Clinicopathological Conference

Refractory hypertension and multiple organ dysfunction in the elderly

(The seventh case)

Case Presentation

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A male patient aged 63 with a history of hypertension for ten years and gout for two years was admitted to our hospital on Dec 23rd, 2001.

Ten years ago, he was diagnosed as essential hypertension because of recurrent dizziness, chest distress and the highest blood pressure of 260/150 mmHg. He had received antihypertensive therapy, including nifedipine, metoprolol and captopril, but his blood pressure was still above 170/110 mmHg. Two and one half hours before admission, he suddenly developed dyspnea, orthopnea, cyanosis and cough with profuse white foam sputum, which occurred shortly after defecation. He was admitted to our Emergency Department and was diagnosed as acuteleft-heart failure. After receiving intravenous urapidil, furosemide and lanatoside(Cedilanid), his clinical condition tended to be stable. He was transferred to the Cardiology Department.

Physical examination: the temperature was 36.3℃, pulse rate 80/min, the respiratory rate 20/min and blood pressure 200/120 mmHg. Harsh breath, dry and moist rales could be heard at both lungs. Heart was enlarged to the left, heart rate was 80 bpm and systolic murmur of grades Ⅲ/Ⅵ was heard at auscultation area of mitral valve. Vascular bruit was heard at auscultation area of abdomen. Laboratory examinations: creatinine (Cr) 218 μmol/L, blood urea nitrogen(BUN) 10.87 mmol/L, uric acid(UA) 705 μmol/L. Electrocardiogram showed ST segment with 0.1 - 0.3mV downslope depression and T wave inversion in leads I, aVL and $V_{[3-6]}$. Chest X-ray showed left ventricular enlargement. The two kidneys detected by abdomen echogram were slightly shrunk. Echocardiography showed thickening of interventricular septum and posterior wall of left ventricle, enlargement of left atrium and left ventricle, and left ventricle ejection fraction being 57%.

After receiving intravenous sodium nitroprusside, lanatoside C, furosemide and antibiotics, the clinical symptoms of heart failure disappeared. His blood pressure was maintained at 160 - 220/100 - 120 mmHg after antihypertensive therapy with drugs such as nifedipine, indapamide, terazosin, metoprolol. On Jan 10th 2002, coronary angiography showed diffuse and irregular lesions in the proximal segment of the left anterior descending (LAD) artery with 80-90% stenosis at most. Selective renal artery angiography showed severe stenosis of bilateral renal arteries.

The final diagnosis was renovascular hypertension, chronic renal and cardiac dysfunction, ischemic nephrosis, coronary heart disease. Percutaneous transluminal renal angioplasty was performed, and two stents were implanted in two renal arteries. The blood pressure was decreased to 150/90 mmHg immediately after interventional therapy. The patient was discharged and continued to receive antihypertensive therapy. During 1.5 years' follow-up, his blood pressure was 150/90 mmHg and no symptoms appeared.

Clinical Discussion

Dr. Cao Guangmin: The patient had hypertension for 10 years and his blood pressure was not adequately controlled by antihypertensive drugs. He was admitted because of acute left-side heart failure. Examination revealed heart enlargement, cardiac and renal dysfunction, bilateral renal shrinkage, coronary artery stenoses and bi-

lateral renal artery stenoses. All these manifestations were related to refractory hypertension.

Dr. Zhao Xizhe: Five to fifteen percent patients with hypertention are refractory to standard medical treatment. Of these patients, 5% are secondary hypertension. Of all kinds of secondary hypertension, renovascular hypertension and primary aldosteronism are often misdiagnosed, while pheochromocytoma, chronic renal parenchymal disease and Cushing's syndrome can be diagnosed without much difficulty. As for the elderly patient with refractory hypertension, secondary hypertention was highly probable and abdominal vascular bruit should lead to the consideration of the possibility of hypertension induced by renal artery stenosis.

