

- treatment of ROP: a multi-disciplinary perspective [J]. *Prog Retin Eye Res*, 2018, 62: 77-119. DOI: 10. 1016/j. preteyeres. 2017. 09. 002.
- [28] Cao M, Zhang L, Wang JH, et al. Identifying circRNA-associated-ceRNA networks in retinal neovascularization in mice [J]. *Int J Med Sci*, 2019, 16(10): 1356-1365. DOI: 10. 7150/ijms. 35149.
- [29] Shan K, Liu C, Liu BH, et al. Circular noncoding RNA HIPK3 mediates retinal vascular dysfunction in diabetes mellitus [J]. *Circulation*, 2017, 136(17): 1629-1642. DOI: 10. 1161/CIRCULATIONAHA. 117. 029004.
- [30] Zhang D, Yi Z, Fu Y. Downregulation of miR-20b-5p facilitates *Mycobacterium tuberculosis* survival in RAW 264. 7 macrophages via attenuating the cell apoptosis by Mcl-1 upregulation [J]. *J Cell Biochem*, 2019, 120(4): 5889-5896. DOI: 10. 1002/jcb. 27874.
- [31] Zhang SJ, Chen X, Li CP, et al. Identification and characterization of circular RNAs as a new class of putative biomarkers in diabetes retinopathy [J]. *Invest Ophthalmol Vis Sci*, 2017, 58(14): 6500-6509. DOI: 10. 1167/iovs. 17-22698.
- [32] Liu C, Yao MD, Li CP, et al. Silencing of circular RNA-ZNF609 ameliorates vascular endothelial dysfunction [J]. *Theranostics*, 2017, 7(11): 2863-2877. DOI: 10. 7150/thno. 19353.
- [33] Wang JJ, Liu C, Shan K, et al. Circular RNA-ZNF609 regulates retinal neurodegeneration by acting as miR-615 sponge [J]. *Theranostics*, 2018, 8(12): 3408-3415. DOI: 10. 7150/thno. 25156.
- [34] Wang JJ, Shan K, Liu BH, et al. Targeting circular RNA-ZRANB1 for therapeutic intervention in retinal neurodegeneration [J/OL]. *Cell Death Dis*, 2018, 9(5): 540 [2022-05-19]. <http://www. ncbi. nlm. nih. gov/pubmed/29748605>. DOI: 10. 1038/s41419-018-0597-7.
- [35] Charteris DG, Sethi CS, Lewis GP, et al. Proliferative vitreoretinopathy-developments in adjunctive treatment and retinal pathology [J]. *Eye (Lond)*, 2002, 16(4): 369-374. DOI: 10. 1038/sj. eye. 6700194.
- [36] Yao J, Hu LL, Li XM, et al. Comprehensive circular RNA profiling of proliferative vitreoretinopathy and its clinical significance [J]. *Biomed Pharmacother*, 2019, 111: 548-554. DOI: 10. 1016/j. biopha. 2018. 12. 044.
- [37] Meganck RM, Borchardt EK, Castellanos Rivera RM, et al. Tissue-dependent expression and translation of circular RNAs with recombinant AAV vectors *in vivo* [J]. *Mol Ther Nucleic Acids*, 2018, 13: 89-98. DOI: 10. 1016/j. omt. 2018. 08. 008.
- [38] 吴宛玲, 李爽. 环状 RNA 在肿瘤疾病中的研究进展 [J]. *中国肿瘤临床*, 2018, 45(5): 251-255. DOI: 10. 3969/j. issn. 1000-8179. 2018. 05. 082.
- Wu WL, Li S. Progress in research on the role of circular RNAs in tumors [J]. *Chin J Clin Oncol*, 2018, 45(5): 251-255. DOI: 10. 3969/j. issn. 1000-8179. 2018. 05. 082.
- [39] Klingeborn M, Dismuke WM, Bowes Rickman C, et al. Roles of exosomes in the normal and diseased eye [J]. *Prog Retin Eye Res*, 2017, 59: 158-177. DOI: 10. 1016/j. preteyeres. 2017. 04. 004.

