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·临床研究·

聚多卡醇经皮硬化治疗成人巨大唇颊部微静脉畸形

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【摘要】　目的　探讨聚多卡醇硬化治疗成人巨大唇颊部微静脉畸形的临床疗效。**方法**　2019年9月至2020年9月在徐州市中心医院就诊，临床诊断为巨大唇颊部微静脉畸形的5例患者。使用聚多卡醇泡沫硬化剂瘤体内注射治疗，注射3周后复诊，对于临床症状未缓解，MRI检查示病灶残留＞25%，或症状稳定后再次复发，则需再次治疗。治疗终点为：①临床症状消退且MRI检查显示病灶残留＜25%；②连续治疗4次症状无缓解或加重者；③放弃治疗者。**结果**　5例患者完成全程治疗，注射治疗次数为2～4次，参照Achauer标准评价疗效，达Ⅰ级疗效者1例，Ⅱ级疗效者2例，Ⅲ级疗效者2例。其中1例患者术前病灶出现糜烂出血，术后症状得到明显改善。1例患者术后病灶处出现色素沉着，其它无明显严重不良反应。**结论**　聚多卡醇泡沫硬化剂局部注射治疗成人巨大唇颊部微静脉畸形是一种安全有效治疗方法，且对自发性出血的微静脉畸形有一定的止血作用。

【关键词】　脉管畸形；　微静脉畸形；　葡萄酒色斑；　硬化治疗；　泡沫硬化剂；　聚多卡醇；　硬化剂
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Polydocanol percutaneous sclerotherapy for the treatment of giant venular malformation of the lips and cheeks in adults

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【Abstract】　Objective　To investigate the clinical effect of polidocanol sclerotherapy in the treatment of giant venular malformations of the lips and cheeks in adults. **Methods**　From September 2019 to September 2020, 5 patients with huge venular malformations of the lips and cheeks (4 males, 1 female) admitted to Xuzhou Central Hospital were included in the study. All the patients were treated with local injection of polidocanol foam scleroagent, and all patients were followed up with a 3-week treatment course. If the clinical symptoms were not alleviated and the MRI examination showed that > 25% of the lesion remained, or it relapsed again after symptoms are stable, the patient needed to be treated again. The endpoints of treatment were: ①subsidence of clinical symptoms and MRI showing residual lesions < 25% in size; ②continuous treatment for 4 times without relief or aggravation of symptoms; ③a discontinuation of treatment. **Results**　All 5 patients successfully completed the treatment and were injected 2 to 4 times during treatment. The curative effect was evaluated according to the Achauer standard, including grade Ⅰ curative effects in 1 patient, grade Ⅱ in 2 patients, grade Ⅲ in 2 patients. Among them, one patient suffered from erosion and bleeding in the lesion before the operation, and the symptoms were significantly improved postoperatively. No serious side effects were found except skin

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pigmentation in 1 case. **Conclusion**　Local injection of polidocanol foam scleroagent is a safe and effective treatment method for adult giant venular malformations of the lips and cheeks, and it has a hemostatic effect on spontaneous bleeding invenular malformations.

【Key words】 vascular malformations;　venular malformation;　port wine stain;　sclerotherapy;　foam scleroagent;　polidocanol;　scleroagent

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微静脉畸形(venular malformation,VM)又称葡萄酒色斑(port wine stain,PWS)或鲜红斑痣,是一种先天性脉管疾病。该病发病率约0.3%~0.5%[1],85%发生在面颈部,且多沿三叉神经分布区域单侧发生。病变初期常表现为无痛性缓慢生长的粉红色斑块,发展到晚期常形成多发性隆起性结节,影响美观[2]。累及口唇时,可表现为唇的厚度、长度、宽度均增加,形成鲜红斑痣巨唇症[3],增大自发性出血的风险,临床治疗比较棘手。本研究采用聚多卡醇泡沫硬化剂局部注射的方法治疗巨大唇颊部微静脉畸形患者,取得了较为满意的临床效果,报道如下。

1　资料和方法

1.1　临床资料

徐州市中心医院口腔科2019年9月至2020年9月收治的影像学和病理学明确诊断为巨大唇颊部微静脉畸形患者5例,其中男4例,女1例,年龄35~68岁,平均年龄41岁。累及唇部2例,颊部1例,唇颊联合2例。临床表现为出生时浅表皮肤淡红或鲜红色斑块,无痛性缓慢生长,且随着年龄增长,斑块逐渐增大,颜色逐渐加深呈紫红色,病变处皮肤增厚或呈结节样增生,表面皮肤隆起,其中1例伴有溃疡、出血、局部疼痛。所有患者行MRI检查,全部病例均为首次接受治疗,且对聚多卡醇无过敏反应。

1.2　治疗方法

患者仰卧位,建立好静脉通道后病变区皮肤常规消毒、铺巾。

使用Tessari法[4]将1%聚多卡醇注射液1mL(Hameln pharmaceuticals GmbH公司,德国,批准文号:H20160033)与空气1∶3制成泡沫混合液备用。

2%盐酸利多卡因注射液2 mL(上海朝晖药业有限公司,国药准字H31021072)及地塞米松磷酸钠注射液1 mL(辰欣药业股份有限公司,国药准字H37021969)配成溶液,于病变周围正常皮肤切线方向进针,回抽有血性液体流出,注入麻药,更换聚多卡醇泡沫硬化剂酌情注射。用药剂量根据病灶的部位、大小而定,剂量不超过2 $mg \cdot kg^{-1} \cdot d^{-1}$。

对于体积较大的病变,采用多点注射,必要时采用双针法注射[5]。推注硬化剂时密切观察瘤体颜色变化,注射结束后用小纱布对针孔部位进行压迫止血,并防止药物外溢。注射后1~3 d严密观察,针对术后出现的疼痛,红肿对症处理。

3周后复诊,对于临床症状未缓解,MRI检查示病灶残留>25%,或症状稳定后再次复发,则需再次治疗。治疗终点为:①临床症状消退且MRI检查显示病灶残留<25%;②连续治疗4次症状无缓解或加重者;③放弃治疗者。

1.3　疗效评价

所有患者术后1、2、3个月门诊随访,依据临床症状及MRI检查进行疗效评估。疗效评价参照Achauer标准[6],无效:病灶体积不缩小或继续增大;Ⅰ级:病灶缩小≤25%;Ⅱ级:病灶缩小26%~50%;Ⅲ级:病灶缩小51%~75%;Ⅳ级:病灶缩小>76%,皮肤有轻度色素沉着或接近正常,无功能障碍。

2　结　果

5例患者共行局部注射治疗16次,其中最少注射次数为2,最多注射次数为4。1例患者术前病

灶出现破溃出血，经首次聚多卡醇治疗后，唇红糜烂面愈合，不再出血，末次治疗后达到Ⅱ级疗效。5例患者中无效者0例，达Ⅰ级疗效者1例(20%)，Ⅱ级疗效者2例(40%)，Ⅲ级疗效者2例(40%)，Ⅳ级疗效者0例。

有3例在术后1～2 d出现局部软组织肿胀，常规抗炎消肿对症治疗，4 d后肿胀缓解。1例术后5 d出现病灶处色素沉着，未行特殊处理，定期随访过程中发现色素沉着逐渐变淡。所有病例均未出现皮肤破溃、过敏、组织坏死、肺栓塞与呼吸衰竭等严重不良反应。目前所有随访患者病情稳定。

3　典型病例

患者，男，61岁，因下唇肿胀畸形伴破溃出血3月余入院。

患者自述出生时即见右面颈部斑片状紫红色改变，生长缓慢，无不适症状。约20年前右颊面部皮肤隆起，形成一赘生物，缓慢生长。约3个月前，下唇开始肿胀，继之破溃、反复出血，局部压迫，效果不佳，且长期不愈。

患者智力正常，否认下唇创伤史，既往无癫痫病史，且家族中无类似病史。

检查见右面颈部、颏部及下唇大片紫红色病损，其中右颊面部有一赘生肿物，大小约2.5 cm × 1 cm × 1 cm，有蒂、可活动(图1a、1b)；下唇增生肥厚，唇黏膜外翻，表面破溃出血，颏部皮肤增生呈多个鹅卵石样小结节，质韧(图1c)。

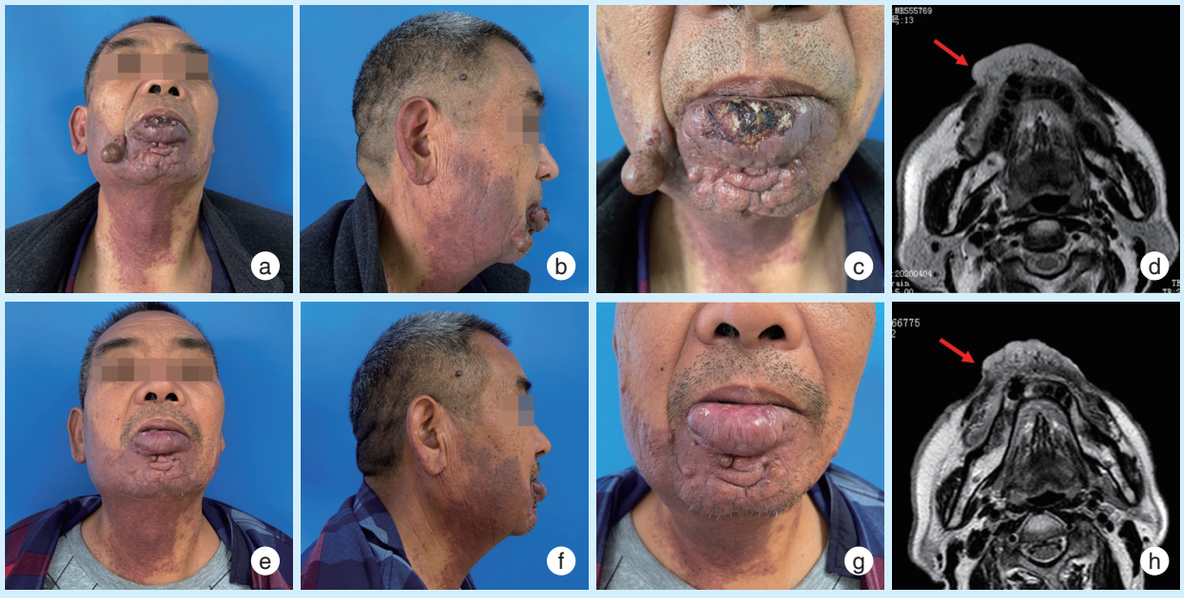
面部MRI示：下唇软组织增厚，右侧颊部软组织结节状隆起，T1W呈低信号，T2W呈高信号，邻近骨质未见明显破坏(图1d)。

实验室检查无血小板减少，无凝血功能障碍。

诊断：巨大唇颊部微静脉畸形。

按上述方法治疗，术后1周出院时，下唇肿胀较入院时稍减轻，唇红血痂已脱落，糜烂面基本愈合，不再出血。

术后每间隔3周住院在局麻下再次行聚多卡醇硬化剂注射治疗2次后，下唇糜烂面完全愈合，随访至2021年1月未有出血，且其肿胀畸形的程度也有明显改善(图1e～1h)。



a: frontal view showed a large red lesion and a neoplastic mass on the right side of the face and neck; b: side view showed the lip hypertrophy and infrared turns; c: local lesion view showed the lip ulceration covered with scabs; d: MRI image showed thickened lip tissues and malformed vasculature (indicated by arrow); e&f: frontal view (e) and side view (f) showed alleviation of lip hypertrophy and infrared turns compared with that before treatment; g: local lesion view showed the lip erosion surface was healed; h: MRI image showed the lip tissue fibrosis, the lumen was atresia and the lesion size was smaller compared with that before treatment (indicated by arrow)

Figure 1　Preoperative and postoperative images of the patient's lesion and imaging examination of typical case with venular malformations of the giant lip and cheek

图1　巨大唇颊部微静脉畸形患者手术前后病灶及影像学检查

4　讨　论

4.1　病因病理

微静脉畸形是一种常见的先天性、进行性脉管畸形[7]，其确切病因迄今尚不明确，但有理论认为基因突变是造成早期血管发育异常的原因之一。近年来，GNAQ体细胞基因发生突变已成为微静脉畸形的主要病因学说[8]。Tan等[9]发现其突变的基因主要存在血管内皮上，另有学者又相继发现了其他突变[10-12]。另有学者认为微静脉畸形的发生可能与神经、血管、细胞因子等因素有关[13]。微静脉畸形在病理上通常表现为真皮浅层异常扩张的毛细血管，而且数量不等，深部可见管壁增厚的畸形静脉样血腔，不伴有明显的内皮细胞增殖[14]。

对于晚期微静脉畸形继发自发性出血的机制，尚不完全清楚，有学者推测可能是由于病变晚期扩张的血管通透性增加，使病灶内炎症因子增多，加上唇颊部位置表浅、黏膜较薄，易受外界刺激，从而使其发生出血的风险增加[15]。

4.2　临床表现

微静脉畸形在出生时即可表现为鲜红或紫红色的斑块，与皮肤表面平、界限清楚，压之可褪色；随年龄增长病变逐渐增厚甚至呈现瘤样增生，颜色逐渐加深，据报道约有65%的患者会出现病灶增厚和结节，且出现上述症状的年龄段为20～39岁，并终生持续发展[16]。

临床上根据病变颜色和增生情况，将其分为3型——粉红型、紫红型、增生型，本研究5例患者临床症状比较典型，均属于增生型。有学者认为微静脉畸形局部增生主要与雷帕霉素靶蛋白信号通路被过度激活相关，p-p70S6、p-eIF4EBP1高表达促使下游通路改变，进而导致血管不断扩张畸形，管壁增厚，扩张的血管通透性增加，使病灶内营养物质增多，继之造成病灶增厚[17]。