Dr. Ma Fengyun: Renovascular hypertension is the most common cause of curable secondary hypertension, but many of such patients are misdiagnosed as primary hypertension, and so treatment is delayed, causing impairment of multiple organs. It is, therefore, necessary to carefully differentiate the causes of refractory hypertension, especially to exclude renovascular hypertension. Those with following characteristics have 5-15% likelihood of the diagnosis, including severe hypertension, refractory to standard therapy, abrupt onset of sustained, moderate to severe hypertension at age <20 or >50, hypertension with a suggestive abdominal bruit at the region of the renal artery, moderate hypertension in a smoker, in a patient with evidence of occlusive vascular disease. Those with following characteristics have a greater than 25% likelihood of the diagnosis, including severe hypertension with either progressive renal insufficiency or refractoriness to aggressive treatment, accelerated or malignant hypertension, hypertension with recent elevation of serum creatinine, unexplained or reversibly induced by an angiotensin-converting enzyme inhibitor, moderate to severe hypertension with incidentally detected asymmetry of renal size.

Dr. Chen Buxing: The detection of renal stenosis involves radiologic imaging and functional examination. The treatment of renal artery stenosis includes interventional, surgical and drug therapies. Recently, interventional therapy of renal artery stenosis has developed rapidly and become the first choice to treat renal artery stenosis. Compared with surgical therapy, interventional therapy is less traumatic and has less complications and lower death rate. The indication for interventional therapy should include unilateral or bilateral renal stenosis equal to or more than 70 percent, accompanied with one of the following characteristics: hypertension, mild or moderate renal dysfunction, recurrent pulmonary edema, recurrent hypertensive crises accompanied with angina pectoris, acute or subacute renal failure induced by total or subtotal occlusion of renal arteries.

The patient presented acute pulmonary edema on a background of slight left ventricle systolic dysfunction. Recurrent pulmonary edema is a common complication of severe bilateral renal artery stenosis and an absolute indication for interventional therapy. His blood pressure was controlled after implanting stent in the stenotic renal artery. The major dilemma of renal artery angioplasty is a restenosis rate of 1.6～25% in 6 months after the procedure. During 1.5 years follow-up of this patient after stent implantation, the blood pressure and renal function is stable, hence repeated renal artery angiography is not performed.

(Translator SUN Shuhong)

(收稿日期:2003-08-04)
(本文编辑 程述)

老年难治性高血压合并多脏器功能障碍

1 临床资料

患者，男，63 岁，发现高血压 10 年，因呼吸困难 2.5 h，于 2001 年 12 月 23 日急诊入院。患者于 10 年前因出现头晕、胸闷，查体发现血压增高，最高达 260/150 mmHg，在门诊服用多种降压药物，包括硝苯地平、美托洛尔（倍他乐克）、卡托普利（开博通）等药物治疗，血压一直控制不理想，一般约在 170/110 mmHg。患者于入院前 2.5 h，排便时突发呼吸困难，呈端坐呼吸，口唇发绀，咳嗽，咳白色泡沫样痰，伴大汗淋漓，急诊入院，诊断为急性左心功能不全，给予吸氧、静脉注射乌拉地尔、呋塞米、毛花甙丙等药物治疗，症状好转后入院进一步治疗。既往有痛风病史 2 年，大量吸烟史 50 年。

入院查体：体温：36.3℃，脉搏 80 次/min，呼吸 20 次/min，血压 200/120 mmHg。神清，急性病容，营养好，双肺呼吸音粗，双肺中下满布干湿性啰音，心界向左侧扩大，心率 80 次/min，律齐，二尖瓣听诊区可闻及Ⅲ/6 级收缩期杂音，腹软，肝脾肋下未触及，脐周可闻及响亮的血管杂音。