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· 病例报告 ·

神经营养性角膜炎患者感染性角膜溃疡诊疗一例

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患者,男,41岁,因左眼视物不清2年伴耳鸣1个月余,于2021年4月19日至南京中医药大学附属南京中医院眼科就诊,眼科检查:左眼视力0.08,矫正视力0.8;双眼眼压均为18 mmHg(1 mmHg=0.133 kPa);左眼瞳孔正圆,瞳孔直径约5 mm,直接对光反射迟钝;右眼瞳孔正圆,瞳孔直径约3 mm,直接对光反射灵敏,余眼前节及眼底未见明显异常;双眼视野检查示可见生理盲点,全视野范围内各部位光敏感度正常。请神

经外科医师会诊,头颅CT检查后诊断为头颈部腺样囊性癌,行肿瘤次全切除术及放射治疗。术后6个月,患者因左眼视物不清伴分泌物增多及左耳胀痛2周,再次就诊。眼科检查:左眼视力指数20 cm;眼压19 mmHg,球结膜中度充血,角膜中央可见4 mm×4 mm溃疡,荧光素钠染色阳性,前房可见积脓,眼后段结构窥不清(图1)。激光扫描角膜共焦显微镜示病灶内大量炎性细胞浸润(图2)。结膜囊分泌物培养未见细菌及真菌

生长。角膜知觉检查显示左眼角膜知觉反射迟钝。耳鼻喉科医师会诊诊断为左中耳炎。临床诊断为左眼感染性角膜溃疡,左眼神经营养性角膜炎,左中耳炎。给予氧氟沙星眼膏(日本参天制药株式会社)1次/2h点眼,头孢曲松钠3.0g 1次/d静脉滴注。治疗5d后,患者眼部及耳部症状明显减轻,左眼角膜溃疡范围缩小至3mm×3mm(图3A、B),前房积脓消失。停用全身抗感染药物,加用小牛血去蛋白提取物滴眼液(沈阳兴齐眼药股份有限公司)1次/2h点眼并佩戴角膜绷带镜。持续治疗5d后检查发现左眼角膜上皮缺损持续不愈,予利多卡因联合罗哌卡因1:1约0.2ml球结膜下浸润麻醉后行左眼角膜羊膜覆盖术。术中羊膜覆盖全角膜,于角膜缘进行间断缝合。术后1d,羊膜贴敷紧密,角膜缘无渗出及分泌物(图4A)。术后1周羊膜贴敷紧密、无溶解,拆除缝线(图4B)。术后2周羊膜仍覆盖角膜,未见溶解迹象(图4C)。术后1个月检查发现溃疡病灶愈合合并呈片状云翳,球结膜中度充血,角膜缘上方可见一新发1.5mm×1.5mm角膜溃疡灶,前房下方积脓(图4D);压迫泪囊区可见大量脓性分泌物自下泪小点溢出,泪囊区皮肤无红肿和压痛;结膜囊分泌物培养结果为金黄色葡萄球菌。综合诊断为左眼泪囊炎、左眼感染性角膜溃疡、左眼神经营养性角膜炎、左中耳炎。给予全身头孢曲松钠3.0g 1次/d静脉滴注,局部氧氟沙星眼膏、小牛血去蛋白提取物滴眼液1次/2h点眼抗感染治疗,治疗5d后行左泪囊鼻腔吻合术;术后随访1年角膜溃疡已形成角膜云翳(图5),泪道冲洗通畅。

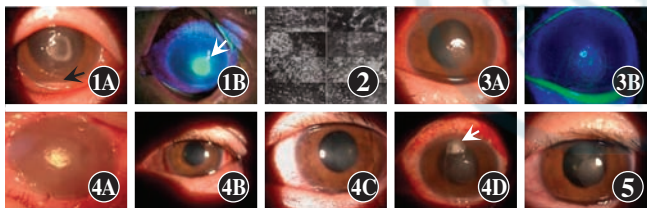


图1 治疗前患眼前节照相检查 A:眼前节照相示左眼角膜中央一约4mm×4mm溃疡灶下方可见前房积脓(黑色箭头) B:角膜荧光素钠染色呈阳性(白色箭头) 图2 治疗前患眼角膜激光扫描共焦显微镜检查 病灶内见大量炎性细胞浸润,病灶区及内皮面见大量炎性反光物 图3 治疗5d后患眼前节照相 A:眼前节照相示左眼角膜溃疡范围缩小至3mm×3mm B:角膜荧光素钠染色示中央缺损区着色 图4 羊膜覆盖术后眼前节照相 A:术后1d,羊膜贴敷紧密 B:术后1周,羊膜仍覆盖角膜缘 C:术后2周,羊膜仍覆盖角膜,未见溶解 D:术后1个月,溃疡病灶愈合合并呈片状云翳,云翳上方可见一新发1.5mm×1.5mm角膜溃疡灶(白色箭头) 图5 治疗后1年眼前节照相 左眼角膜上方可见两处角膜云翳

