

·短篇论著·

儿童嗜酸性粒细胞性膀胱炎 2 例报道并文献复习

宁峰¹ 何军¹ 涂磊¹ 胡建军¹ 陈卫坚² 赵天望¹

【摘要】 目的 探讨儿童嗜酸性粒细胞性膀胱炎的临床表现、病理特点与治疗方法。**方法** 收集 2016 年 1 月至 2017 年 3 月本院收治的 2 例嗜酸性粒细胞性膀胱炎患儿临床资料,并结合文献复习进行分析。**结果** 病例 1,男,6 岁,间断性肉眼血尿,伴尿频、尿急、排尿困难和腹痛,尿沉渣每高倍视野下可见 20~25 个红细胞,户尘螨粉尘螨(D1D2)2 级 IU/mL。病例 2,男,7 岁,尿频、尿急、尿痛,无血尿、排尿困难和耻骨上疼痛,均无过敏史。2 例血常规嗜酸性粒细胞明显增高,骨髓穿刺检查嗜酸性粒细胞均增多,尿培养均阴性,B 超、CT、膀胱逆行造影等影像学检查发现膀胱壁不均匀增厚明显,黏膜弥漫性病变。膀胱镜检查显示膀胱容量变小,未见占位性病变,膀胱底及膀胱颈部黏膜发红,病变区活组织检查病理学提示黏膜水肿,嗜酸性粒细胞大量浸润至固有肌层,及局灶性肌坏死。病例 1 给予抗生素,西地利嗪并辅以 6 周剂量递减的强的松治疗;病例 2 仅给予抗生素,西地利嗪治疗。2 例术后随访 6 个月,排尿异常症状消失,B 超、CT 影像学未见膀胱壁增厚及占位性病变。**结论** 儿童嗜酸性粒细胞性膀胱炎临床少见,易误诊为膀胱非特异性炎症及膀胱占位性病变,膀胱镜检查与病理学检查是诊断的必要步骤,治疗以抗炎、抗过敏及皮质激素非特异性药物保守治疗为主。

【关键词】 膀胱炎;嗜酸性粒细胞;病理学;活组织检查;儿童

Eosinophilic cystitis of children: a report of two cases. Ning Feng¹, He Jun¹, Tu Lei¹, Hu Jianjun¹, Chen Weijian², Zhao Yaowang¹. Hunan Children's Hospital, Changsha 410007, China

【Abstract】 Objective To explore the clinical features, pathological examinations and treatments of eosinophilic cystitis. **Methods** Two male cases of eosinophilic cystitis were reviewed from January 2016 to March 2017. **Results** Case 1, 6-year-old, had intermittent hematuria with urinary frequency, urgency, difficult urination and abdominal pain; Case 2, 7-year-old, complained of urinary frequency, urgency, urine pain, dysuria and pubic bone pain. Neither had any history of allergy. Counts of eosinophils increased obviously. Bone marrow biopsy indicated eosinophil increased, urine culture was negative, urine microscopy examination, 6-year-old boy of every 20 to 25 red blood cells at a high magnification and household dust mites (D1D2) level 2 IU/ml. Ultrasound, computed tomography (CT) and cystography showed that bladder wall became thickened obviously with diffuse mucosal lesions. Microscopic examination indicated bladder capacity decreased and there was no occupying lesion. Mucosal redness was found at bottom and neck of bladder. And biopsy pathology revealed mucosal edema, numerous eosinophils infiltrating through intrinsic muscle layer and focal necrosis. Case 1 received cetirizine hydrochloride supplemented by 6-week decreasing doses of prednisone treatment while case 2 had cetirizine hydrochloride alone. During a postoperative follow-up period of 6 months, abnormal symptoms of micturition disappeared. Neither ultrasound nor CT revealed no wall thickening or occupying lesions. **Conclusion** Eosinophilic cystitis is rare in children. Easily misdiagnosed as nonspecific inflammation and bladder occupying lesions, it is definitely diagnosed by cystoscopy and biopsy pathology. Anti-inflammatory, anti-allergic and corticosteroid hormone nonspecific drugs are routinely offered.

