM, aiming to provide evidence and basis for management standard for these patients.

【**Key words**】 Cerebral arteriovenous malformations;　Microsurgery;　Cerebral angiography;　Child

Conflicts of interest: none declared

脑动静脉畸形(CAVM)是一种动静脉分化失败使动静脉之间形成异常沟通的先天性血管畸形，是儿童最为常见的自发性脑出血病因。儿童脑动静脉畸形的自然史与成人有所不同，其破裂出血风险明显高于成人、预后更差，且部分儿童患者颅内畸形血管团具有生长倾向[1]；鉴于儿童预期寿命较长，上述风险对儿童造成的影响更大。因此，对于儿童脑动静脉畸形应采取更为积极的治疗策略，最大限度地降低疾病对儿童生命和生活质量所造成的威胁。目前，儿童脑动静脉畸形的治疗方式主要包括显微外科手术、立体定向放射外科(SRS)治疗及血管内介入治疗，但有关治疗方式的选择至今尚存争议。本文拟就儿童脑动静脉畸形的不同治疗方式和整体治疗现状进行概述，以为临床医师充分了解不同治疗方式的特点与适应证并制定个体化治疗方案提供依据和思路。

一、显微外科手术

早在1908年，即有学者尝试通过外科手术切除畸形血管团，但终因手术失败而对这一治疗方法的探索趋于停滞[2]。随着20世纪20年代脑血管造影术的问世，人类对脑动静脉畸形的血管构筑有了更深入的了解，再次开始尝试对该病进行外科手术治疗。1969年，美国波士顿儿童医院首次报道一组儿童病例，共切除了34例患儿颅内畸形血管团，其中12例获全切除[3]。近10年来，对儿童脑动静脉畸形的大样本病例系列报道显示，儿童脑动静脉畸形手术切除治愈率可达94%～99%[4-6]；对于术前存在癫痫发作的患儿，术后达到Engel Ⅰ级标准(无致残性癫痫发作)的比例可达到92.31%[7]，而全年龄组达到Engel Ⅰ级标准的比例仅约70%[8-9]；儿童患者术后新发癫痫发作、再出血、神经功能缺损、感染等并发症的比例为8.3%～19%[4,6]，其中，低龄患儿术后

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新发癫痫发作的比例较大龄儿童和成人更低(3%～4%对20%)[6,8]。

儿童脑动静脉畸形手术后复发率高于成人[10],为3.5%～16%[10-14],而成人仅为0～2.7%[10,13],全年龄组平均影像学复发时间为术后4.2年,出现复发症状的平均时间为术后6.3年[10]。影响术后复发的因素有多种,其中手术年龄、畸形血管团结构弥散、有深静脉引流、畸形血管团破裂出血等为主要危险因素[14-16];由于脑动静脉畸形为先天性病变,也有观点认为,术区复发系术中未发现的少量残留病灶所致。复合手术[亦称杂交手术(hybrid operation)]指血管内介入操作与开颅手术同期进行,通过术中脑血管造影辅助判断病灶残留情况,可为全切除畸形血管团提供保障[17]。多项文献报道,术中脑血管造影发现的病灶残留率高达11%～29%[12,18],笔者团队于复合手术中脑血管造影显示的畸形血管团残留率为15.8%[19],说明仅凭开颅手术术野判断是否全切除并不可靠。根据笔者经验,造成术后复发的主要原因仍是术中残留,而通过复合手术模式可将术中脑血管造影"治愈率"提高至100%[19]。

合理选择手术适应证也是保证手术治愈率、降低并发症风险的关键因素。目前认为,位于皮质、非功能区的中小型畸形血管团为手术切除的首选适应证。但对畸形血管团破裂出血者而言,手术切除是一把"双刃剑",虽然血肿腔的存在使畸形血管团边界的分离更加容易,但病灶残留复发的风险亦随之增加,尤其是在出血急性期。2010年,Lawton等[20]提出Spetzler-Martin分级补充分级,进一步加强了对手术风险与疗效的术前预测,是目前公认的脑动静脉畸形术前风险评估系统,评估项目主要包括破裂出血史、畸形血管团结构弥散和年龄,其中年龄<20岁计1分、20～40岁计2分、>40岁计3分,总评分越低越倾向手术切除,尤其适用于6分以内的患儿[21],提示儿童脑动静脉畸形应采取更加积极的外科手术态度。

