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肾小球毛细血管内皮病合并甲状腺功能减低 1 例病例报道并文献复习 *

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摘要 目的：通过分析我院收治的 1 例肾小球毛细血管内皮病合并甲状腺功能减退患者的诊治过程，结合相关文献，探讨此病的临床特点和诊疗方法。**方法**：报告北京军区总医院收治的 1 例肾小球毛细血管内皮病合并甲状腺功能减退病例的其临床资料及诊疗过程，并复习相关文献，对肾小球毛细血管内皮病合并甲状腺功能减退的病因、临床表现、诊断、治疗及预后进行分析，并总结其诊疗经验。**结果**：1 例肾小球毛细血管内皮病合并甲状腺功能减退患者经综合治疗后病情好转出院，出院后继续接受对症治疗，目前患者恢复良好。**结论**：肾小球毛细血管内皮病的发病率低，合并甲状腺功能减退更少见，其发病原因不明，部分与药物、毒物或者病毒感染有关，多数病例对症治疗后预后较好。

关键词：肾小毛细血管内皮病；甲状腺功能减低；诊断；治疗

中图分类号：R692；R581.2 **文献标识码**：A **文章编号**：1673-6273(2015)05-870-03

A Case Report of Glomerular Capillary Endothelial Disease Complicated by Hypothyroidism and Literature Review*

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ABSTRACT Objective: To study the clinical characteristics and treatment methods of this disease by reporting one case of glomerular capillary endothelial disease patient associated with hypothyroidism and discussing the early diagnosis and treatment of the patient. **Methods**: One case of glomerular capillary endothelial disease associated with hypothyroidism cases was reported. Clinical data and the treatment process were reported. The literatures were reviewed. The etiology, clinical presentation, diagnosis, treatment and prognosis were analyzed, then the treatment experience was summarized. **Results:** The patient of glomerular endothelial disease with hypothyroidism was discharged after combined treatment. She continued to receive symptomatic treatment after discharge and the patient recovered well. **Conclusions:** The incidence of glomerular capillary endothelial disease associated with hypothyroidism is very rare, its etiology is unknown, and some drugs, toxins or viral infection maybe are involved. Major patients prognosis are good after symptomatic treatment.

Key words: Glomerular capillary endothelial disease; Hypothyroidism; Diagnosis; Treatment

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前言

流行病学资料显示，临床中继发性肾脏病的发病率逐年升高，其中各种药物、毒物引发的继发性肾脏病越来越多[1,2]，这些继发性肾脏病中病理类型除间质性肾炎以外，以膜性肾病最常见[3]，而肾小球毛细血管内皮病非常少见。近些年来，甲状腺功能减退的发病率也逐年升高，而且继发性甲状腺功能减低的比例逐渐增大，药物、毒物均是继发原因[4,5]。药物毒物、肾病综合征与甲状腺功能减低似乎有某种联系，此时肾病综合征病理类型多以膜性肾病为主[6]。以肾病综合征为表现的肾小球毛细血管内皮病合并甲状腺功能减低的病例非常罕见，国内外很少报道这样的病例。本文拟报道 1 例以肾病综合征为表现的肾小球毛细血管内皮病合并甲状腺功能减低患者的临床资料，并复习相关文献，旨在总结肾小球毛细血管内皮病合并甲状腺功能减退病因、临床表现、诊断、治疗及预防等要点。

1 临床资料

患者女，42 岁，1 月前无明显诱因开始出现双下肢凹陷性浮肿，伴眼睑浮肿，尿量减少，排尿频次减少，伴间断上腹部隐痛，可耐受，发作无诱因，约 1 次 / 周。在当地医院查尿常规：潜血(++)，尿蛋白(+++)，腹部超声：腹水，脾大，腹部 CT：肝脾增大，考虑为早期肝硬化，胸部 CT：右侧胸腔少量积液，妇科超声：左侧盆腔囊性包块。既往否认高血压、糖尿病、心脏病等慢性病，否认乙肝、丙肝病史，6 年前因子宫肌瘤行子宫切除术。

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入本院肝病科后查体:血压 140/90 mmHg,神情淡漠,皮肤粘膜无出血点及黄染,浅表淋巴结未及,眼睑略浮肿,双肺呼吸音清晰,未闻及干湿性啰音,心界不大,各瓣膜听诊区未闻及病理性杂音,腹部平软,移动性浊音阴性,双下肢轻度浮肿。行肝组织活检,光镜下见肝细胞排列拥挤,细胞水肿,局部脂肪变性,可见肝细胞内淤胆,有点灶状坏死及肝细胞增生,汇管区慢性炎细胞浸润,未见明显纤维组织增生。追问病史:患者间断双下肢水肿 2 年,尿蛋白阳性,曾按 " 肾炎 " 应用激素治疗约半年,水肿好转,尿蛋白持续阳性。后患者转入肾内科,查超声:双下肢静脉未见异常,尿蛋白量 0.70 g/24 h,血白蛋白 23.9 g/L,肾功能正常,ANA、抗双链 DNA、ENA 多肽酶谱、抗中性粒细胞胞浆抗体阴性、抗肾小球基底膜抗体阴性、抗平滑肌抗体阴性、抗心磷脂抗体均阴性,免疫球蛋白正常,补体 C3、C4 正常,类风湿因子阴性,C 反应蛋白 93.9 mg/L,肿瘤标志物阴性,三碘甲状腺氨酸 1.0 nmol/L,游离三碘甲状腺氨酸 1.0 nmol/L,促甲状腺素 8.84 uIU/mL,游离甲状腺素 9.1 pmol/L。行肾组织活检,免疫荧光:4 个肾小球,IgM(+),沿毛细血管壁沉积,IgG、IgA、C3、Clq 均阴性;光镜:镜下可见 2 条肾皮质,共计 18 个肾小球,1 个肾小球缺血硬化,其余小球内皮细胞弥漫增生,毛细血管管腔狭窄;系膜区嗜复红蛋白沉积,肾小管上皮细胞颗粒及空泡样变性,肾间质未见明显病变;小动脉壁增厚,内皮细胞增生,病理诊断:毛细血管内皮细胞病(见图 1)。电镜:可见 4 个肾小球,肾小球系膜细胞和基质轻度增生,节段性内皮细胞增生、肿胀,基底膜内疏松层弥漫增宽,上皮足突节段融合;肾小管上皮溶酶体增多;肾间质无明显病变,诊断符合毛细血管内皮细胞病。追问患者近 3 年从事洗车工作,大量接触清洁剂、雾化剂,留取血尿标本检测出汞、铅、砷、铬、镉、铊元素,但是均在正常范围内。给予扩容、利尿、抗凝、降低蛋白尿等对症治疗,补充左甲状腺素钠,临床症状缓解明显。出院后随访病情稳定。