【Key words】 Cystitis; Eosinophil Cells; Pathology; Biopsy; Child

嗜酸性粒细胞性膀胱炎 (eosinophilic cystitis,

EC) 是一种病因不明的膀胱炎症性疾病,1960 年由 Brown^[1,2] 首次报道,该病在儿童中极少发病,迄今文献报道仅 59 例^[3,4]。临床常表现尿血和膀胱壁增厚,常被误诊为肿瘤^[5]。病理表现为嗜酸性粒细胞广泛浸润膀胱壁各层,病因可能是免疫系统调控

DOI: 10.3969/j.issn.1671-6353.2018.05.015

作者单位: 湖南省儿童医院 (湖南省长沙市,410007); 1. 泌尿外科, 2. 病理科

通讯作者: 何军, Email: hjys840808@163.com

障碍,诱导抗原刺激,导致 IgE 介导的嗜酸性粒细胞激活,肥大细胞脱颗粒,进而引起炎症介质释放和膀胱壁损伤^[6]。EC 在成人可表现出多种泌尿系统症状,如尿频、尿急、尿痛、尿血、排尿困难和耻骨上疼痛,儿童也表现相似的症状。治疗方法包括观察,识别过敏原,抗生素、抗组胺药以及类固醇等药物治疗^[7]。对于顽固性血尿,也可采用经尿道膀胱病变切除和膀胱部分切除术^[6]。小儿嗜酸性粒细胞性膀胱炎发病较少,临床表现特异性不强,易与膀胱炎症和肿瘤相混淆。本文收集 2 例嗜酸性粒细胞性膀胱炎病例,对其临床表现、病理特点和相应治疗进行描述,旨在为嗜酸性粒细胞性膀胱炎的诊治提供参考。

临床资料

病例 1:男,6 岁,间断性肉眼血尿,尿频、尿急、尿痛、腹痛,尿频多时达 30 次/d,以夜尿增多为主,且排尿困难、费力,排尿能成线,无它部位出血病史或类似膀胱出血病史,无腰痛、发热等不适,无过敏史,既往于 2013 年 7 月因尿频、B 超提示膀胱壁增厚,考虑“泌尿系感染”予抗感染治疗 3 d,症状完全

消失。此次以“泌尿系感染”抗炎治疗 1 周,症状加重。入院检查:血压正常,血常规:入院第 1 天、第 1 周、第 2 周嗜酸粒细胞比值(EO)分别为 24.6%、33.0%和 29.4%,外周血涂片见正常红血球和正常血色素。尿培养为阴性,尿常规加显微镜检查,每高倍视野下可见 20~25 个红细胞,尿比重为 1.025,尿亚硝酸盐为阴性。肾功能检查正常,补体 C3 为 122 mg/dL。PPD 实验(-),尿 PCR 未检测到腺病毒和结核分枝杆菌,户尘螨粉尘螨(D1D2)2 级 IU/mL。B 超提示膀胱壁增厚明显(图 1),CT 检查显示局部黏膜病变,伴有膀胱右侧和后侧壁增厚(图 2)。膀胱逆行造影显示膀胱容量变小,膀胱壁不规整(图 3)。膀胱镜检查,膀胱容量变小,膀胱底及膀胱颈部黏膜发红,根据上述影像学 and 膀胱镜检查结果,首先考虑膀胱横纹肌肉瘤,经尿道取材活检,组织病理检查提示膀胱黏膜充血水肿,血管和嗜酸性粒细胞浸润至肌层,伴有局灶性肌坏死(图 4~6)。骨髓穿刺检查可见嗜酸性粒细胞增生(图 7)。给予抗感染和西地利嗪治疗,加 6 周强的松剂量递减治疗。1 个月后复查症状消失,影像学检查基本正常(图 8),血液嗜酸性粒细胞 1.19%。继续服用强的松小剂量维持 2 个月,血液嗜酸性粒细胞正常,影像学检查完全正常(图 9)。