实验室检查及其他辅助检查：血尿常规化验正常，血 Na^+、K^+、Cl^- 化验正常。肌酐为 218 μmol/L，尿素氮 10.87 mmol/L，尿酸 705 μmol/L。总胆固醇 5.03 mmol/L，甘油三酯 0.42 mmol/L，高密度胆固醇脂蛋白 1.79 mmol/L，低密度胆固醇脂蛋白 2.41 mmol/L。卧、立位肾素、血管紧张素、醛固酮化验正常。心电图：ST 段在Ⅰ，aVL，$V_{3\sim6}$ 导联呈下斜型下移 0.1～0.3 mV，T 波倒置，住院期间 ST－T 无明显动态改变。胸部 X 线检查：左心室增大。腹部超声：双肾轻度萎缩，左肾 8.3 cm×5 cm，右肾 8.5 cm×4 cm；超声心动图检查：室间隔 13 mm，左室后壁厚度 12 mm，左房 40 mm，左室舒张末径 60 mm，左室收缩末径 42 mm，射血分数 57%，升主动脉 40 mm，轻度扩张。双肾上腺 CT 扫描：未见异常。肾动态显像：右肾血流实质影像功能曲线正常，左肾血流灌注时间明显延长。

入院后继续给予静脉注射硝普钠、毛花甙丙，呋塞米及抗生素等治疗，左心功能不全症状消失。口服硝苯地平（拜新同）、吲达帕胺、特拉唑嗪（高特灵）、美托洛尔等治疗，血压维持在 160～220/100～120 mmHg之间。2002 年 1 月 10 日行冠状动脉及肾动脉造影，冠脉造影结果显示前降支近段弥漫性病变，最窄处为 80%～90%狭窄，回旋支及右冠状动脉正常；肾动脉造影显示双肾动脉有明显狭窄性病变，其中左肾动脉中段 99%偏心性狭窄，右肾动脉分上下二支，开口处均有明显狭窄，分别为 90%和 80%～90%。最后诊断为：肾血管性高血压，慢性肾功能不全，缺血性肾病，冠状动脉粥样硬化性心脏病。2002 年 1 月 22 日行经皮腔肾动脉成形术加支架置入术，左肾动脉狭窄处置入 6.0 mm×10 mm AVE bridge 支架，右肾动脉上支置入 7.0 mm×15 mm AVE bridge 支架。术后即刻血压下降至 150/90 mmHg，继续服用美托洛尔（50mg，bid），硝苯地平（30mg，bid），吲达帕胺（2.5 mg，qd）等治疗，血压维持在 150/90 mmHg，血尿素氮 6.97 mmol/L，血肌酐 159 μmol/L。随访至今无其他临床症状，继续服用美托洛尔（50 mg，bid），哨苯地平（30 mg，bid）治疗，血压水平为 150～160/80～90 mmHg。

2 病例讨论

高光敏医师：患者为老年男性，有高血压病史 10 年，长期在门诊服用多种降压药物治疗，降压效果不理想，一般血压在 170/110 mmHg 以上，临床上应考虑为顽固性高血压。这次主要以急性左心功能不全为表现而入院治疗。入院后经过仔细检查，发现有心肾功能不全，心脏扩大，双肾轻度萎缩，冠状动脉造影提示有冠心病，肾动脉造影显示双侧肾动脉严重狭窄。从整个病史过程看，该患者出现心功能不全、冠心病、肾功能不全与长期血压未能得到良好控制有关。

赵希哲医师：对顽固性高血压的诊断标准不统一，为 5%～15%不等。因顽固性高血压转至专家门诊患者中约 5%是继发性，其中以肾血管性高血压和原发性醛固酮增多症易误诊，肾实质性疾病、柯兴综合征、嗜铬细胞瘤等由于易被发现不难诊断。至于该患者长期在门诊漏诊的原因，在于患者临床症状不明显，同时对老年才发现的明显高血压，各种药物治疗反应不佳，没有想到应除外继发性高血压的可能。查体时发现脐周围血管有杂音，应考虑肾动脉狭窄引起高血压的可能性较大。最后经过肾动脉造影证实了当时的临床判断，为制定下一步治疗方案提供了重要依据。