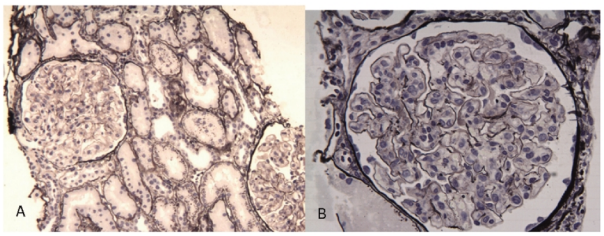

图 1 肾组织病理 A:HE× 200;B:PASM× 400

Fig.1 Renal pathology A:HE× 200;B:PASM× 400

2 文献资料分析

经中国医院知识仓库 CHKD 期刊文库及 PubMed 检索,目前国内尚未报道肾小球毛细血管内皮病合并甲状腺功能减低的病例文献,国外报道了 2 例[7,8],均为女性,年龄分别为 69 岁、24 岁,临床诊断为肾病综合征合并甲状腺功能减退,肾脏病理类型为肾小球毛细血管内皮病。

3 讨论

本例患者临床表现为肢体浮肿,实验室检查提示低蛋白血症、高脂血症,虽然尿蛋白定量不足 3.5 g/24 h,但是随着病情发展或者变化临床诊断肾病综合征的可能性极大[9]。临床表现及实验室检查提示患者呈多系统、多器官损伤,排除了系统性红斑狼疮、类风湿性关节炎、干燥综合征、自身免疫性肝炎、乙型肝炎病毒感染、糖尿病等常见继发肾脏病病的可能。根据实验室检查可以诊断甲状腺功能减低,临床中甲状腺功能减低与肾病综合征可以互为因果[10]。

根据以往文献报道,此类肾病综合征不论原发还是继发,病理表现均为膜性肾病(不典型膜性肾病及Ⅰ、Ⅱ期膜性肾病多见)[11-13]。本病例肾活检病理类型为毛细血管内皮细胞病,极为罕见,提示本病例的肾病综合征与甲状腺功能减低另有诱因。毛细血管内皮细胞病病理学特点是:免疫荧光常为阴性;光镜下可见肾小球毛细血管内皮细胞弥漫增生和肿胀,基底膜弥漫增厚,可呈分层状;电镜是诊断的关键,内皮细胞增生、肿胀,基底膜内疏松层增宽是其最大特点[14]。上述内皮细胞表现常见于血栓性微血管病,还有表现为内皮细胞病的 Castleman 病的报道[15],但均有特异的病因和伴随的其他病变。

该病的病因尚不清楚,各种原因造成毛细血管内皮细胞损伤,进而出现内皮细胞增生和变性的病变。复习相关国内外文献,部分肾小球毛细血管内皮细胞病与多种病毒感染、接触毒物药物等相关[16,17]。追问患者近 3 年从事洗车工作,大量接触清洁剂、雾化剂,虽然留取血尿标本检测出汞、铅、砷、铬、镉、铊等元素均在正常范围内,但是本病无直接的病毒感染证据,根据临床表现、病史,因此不能排除接触毒物后诱发此病的可能。

毛细血管内皮细胞病在各年龄组均可发病,无性别差异,临床以急性肾功能损伤多见,少部分以肾病综合征为表现,也可表现为少量蛋白尿和血尿,常呈现多器官的损伤,尤以肝和消化道损伤多见,在肾脏损伤的同时可出现肝脾肿胀、消化道功能异常,乃至腹腔积液[18-20],本病例符合上述特点。

该病多数预后较好,有自限性,有报道该病对类固醇及细胞毒药物反应较好。临床中导致甲状腺减低原因很多,其中病毒感染、接触毒物药物也是甲状腺功能减低的一类原因[21],根据临床表现、病史,不能排除接触毒物后诱发此病的可能。综合分析本病例特点,同时结合复习相关文献,考虑患者由于职业原因长期接触毒物,同时诱发了以肾病综合征为表现的肾小球毛细血管内皮病合并甲状腺功能减低。

4 小结

本文结合 1 例病例报告,系统性回顾总结了近年来国内外有关报道,尤其是复习了肾小球毛细血管内皮病合并甲状腺功能减低的文献,发现肾小球毛细血管内皮病合并甲状腺功能减低的发病率极其低,多与接触毒物或者病毒感染有关。为明确该病的临床诊断及给予合理的预防及治疗,除了完善包括肾脏组织活检在内的各项实验室检查以外,掌握患者详细的接触史、职业状况更为重要。

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