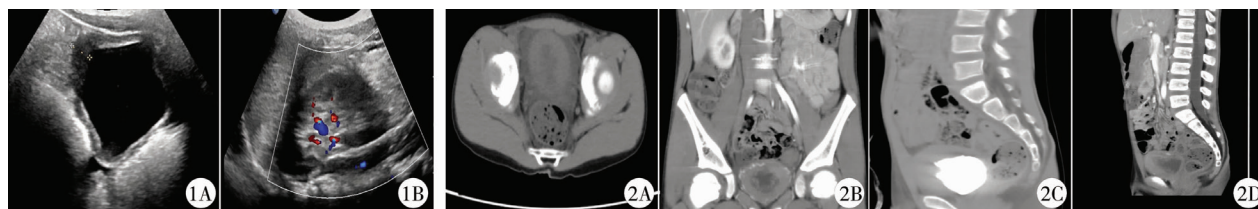


图 1 典型病例超声检查图像。A. 超声显示不规则的膀胱壁增厚达 1 cm,类似于肿瘤。B. 多普勒彩超见膀胱壁内血流丰富。图 2 典型病例 CT 图像。A. 膀胱壁弥漫性增厚,边缘毛糙。B. 膀胱腔内体积较小,增厚膀胱壁密度不均匀。C. 对比增强 CT 显示膀胱壁血供丰富,呈明显不均匀强化。D. 膀胱内壁尚光整,未见明显充盈缺损。

Fig. 1 Ultrasonography of bladder wall. A. Ultrasound showed irregular thickening of bladder wall. B. Color Doppler ultrasound showed abundant blood flow in bladder wall. **Fig. 2** Computed tomography. A. Bladder wall showed diffuse thickening and rough edges; B. The volume of bladder cavity was small and the density of thickened bladder wall was uneven; C. Contrast enhanced computed tomography showed abundant blood flow in bladder wall and uneven enhancement; D. Bladder wall was smooth and no obvious filling or defect was observed.

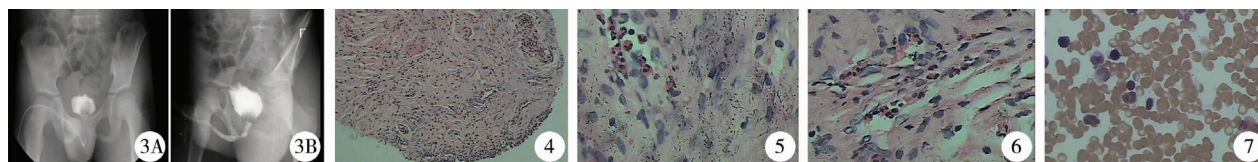


图 3 膀胱逆行造影图像。A. 膀胱容量减小,膀胱壁不规整。B. 膀胱壁不均匀增厚明显,粘膜弥漫性病变。图 4 膀胱镜检查。黏膜被覆少量移行上皮,上皮纤维组织增生,可见少量平滑肌组织,伴有炎症细胞浸润,以嗜酸性粒细胞为主,散在淋巴细胞和浆细胞(H&E ×100)。图 5 嗜酸性粒细胞浸润到右后肌肉束(H&E ×400)。图 6 上皮纤维间质中嗜酸性粒细胞浸润(HE ×400)。图 7 骨髓粒系增生活跃,嗜酸性粒细胞比值增加,各阶段形态无明显异常。

Fig. 3 Retrograde angiography of bladder. (A) Front view; (B) Left view. Bladder volume decreased. Bladder wall became irregular and thickened and there were diffusive mucosal lesions. **Fig. 4** Hematoxylin & eosin (H&E) staining of bladder wall tissues (magnification, ×100). A small amount of transitional epithelium was found on mucosa. Subepithelial fibrous hyperplasia and inflammatory cell infiltration. Eosinophilic granulocytes were predominant with a scattering of plasma cells and lymphocytes. **Fig. 5** H&E staining of bladder wall tissues (magnification, ×400). Eosinophils infiltrated into right posterior muscular bundle. **Fig. 6** Infiltration of eosinophils was present in subepithelial fibrous stroma. **Fig. 7** Bone marrow biopsy. Myeloid granulocytic hyperplasia was active, eosinophil ratio increased and each stage had no obvious abnormality.