讨论 本例患者为头颈部腺样囊性癌手术中三叉神经和角膜神经损伤导致的继发性神经营养性角膜炎,同时因有中耳炎和慢性泪囊炎反复发作,最终造成反复角膜溃疡。神经营养性角膜炎的治疗应根据角膜上皮缺损范围及程度采取不同的方案^[1-2]。本例患者在感染性角膜溃疡得到有效控制的前提下应用角膜营养药物及佩戴角膜绷带镜治疗。但由于角膜神经营

养作用丧失,角膜上皮缺损仍迁延不愈,为防止角膜溃疡穿孔,对患眼行全角膜湿态羊膜覆盖术。羊膜含有许多生长因子^[3],具有抗炎、抗瘢痕和抗血管生成的生物特性^[4-5],广泛用于角膜病变和多种眼表相关病变的治疗^[6]。但新鲜羊膜存在取材受限、易受污染等问题,限制了其在临床上的使用^[7]。湿态羊膜具有与新鲜羊膜相同的生物活性,且有效保存了多种营养因子和抗炎因子,防止角膜顽固性溃疡的进展,促进角膜上皮缺损的愈合^[8-9]。本例患者全角膜湿态羊膜覆盖术后2周羊膜无溶解迹象,透明度高,且在1年的随访中角膜溃疡未再发作,表明湿态羊膜可有效治疗神经营养性角膜炎。

本例患者的诊疗过程中的教训也值得注意,该患者第一次出现角膜溃疡时我们仅关注了角膜病变区的检查,忽视了泪囊的检查,导致慢性泪囊炎引起的第二次感染性角膜溃疡。因此在眼部感染性疾病的诊治过程中要明确感染源并及时处理,以免导致病情恶化。

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参考文献

- [1] Dohlman TH, Singh RB, Dana R. Advances in the medical management of neurotrophic keratitis [J]. *Semin Ophthalmol*, 2021, 36(4): 335-340. DOI: 10.1080/08820538.2021.1900282.
- [2] Dana R, Farid M, Gupta PK, et al. Expert consensus on the identification, diagnosis, and treatment of neurotrophic keratopathy [J/OL]. *BMC Ophthalmol*, 2021, 21(1): 327 [2022-11-20]. <http://www.ncbi.nlm.nih.gov/pubmed/34493256>. DOI: 10.1186/s12886-021-02092-1.
- [3] Jahanafrooz Z, Bakhshandeh B, Behnam Abdollahi S, et al. Human amniotic membrane as a multifunctional biomaterial; recent advances and applications [J]. *J Biomater Appl*, 2023, 37(8): 1341-1354. DOI: 10.1177/08853282221137609.
- [4] Dhall S, Sathyamoorthy M, Kuang JQ, et al. Properties of viable lyopreserved amnion are equivalent to viable cryopreserved amnion with the convenience of ambient storage [J/OL]. *PLoS One*, 2018, 13(10): e0204060 [2022-11-20]. <http://www.ncbi.nlm.nih.gov/pubmed/30278042>. DOI: 10.1371/journal.pone.0204060.
- [5] Walkden A. Amniotic membrane transplantation in ophthalmology: an updated perspective [J]. *Clin Ophthalmol*, 2020, 14: 2057-2072. DOI: 10.2147/OPHT.S208008.
- [6] Nubile M, Dua HS, Lanzini M, et al. *In vivo* analysis of stromal integration of multilayer amniotic membrane transplantation in corneal ulcers [J]. *Am J Ophthalmol*, 2011, 151(5): 809-822. DOI: 10.1016/j.ajo.2010.11.002.
- [7] Jirsova K, Jones G. Amniotic membrane in ophthalmology: properties, preparation, storage and indications for grafting-a review [J]. *Cell Tissue Bank*, 2017, 18(2): 193-204. DOI: 10.1007/s10561-017-9618-5.
- [8] Rodríguez-Ares MT, López-Valladares MJ, Touriño R, et al. Effects of lyophilization on human amniotic membrane [J]. *Acta Ophthalmol*, 2009, 87(4): 396-403. DOI: 10.1111/j.1755-3768.2008.01261.x.
- [9] Russo A, Bonci P, Bonci P. The effects of different preservation processes on the total protein and growth factor content in a new biological product developed from human amniotic membrane [J]. *Cell Tissue Bank*, 2012, 13(2): 353-361. DOI: 10.1007/s10561-011-9261-5.

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