· 临床病理讨论 ·

Clinicopathological Conference

An elderly infective endocarditis patient with endocapillary proliferative glomerulonephritis

(the 28th case)

Center of Nephrology, China-Japan Friendship Hospital

Case presentation

A 61-year-old male farmer from Changping District, Beijing was admitted to the hospital on January 25, 2008 because of intermittent fever with chills for half a month, and edema for ten days. The patient has been suffered from fever with no obvious reason since January 10, 2008. His fever was about 38.5℃, accompanied by chills, lasted about 1-2 h after every onset, without night sweat, cough, sputum, hemoptysis, chest pain, chest distress, and palpitation. Urine volume and color were regular. Skin rash was not found, no joint and muscle pain were experienced. The patient had been admitted to the Beijing University People's Hospital on January 20, 2008 because of eyelid and ankle joint edema. