Corneal ulcer following use of tobramycin-dexamethasone eye drops in two patients

Ma Jin, Zhong Yong (Department of Ophthalmology, Peking Union Medical College Hospital, Beijing, 100073, China)

ABSTRACT Two patients developed corneal ulcer following use of tobramycin-dexamethasone eye drops.

Patient 1, a 54-year-old man with neovascular glaucoma and central retinal vein occlusion in his right eye, underwent glaucoma valve in plantatium. Postoperatively, one drop of tobramycin-dexamethasone eye drops as instilled into his operated eye every one hour. On day 7, superficial oval ulcer with grey edema along its edge occurred in the temporal part of corneal limbus in his right eye. The ulcer depth was one-third of corneal thickness. Swab cultures were negative for bacteria and fungi. Corneal ulcer was considered to be tobramycin-dexamethasone eye drops-induced. The eye drops were discontinued immediately, and recombinant bovine basic fibroblast growth factor eye drops, sodium carboxymethylcellulose eye drops, vitamin C tablets, and vitamin B1 tablets were given. Two days later, his corneal ulcer was complete healing.

Patient 2, a 28-year-old woman with traumatic cataract and subluxation of lens in her left eye, underwent cataract extract and intraocular lens implantation in her left eye. After surgery, one drop of tobramycin-dexamethasone eye drops was instilled into her operated eye every one hour. On day 3, a belt-like ulcer with grey oedema along its edge occurred in temporal part of corneal limbus in her left eye. The ulcer depth was two-third of corneal thickness. Swab cultures were negative for bacteria and fungi. Tobramycin-dexamethasone eye drops were stopped as the drops were suspected as a causative factor for the corneal ulcer. Recombinant bovine basic fibroblast growth factor eye drops, sodium carboxymethylcellulose eye drops, vitamin C tablet, and vitamin B1 tablets were administrated. After 3 days, her corneal ulcer was complete healing.

KEY WORDS tobramycin-dexamethasone eye drops; corneal ulcer; adverse reactions
例2女，28岁，以“左眼外伤性白内障，左眼晶状体半脱位”为诊断入院。入院后查：远视力：右1.5，左指数/20 cm，眼压：右12 mmHg，左13 mmHg，左角膜后可见色素性KP (+)，上方前房浅，房闪（-），左上方虹膜缺损，瞳孔固定，晶状体白色混浊并向前，上方移位，眼底窥不清。入院后于第2天在局麻下行左眼超声乳化白内障摘除+人工晶状体植入术，手术顺利。术后给予泼尼松50 mg/d，一次口服，妥布霉素—地塞米松滴眼液1滴/次，1次/日。术后第3天患者诉视物闭光，不适。检查：视力右0.7（小孔），切口愈合好，左眼睑及角膜缘可见条状裂伤（见图2），深达2/3角膜厚度。溃疡边缘呈灰色水肿，基底透明，相应基质轻度水肿，KP（-），房闪（-），人工晶体在位透明。经角膜刮片检查及细菌、真菌培养均为阴性。考虑角膜溃疡与局部应用妥布霉素—地塞米松滴眼液有关，立即停用妥布霉素—地塞米松滴眼液，给予重组牛碱性成纤维细胞生长因子（融合蛋白）滴眼液，凝甲基纤维素滴眼液每日2次，维生素A、维生素B1、2片口服。停药后3天角膜溃疡完全愈合，局部改用0.1%氟米龙眼滴眼液，继续治疗12d停药。

图1 例1患者角膜溃疡
图2 例2患者角膜溃疡
Fig1 Corneal ulcer in patient 1
Fig2 Corneal ulcer in patient 2

讨论 例2患者均于左眼手术后局部频繁妥布霉素—地塞米松滴眼液使用抗炎、消炎治疗，用药3～7d后出现角膜溃疡，微生物检查结果均为正常，用其他原因引发的角膜溃疡难以解释；例2患者均无全身免疫性疾病，且用药时间不长，排除真菌感染之可能，溃疡部位又远离切口，且停药后2～3d，溃疡均自行愈合。考虑角膜溃疡为局部应用妥布霉素—地塞米松滴眼液所致，但2例视力未受影响。0.3%妥布霉素和0.1%地塞米松的局部毒性以及滴眼液内防腐剂的作用可能是导致药源性角膜溃疡发生的原因。药源性角膜病变（drug-induced keratopathy）是指局部及全身用药导致的眼角膜病变，也称为毒性角膜病变（toxic keratopathy）。常因在治疗原发病过程中发生，且不易与原发病相鉴别，诊断带来一定困难，药源性角膜病变轻重程度出现角膜上皮点状糜烂，中度会出现角膜知觉减退，上皮损伤和角膜基质水肿增厚，重度则会出现角膜溃疡，前房积脓，以及内皮细胞损害等。导致药源性角膜病变的局部用药主要有抗生素、抗病毒药、皮质类固醇激素及免疫抑制剂，局部麻醉剂、非甾体类药物及防腐剂等[1]。常用的局部抗菌治疗中氨基糖苷类是最易产生眼部局部病变的抗生素，可导致角膜上皮剥脱，形成角膜溃疡性溃疡。国外邓世雄等报道的15例药源性角膜溃疡中8例（53%）出现角膜溃疡，其中6例为角膜上注射氨基糖苷类抗生素引起[2]。其发病机制可能为药物的直接毒性作用，如药物直接抑制蛋白、核酸合成、破坏细胞膜或细胞间连接、破坏细胞外基质的合成等[2]。这类药物呈现出剂量依赖性细胞毒性作用，其毒性与药物浓度和作用时间正相关[3]。防腐剂（尤其是目前常用的苯扎氯铵）可破坏角膜上皮细胞的紧密连接，使角膜上皮细胞容易脱落，引起角膜上皮细胞变性[3]和结膜纤维化[2]。

药源性角膜溃疡往往在治疗原有眼部疾病时发生，尚无实验室特异性检查指标。因此，目前对药源性角膜溃疡的临床诊断主要根据病史、临床症状、用药史以及微生物学检查来排除感染等方法进行。在临床上，还应该注意其与其它病因引起的角膜炎相鉴别。对药源性角膜病变治疗应遵循3条原则：(1)停止原局部用药；(2)保护角膜，减少机械损伤；(3)促进角膜生长修复。本文2例报道提示，在使用妥布霉素—地塞米松滴眼液时应警惕角膜溃疡的发生。

参考文献

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