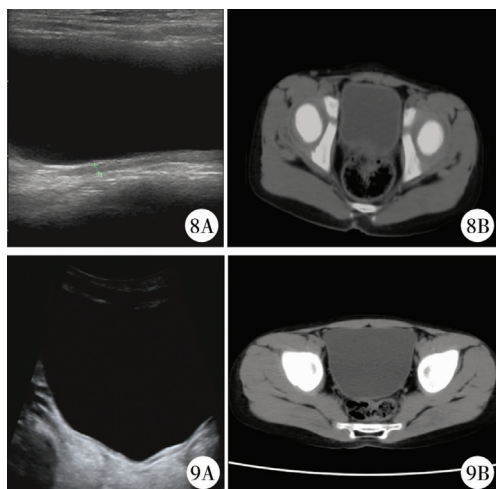


图8 A和B分别为治疗后1个月B超和CT复查图像。

图9 A和B分别为治疗后3个月B超和CT复查图像。

Fig.8 Follow-ups at 1 month post-treatment. Fig.9 Follow-ups at 3 months post-treatment.

病例2:男,7岁,急性发作排尿困难、耻骨上疼痛,尿频、尿急、急迫性尿失禁和尿痛。既往无特殊病史。无过敏史。发育正常。血压正常。入院第1天、第1周、第2周嗜酸性粒细胞比值(EO)分别为7.9%、5.6%和0.09%,外周血涂片见正常红细胞和正常血色素。尿培养为阴性,尿常规和显微观察无异常。尿比重为1.030,尿亚硝酸盐为阴性。肾功能检查正常。补体C3为109 mg/dL。PPD实验(-),尿PCR未检测到腺病毒和结核分枝杆菌,过敏源筛查未见明显过敏源。CT和膀胱逆行造影等放射性检查显示局部黏膜病变,伴有膀胱两侧和后侧壁增厚。膀胱镜检查显示膀胱容量变小,膀胱底及膀胱颈部黏膜发红,尿道取材活检显示病变区血管和嗜酸性粒细胞浸润至肌层,伴有局灶性肌坏死,考虑嗜酸性粒细胞性膀胱炎,骨髓穿刺检查未见嗜酸性粒细胞增生。给予抗感染和西地利嗪治疗,2个月后复查症状消失,影像学检查正常,血液嗜酸性粒细胞正常。

讨论

嗜酸性粒细胞性膀胱炎临床罕见,尤其儿童,病因不明。成人男性发病明显多于女性,与成人情况一样,EC多见于男童,儿童平均发病年龄为6岁^[8,9]。本组2例分别为6岁和7岁男童,与相关报道一致。EC的确切病因尚不明确,有研究提出过敏反应是其病因,过敏原包括食物、尘螨、花粉、安全套抗原、碘或麻醉药膏。哮喘和乳糜泻也与EC有关^[6]。本组2例中1例户尘螨粉尘螨过敏,另1例

未发现特定的过敏原。发病机制涉及IgE介导的嗜酸性粒细胞的激活,与随后的肥大细胞脱颗粒和肌肉损伤^[6]。患者表现出一系列泌尿系统症状如尿频、尿血、耻骨上疼痛、排尿困难、日间和夜间遗尿等,儿童患者可出现明显的耻骨上肿块^[10]。本组2例临床表现和嗜酸性膀胱炎契合,只是EC的临床表现形式多样,容易和非特异性膀胱炎相混淆。