二、立体定向放射外科治疗

该项技术用于治疗儿童脑动静脉畸形的时间最早可追溯至1989年[22],近10年来,针对儿童脑动静脉畸形的大样本报道逐渐增多。SRS治疗旨在通过大剂量放射线照射,诱导血管平滑肌细胞增殖和细胞外胶原累积,使血管内膜进行性增厚,受照射血管管腔逐渐闭塞[23],一般需3～5年方能达到治疗目的,在畸形血管团完全闭塞前,年出血率接近未经治疗的脑动静脉畸形[24]。Meta分析表明,SRS治疗儿童脑动静脉畸形的中位边缘照射剂量为15～25 Gy,单次照射后畸形血管团完全闭塞率为65.9%,达到闭塞的中位时间为16～49个月,伽马刀与其他SRS治疗方式(质子刀、X刀)相比,疗效与并发症发生率相当[25]。根据文献检索,SRS治疗后畸形血管团完全闭塞率分别为:照射2年36%、3年46%～84%、5年51%～95%,之后闭塞情况趋于稳定[26-29]。对于闭塞率的影响因素,其研究结论尚不一致。一般而言,Spetzler-Martin分级低级别(Ⅰ～Ⅲ级)者疗效优于高级别(Ⅳ～Ⅴ级)者[26,30],而边缘照射剂量、病灶大小以及畸形血管团破裂出血与闭塞率之间的关系仍存争议[25,30-31]。SRS治疗总体并发症发生率约为10.8%,病死率为0.6%～3%[25,32];短期并发症发生率为3%～15.8%,随访20年时累积并发症可达17%[33]。常见并发症包括照射区域水肿、出血、囊性变,以及神经功能缺损、癫痫发作等,儿童患者SRS治疗后畸形血管团闭塞率和并发症发生率与成人患者无显著差异[34]。但考虑到放射线对低龄儿童的影响,Winkler等[4]将儿童患者接受SRS治疗的年龄限定为5岁以上,截至目前,SRS治疗的最小年龄为2.8岁[35],其远期影响尚待进一步观察研究。

三、血管内介入治疗

血管内介入治疗是治疗脑动静脉畸形的重要方法之一,而全脑血管造影术是儿童脑动静脉畸形诊断的"金标准"。尽管单纯栓塞术治疗脑动静脉畸形的治愈率较低,但因其适应证广泛且微创,尤其是对存在动脉瘤样结构等危险结构的脑动静脉畸形具有得天独厚的优势,因此被广泛应用于各类儿童脑动静脉畸形的治疗。血管内介入治疗亦可作为显微外科手术或SRS的协同治疗措施,以提高治愈率、降低出血风险,极具临床实用价值。

近20年来,随着介入材料与介入技术的进步与发展,脑血管病变的治疗效果有了明显提高,如Onyx胶[36]的临床应用使脑动静脉畸形总体治愈率提高,"高压锅"技术[37]和经静脉途径栓塞术[38]在部分复杂儿童脑动静脉畸形的治疗中获得成功。尽管有关新技术应用的安全性尚未取得一致性临床证据,但近年来血管内治疗技术与材料的革新使越来越多的儿童脑动静脉畸形患者通过血管内介入治疗治愈成为现实。1995年单纯栓塞术治疗脑动静脉畸形的治愈率仅为5%,总体并发症发生率近

20%[39]；至2014年，南方医科大学珠江医院报告的单纯栓塞术治愈率提高至21.21%(14/66)[40]。目前文献报道的血管内介入治疗的直接并发症主要包括出血、非病变区域血栓形成和水肿，少见并发症包括栓塞剂相关肺栓塞或过敏反应、导管撤出失败、导管相关血管破裂等，并发症发生率为7.32%(9/123)～29.41%(15/51)[40-41]。近年来尚缺乏儿童脑动静脉畸形血管内介入治疗治愈率或并发症发生率的报道，相信随着新技术的应用，不久的将来能够看到与血管内介入治疗治愈率与安全性有关的新的研究成果。