马凤云医师：对于肾动脉狭窄，临床上常见病因

有动脉粥样硬化、肌纤维发育不良及大动脉炎。老年人以肾动脉粥样硬化为主，且血管多为弥漫性病变。肾血管性高血压是最常见的可治性高血压，但却有很多被诊断为原发性高血压而得不到及时的治疗，造成多脏器损害的后果。要减少误诊，在临床上必须做好鉴别诊断，从众多的高血压患者中筛选出肾血管性高血压。对于包括重度高血压(DBP＞120 mmHg)、难治性高血压、突发的持续性中重度高血压、年龄＜20岁或年龄＞50岁、伴有腹部血管杂音(局限于肾动脉区的高调长程杂音)或不明原因的腹部症状性高血压患者、吸烟者或伴有闭塞性血管疾病等情况，肾血管性高血压发生的可能性为5%～15%。对于重度高血压伴肾功能不全或采用综合治疗无效者；急进性或恶性高血压；不明原因或可用转换酶抑制剂治疗的伴近期血肌酐升高的高血压；中重度高血压意外发现双肾不等大；属上述情况者，发生肾动脉狭窄的可能性＞25%。当肾动脉狭窄＞50%，伴有肾小球滤过率明显下降和(或)肾脏缩小时，临床可诊断缺血性肾病。该患者双侧肾动脉均有狭窄，达到80%～90%，伴有肾功能的降低及双侧肾萎缩，故考虑临床诊断缺血性肾病。

陈步星医师：肾动脉狭窄的检测方法包括影像学与功能学两方面。影像学的检查有肾血管造影、数字减影肾血管造影、螺旋CT及核磁共振血管成像。继发于肾动脉狭窄的功能不正常的检测有静脉肾盂造影术、肾静脉肾素测定、卡托普利试验、肾图、卡托普利肾图和彩色多普勒超声检测等。每种检测方法各有优缺点，应根据肾动脉狭窄的危险因素和发生概率选择不同的检测方法。肾动脉狭窄的治疗包括介入治疗、外科手术及药物治疗。近年来介入治疗有了较大的发展，与外科手术比较，介入治疗创伤小，并发症少，病死率低，已成为治疗肾动脉狭窄的首选方法，特别是置入支架后可使高血压的改善达到44%～67%。介入治疗的适应证包括单侧或双侧肾动脉狭窄≤70%，同时伴有：(1)高血压，药物依从性差同时有多个心血管危险因素；(2)轻、中度肾功能损害；(3)反复发作的肺水肿；(4)反复发作的高血压危象并有心绞痛；(5)肾动脉闭塞或次全闭塞而出现的急性或亚急性肾功能衰竭。

本例患者此次发病表现为突发急性肺水肿，心脏超声心动图示左室轻度扩大，射血分数为57%。因此，本例患者为左室收缩功能受损不严重基础上突发急性肺水肿，这是双侧重度肾动脉狭窄的一种常见并发症，也是肾动脉介入治疗的绝对适应证。而介入治疗可预防因双侧肾动脉狭窄而出现的反复肺水肿，改善心肾功能。此患者在双侧狭窄的肾动脉置入支架术后，血压明显改善，未再出现肺水肿。对于肾动脉狭窄的介入治疗，其主要缺点就是术后6个月狭窄率为1.6%～25%，本例患者在术后门诊随访1年半，其血压和心肾功能比较稳定，因而未对其进行肾动脉造影检查确定有无再狭窄。

(参加讨论的医师：高光敏，陈步星，马凤云，赵希哲，许玉韵)

(收稿日期：2003-08-04)

(本文编辑 张和起)

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(收稿日期：2003-03-24)

(本文编辑 张和起)