出现耻骨上肿块的患儿还需要和膀胱恶性肿瘤鉴别。本组2例嗜酸性粒细胞计数均明显增高,骨髓穿刺检查嗜酸性粒细胞增多。许多EC患者都会出现外周血嗜酸性粒细胞增多,但不至于到达嗜酸性粒细胞增多综合征的水平。其中1例在住院期间检测血常规嗜酸粒细胞不断下降,症状逐渐好转,仅给予西地利嗪治疗而并没有给予类固醇治疗。提示嗜酸性膀胱炎也可能存在自愈的趋势^[11]。我们病例中6岁患儿3年前有类似症状,B超提示膀胱壁增厚,抗感染治疗3d,症状完全消失,且该患儿有过敏原阳性,我们有理由相信患儿的起病和过敏原有关,随着炎症介质的清除,症状可以消失^[3]。EC患者会出现尿培养阳性^[4],我们2例患儿的尿培养结果为阴性。尿沉渣中很少被发现嗜酸性粒细胞,嗜酸性粒细胞会迅速降解或很少从黏膜脱落^[11]。EC部分患者有尿血症状^[12,13],影像学检查膀胱壁增厚,类似肿块浸润,提示肿瘤;膀胱镜检查结果通常提示膀胱横纹肌肉瘤^[14]。强烈的炎症性改变包括膀胱壁血管充血、水肿,可能会产生堆积的赘生物,类似于膀胱横纹肌肉瘤^[14,15]。EC通常膀胱肌肉受累,必须获得足够深的活组织切片检查,否则可能遗漏。由于这种疾病在儿童罕见,目前尚没有理想的治疗和随访指南。治疗多是经验性治疗^[16]。一线治疗方法通常包括去除任何可疑的过敏原,其次是抗组胺药和皮质类固醇。有研究表明,皮质类固醇因其抗炎作用,可以加速症状的缓解和稳定溶酶体膜^[17]。对难治性病例,可口服环孢素A治疗8个月^[18],对外周血嗜酸性细胞增多的患儿可加用孟鲁斯特钠,研究者还尝试一周两次膀胱内DMSO灌注(50 mL/50%,持续1 h)治疗^[19]。小儿嗜酸性膀胱炎通常是良性、自限性的,不过仍有可能导致膀胱纤维化继发尿路梗阻。诊断和治疗取决于临床怀疑和组织病理学检测。

儿童EC非常像肿瘤,有其特有的表现,是一种罕见疾病,当儿童出现泌尿系统症状及膀胱壁增厚时,应予以警惕。膀胱组织活检、病理组织学评估是诊断的关键,也有助于选择治疗方案。