临床上增生型微静脉畸形常需与血管肉瘤相鉴别，后者多发生在老年人头颈部，临床表现多为紫红色肿块，可有卫星结节，生长速度快，皮肤变薄，表面皮肤可破溃。病理上可见呈浸润生长的、不规则扩张的血管腔隙，内皮细胞核大深染并向腔内突出，或内皮细胞增生且具有异型性[18]。

此外，微静脉畸形在临床上可单独发生，亦可作为综合征与其他病变同时发生，诊断需与Sturge-Weber综合征及Klippel-Trenaunay综合征等相鉴别。Sturge-Weber综合征是指微静脉畸形发生在三叉神经分布区域，同时合并同侧脑、脑膜或者眼部血管畸形的皮肤神经综合征[19]；而当微静脉畸形合并静脉曲张、肢体肥大时则称为Klippel-Trenaunay综合征[20]。本组5例微静脉畸形均为孤立性病变，不属于上述综合征。

4.3　治疗

微静脉畸形的传统治疗方法有脉冲染料激光、光动力治疗、冷冻[21]、硬化治疗、手术切除等[22]。但对于肥厚型出血性微静脉畸形，激光、冷冻等治疗措施往往疗效不佳，手术切除虽可彻底清除病灶，但是由于唇部结构精细，不但有说话、进食、吮吸等功能，还有表情功能，所以不仅要考虑功能，还要兼顾美观。尤其对于本研究患者，若首次直接切除，可能会引起大量出血，有一定风险。所以对本例入院时即出现下唇病灶反复糜烂出血的患者，采用了硬化微创治疗。

硬化微创治疗的原理是通过硬化剂注射栓塞病灶深部的畸形血管，封闭管腔，减少其自发性破溃出血的风险[23]，若后期联合手术切除，即可彻底清除病灶。目前常用的硬化剂有无水乙醇、平阳霉素、博莱霉素、聚桂醇等[24]。

无水乙醇属于强效硬化剂，由于其强烈的侵蚀性作用，易产生较多难以控制的并发症，如疼痛、组织坏死、中枢神经抑制、肺动脉高压等[25]，且注射剂量越大，并发症发生率越高。

平阳霉素作用较温和，但针对一些高流速的脉管畸形，药物瘤内存留时间不足，有效作用时间短，疗效欠佳，且大剂量使用时可能会引起过敏及肺纤维化等[26]。

聚多卡醇作为一种新型泡沫硬化剂，极少引发过敏反应，且疗效显著，已成为国内外最常用的泡沫硬化剂。因泡沫性质不易被血液稀释和被血流冲走，克服了传统硬化剂注射量大、并发症多的缺点，且较传统止血方法微创、作用迅速。本研究应用聚多卡醇泡沫硬化剂经皮注射治疗，不但取得较好的治疗效果，也获得了良好的止血效果，且未见明显严重并发症。

聚多卡醇是一种膜活性化合物，其止血机制是通过与表皮细胞表面的细胞膜相互作用，损伤血管内皮细胞，引发化学性炎症反应，促进血栓形成，血管壁纤维化，进而阻塞血管腔，达到止血的效果，从而消除和预防脉管畸形[27]。聚多卡醇是目前国内外应用最广泛的泡沫硬化剂，它具有良好的起泡性能，相对于同等剂量的其他液体硬化

剂，聚多卡醇具有治疗范围大、过敏反应发生率低、不良反应少、局部微麻作用等优点，不会对机体产生强烈刺激。因此，临床上接受度高，易于推广应用。研究表明，聚多卡醇不但用于不同类型的脉管畸形的治疗[28-29]，还可用于内镜下胃-食管静脉曲张出血急诊止血[30]、下肢静脉曲张[31]、痔疮的止血及硬化治疗[32]。本研究同样使用聚多卡醇进行唇颊部巨大微静脉畸形的硬化及止血治疗，皆达到较好的治疗效果，与其他学者研究结果一致。

综上所述，聚多卡醇治疗成人巨大唇颊部微静脉畸形安全、有效，且副反应少，并对自发性出血的微静脉畸形患者有一定的止血作用，可作为治疗口腔颌面部脉管畸形出血的止血方法之一。但是由于本研究病例数较少，有待收集更多病例加以分析，且远期疗效有待进一步观察。

【Author contributions】 Li FF peformed the research, analyzed the data, and wrote the article. Meng J, Zhuang QW revised the article. All authors read and approved the final manuscript as submitted.

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