四、多模式治疗策略

目前，显微外科手术、血管内介入治疗和SRS治疗是儿童脑动静脉畸形的3种主要治疗手段，无法通过单一方式使所有病例均达到最佳治疗效果。其中，以显微外科手术的治愈率和癫痫缓解率最高，但其适应证较窄，且手术创伤给儿童带来的影响也是不可忽视的；血管内介入治疗适用于绝大多数脑动静脉畸形类型，且可反复多次治疗，尤其对包含危险结构的畸形具有独特优势，但总体治愈率最低；SRS治愈率介于上述两种治疗方法之间，但放射线对儿童的影响不可忽视，因此不适用于低龄患儿，且在畸形血管团未完全闭塞之前不能降低出血风险。因此，对儿童脑动静脉畸形的治疗需在充分了解不同治疗方式适应证与优势的前提下，结合患儿临床特点和畸形血管团病灶特征，在不同的治疗时机，选择最优的治疗方式或组合方式，最终制定个体化多模式治疗策略。对于有治愈希望的患儿，应积极以治愈为最终目标，而难以治愈的患儿，则应以降低畸形血管团出血风险为原则。

基于上述治疗原则，目前的观点认为：对于通过血管内介入治疗即可治愈的病例，可选择单次或分次栓塞，避免开颅手术相关失血、感染等风险；而对于血管内介入治疗难以治愈但显微外科手术能够达到安全切除病灶目的患儿，则应积极选择显微外科手术切除畸形血管团；对于存在动脉瘤样结构等危险结构或伴有深部动脉供血的患儿，可于开颅手术前先行栓塞术对危险结构或深部供血动脉进行栓塞，以降低手术风险与难度，辅助手术顺利进行；建议有复合手术室的医疗中心尽量选择复合手术，以提高手术全切除率和安全性。有研究显示，高达57.5%～83%的儿童脑动静脉畸形以出血为首发表现[1]，故急诊救治至关重要。临床研究表明，破裂出血的畸形血管团切除后残留复发病例主要见于儿童，此类患儿急诊切除残留率高达10.7%～11.5%[42]，5年随访复发率为21.4%，且首次手术年龄越小、复发率越高[14]。因此，儿童脑动静脉畸形破裂出血的急诊开颅手术应慎重，对于整体情况稳定的患儿，应避免急诊开颅手术，建议通过血管内介入治疗处理危险结构、降低再出血风险，待出血吸收后再评估病情、选择个体化治疗方案。而出血量大、须急诊手术者，在缺乏DSA或CTA检查结果，难以对畸形血管团病灶进行有效评估的情况下，可仅行大部分血肿清除术以挽救患儿生命，而后再择期行脑动静脉畸形的治疗。至于既不能通过血管内介入治疗治愈又非手术适应证的患儿或担心短期内治疗风险的患儿，可以选择单次或分次SRS治疗，但需数年时间方能逐渐达到治疗之目的，即畸形血管团完全闭塞。有研究显示，于血管内介入治疗后再行SRS治疗，畸形血管团闭塞率显著低于单纯SRS治疗者[43-44]，而且这一结论与选择何种栓塞剂无关[45]。这些研究结论尚未取得临床共识，其原因仍停留在假说阶段，推测可能与部分栓塞畸形血管团后增加SRS对残留靶区的精确勾画难度有关。当前在儿童脑动静脉畸形多模式治疗被广泛应用的情况下，有待更多临床与基础研究进一步探讨不同治疗方式之间的相互影响，例如，是否需要融合造影与MRI共同进行畸形血管团靶区精确勾画，以及不同栓塞材料对放射线的影响等，以使不同治疗方式之间形成更好的配合、补充，从而提高脑动静脉畸形患儿的治愈率。2020年，Winkler等[4]基于美国加利福尼亚大学旧金山分校20年儿童脑动静脉畸形诊治经验形成一个完整的诊治流程建议，与笔者所述观点基本一致。

儿童脑动静脉畸形患者预后优于成人患者[46]，治疗后5年改良Rankin量表(mRS)评分0～2分者占81.5%～94%[4-6]；随访21年，约62%患儿mRS评分可达0～2分[46]。

儿童脑动静脉畸形是危害儿童生命健康的严重疾病，应采取积极的治疗态度，对于能够有机会治愈的脑动静脉畸形，应以追求治愈为目标，对于难以治愈的患儿，则应力求降低出血风险；在制定治疗方案时，应根据患儿年龄、病灶特点及监护人意愿等，合理选择治疗方式，包括显微外科手术、血管内介入治疗、SRS治疗或多模式治疗方案，以使患儿获得较好的远期预后。

利益冲突 无

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