参考文献

- 1 Verhagen PC, Nikkels PG, De Jong TP. Eosinophilic cystitis [J]. Arch Dis Child, 2001, 84(4): 344-346. DOI: 10. 1136/adc. 84. 4. 344.
- 2 Ahmed Saadi, Abderrazak Bouzouita, Mohamed Cherif. Le léiomyome vésical: À propos de 5 cas [J]. Can Urol Assoc J, 2015, 9(7-8): 471-475. DOI: 10. 5489/cuaj. 2837.
- 3 Hongzoo Park. Eosinophilic cystitis with recurrent urinary retention: case report [J]. Res Rep Urol, 2017, 9: 51-53. DOI: 10. 2147/RRU. S129490.
- 4 Runge SB, Høyer S, Winding L. Acroscopic hematuria and a bladder mass: eosinophilic cystitis in a 7-year-old boy [J]. Case Rep Radiol, 2016, 2016: 9346218. DOI: 10. 1155/2016/9346218.
- 5 Özdoğan EB, Arslansoyu Çamlar S, Bilen S, et al. An unusual cause of terminal hematuria in a child: Eosinophilic cystitis [J]. Can Urol Assoc J, 2014, 8(11-12): 867-871. DOI: 10. 5489/cuaj. 2173.
- 6 Ozcan Kilic, Murat Akand, Murat Gul. Eosinophilic cystitis: a rare cause of nocturnal enuresis in children [J]. Iran Red Crescent Med J, 2016, 18(6): 24562. DOI: 10. 5812/ircmj. 24562.
- 7 Mosholt KS, Dahl C, Azawi NH. Eosinophilic cystitis: three cases and a review over 10 years [J]. BMJ Case Rep, 2014, 2014: bcr2014205708. DOI: 10. 1136/bcr-2014-205708.
- 8 Santosh Kumar, Varun Sharma, Raguram Ganesamoni. Eosinophilic cystitis mimicking tuberculosis: An analysis of five cases with review of literature [J]. Urol Ann, 2013, 5(1): 50-52. DOI: 10. 4103/0974-7796. 106969.
- 9 Elsa Bey, Youssef Teklali, Pierre-Yves Rabattu. Case: eosinophilic cystitis presenting as a bladder mass in an 11-year-old girl [J]. Can Urol Assoc J, 2017, 11(11): 446-448. DOI: 10. 5489/cuaj. 4513.
- 10 Manimaran D, Karthikeyan TM, Sreenivasulu M. Eosinophilic cystitis mimicking bladder tumour: a rare case report [J]. J Clin Diagn Res, 2013, 7(10): 2282-2283. DOI: 10. 7860/JCDR/2013/6018. 3496.
- 11 Jiang P, Wang CJ, Jin BY. Eosinophilic cystitis in a patient with hypereosinophila syndrome: a case report [J]. Exp Ther Med, 2014, 8(1): 49-51. DOI: 10. 3892/etm. 2014. 1706.
- 12 Daniel Chia. Eosinophilic cystitis and haematuria: Case report of a rare disease and common presentation [J]. Int J Surg Case Rep, 2016, 24: 43-45. DOI: 10. 1016/j. ijscr. 2016. 04. 055.
- 13 Venkatesh KS, Bhat S. Eosinophilic cystitis: a rare cause of hematuria in children [J]. Case Rep Nephrol, 2012, 2012: 710230. DOI: 10. 1155/2012/710230.
- 14 Gang Li, Bing Cai, Hualin Song, et al. Clinical and radiological character of eosinophilic cystitis [J]. Int J Clin Exp Med, 2015, 8(1): 533-539.
- 15 Han SG, Chen Y, Qian ZH, et al. Eosinophilic gastroenteritis associated with eosinophilic cystitis: Computed tomography and magnetic resonance imaging findings [J]. World J Gastroenterol, 2015, 21(10): 3139-3145. DOI: 10. 3748/wjg. v21. i10. 3139.
- 16 Kojima K, Maeda J, Mikami S, et al. Eosinophilic cystitis presented as a manifestation of hypereosinophilic syndrome: a case report and review of the literature [J]. Nephron Extra, 2013, 3(1): 30-35. DOI: 10. 1159/00034 6713.
- 17 RJ Popert, JW Ramsay, RA Owen. Eosinophilic cystitis mimicking invasive bladder tumour: discussion paper [J]. J R Soc Med, 1990, 83(12): 776-778.
- 18 Sohaib Aleem, Bharat Kumar, Mary Beth Fasano. Successful use of cyclosporine as treatment for eosinophilic cystitis: a case report [J]. World Allergy Organ J, 2016, 9: 22. DOI: 10. 1186/s40413-016-0113-4.
- 19 Zaman SR, Vermeulen TL, Parry J. Eosinophilic cystitis: treatment with intravesical steroids and oral antihistamines [J]. BMJ Case Rep, 2013, 2013: bcr2013009327. DOI: 10. 1136/bcr-2013-009327.

(收稿日期: 2016-10-13)

本文引用格式: 宁峰, 何军, 涂磊, 等. 儿童嗜酸性粒细胞性膀胱炎 2 例报道并文献复习 [J]. 临床小儿外科杂志, 2018, 17(5): 379-382. DOI: 10. 3969/j. issn. 1671-6353. 2018. 05. 015.

Citing this article as: Ning F, Tu L, He J, et al. Eosinophilic cystitis of children: a report of two cases [J]. J Clin Ped Sur, 2018, 17(5): 379-382. DOI: 10. 3969/j. issn. 1671-6353. 2018. 05. 015.