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个案与短篇

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乙胺丁醇诱发抗中性粒细胞胞质抗体相关性急进性肾小球肾炎1例

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[**关键词**] 利福平;抗中性粒细胞胞质抗体;急进性肾小球肾炎
[**中图法分类号**] R692.31 [**文献标志码**] B

抗中性粒细胞胞质抗体(anti-neutrophil cyto-plasmic antibody, ANCA)是一种与中性粒细胞及单核细胞的细胞质中溶酶体酶发生反应的抗体,可引起多种小血管炎,如侵犯肾脏,可导致肾小球肾炎和肾功能不全。近年报道某些药物如丙基硫氧嘧啶、肼苯哒嗪等可诱发小血管炎,而乙胺丁醇诱发ANCA相关性急进性肾小球肾炎(rapidly progressive glomerulonephritis, RPGN)罕见[1]。现将本科发现的1例报告如下。

1 临床资料

患者,男性,68岁。因"咳嗽、咳痰1个月,双下肢水肿伴少尿5 d"入院。1个月前患者受凉后出现咳嗽、咳痰,在当地医院诊断为"肺结核",当时查肾功、尿常规正常,给予抗结核治疗1周后感厌油、恶心;逐渐出现双下肢水肿,尿量减少(约200 mL/d),转入我科诊治。入院查体:体温正常,血压152/83 mmHg,轻度贫血貌,眼睑轻度浮肿,肺部呼吸音粗,肾区无叩痛,双下肢中度凹陷性水肿。实验室检查血常规:白细胞11.48×10^9/L,中性粒细胞80%,血红蛋白92 g/L;肾功:肌酐847.2 μmol/L,尿素14.84 mmol/L;肝功正常;血沉39 mm/h;C反应蛋白16.9 mg/L;尿常规:蛋白(+),红细胞(+++),尿白细胞(+-);免疫指标:MPO(+),PANCA(+),ANCA滴度1:320,抗核抗体阴性;抗"O"阴性;淋巴细胞刺激转化试验:利福平(-),乙胺丁醇(+)。痰培养阴性。肺CT提示:肺部纹理增粗,未见肺部实质性改变。腹部彩超示:双肾测值增大,实质回声增多、增强,动脉阻力指数增高。肾活组织检查(图1):肾小球总数11个,可见4个细胞性新月体和4个纤维细胞性新月体,球袢与囊壁粘连,囊壁增厚;毛细血管袢腔开放差,可见球袢纤维素样坏死。间质局灶纤维化,炎细胞灶性浸润。系膜细胞及基质:轻~中度增生,系膜区增宽,其中可见4~5个系膜细胞。肾小管病变轻~中度(++);可见肾小管萎缩,基膜增厚,灶性分布;上皮细胞颗粒变性,坏死,基膜裸露,管腔扩张,可见细胞堆积及透明管型;肾间质病变轻度(+),间质纤维化25%~50%,呈局灶纤维化,炎细胞灶性浸润,间质动脉管壁增厚。免疫荧光阴性。病理诊断:新月体性肾小球肾炎。根据上述检查结果,诊断为乙胺丁醇诱发ANCA相关性急进性肾炎。在排除"肺结核"诊断后停用抗结核药物,给予静滴甲泼尼龙1 g/d,冲击治疗3 d,逐渐减量至维持量15 mg/d;并予以静注丙种球蛋白[0.4/(kg·d),5 d]封闭ANCA抗体。同时给予血液透析治疗,3次/周。治疗1周后,血常规正常;肾功:肌酐596 μmol/L,尿素16.97 mmol/L,尿量逐渐增多达500~800 mL/d。出院后予以口服泼尼松片15 mg/d,环磷酰胺片50 mg/d,双嘧达莫25 mg,3次/d,维持性血液透析2次/周。2个月后患者痊愈。

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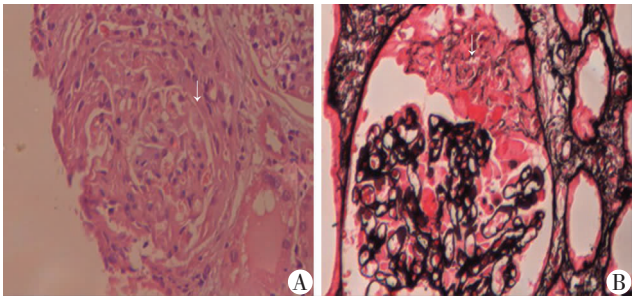
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A:箭头示壁层上皮细胞明显增厚(HE ×200);B:箭头示纤维细胞性新月体(PASM ×200)

图 1 乙胺丁醇诱发 ANCA 相关性 RPGN 患者活检肾脏组织病理学改变

2 讨论

RPGN 以急性肾炎综合征、肾功能急剧恶化及早期出现少尿性急性肾衰竭为临床特征,病理类型为新月体性肾小球肾炎。Couser 分类法将其分为 3 型:Ⅰ型为免疫荧光线条状沉积伴循环抗肾小球基底膜抗体(抗 GBM 抗体型);Ⅱ型为免疫荧光颗粒沉积型(免疫复合物型),此型在我国常见;Ⅲ型为寡免疫复合物型,其中 70% ~80% 患者血清中存在 ANCA,故又称为 ANCA 相关性肾小球肾炎[2]。根据本例患者病史、体征、检查及肾脏活检结果,可诊断为 ANCA 阳性的寡免疫复合物型肾小球肾炎(Ⅲ型)。本例患者既往无肾病史,服用抗结核药期间发病,而既往有抗结核药物诱发急性小管间质性肾炎的报道[1];结合 ANCA 阳性以及肾活检提示新月体肾炎,考虑与抗结核药物有关。为了鉴别何种药物引起发病,本例分别应用利福平和乙胺丁醇刺激培养的患者淋巴细胞,利福平刺激试验显示阴性,而乙胺丁醇刺激试验阳性,与国外报道[1]结果一致,表明乙胺丁醇是引起本例患者 ANCA 相关性 RPGN 的原因。乙胺丁醇引起 ANCA 阳性的新月体性肾小球肾炎的原因仍不清楚。由于乙胺丁醇有诱发视神经血管炎及 Dress 综合征的报道[3-4],提示其可诱发血管及其他多种组织的自身免疫反应,从而参与本病的发病机制。药物诱发的 ANCA 相关性 RPGN 起病急,病情发展迅速,若未及时治疗,90% 以上的患者于 6 个月内死亡或依赖透析生存。由于本例患者发现及时,及时停用乙胺丁醇等抗结核药物,应用免疫抑制治疗,取得了良好的预后。故对临床上应用乙胺丁醇的患者出现急性肾损害症状,应考虑药物诱发 ANCA 相关性 RPGN 可能,及时行血浆 ANCA 测定及肾活检明确诊断,并早期干预。

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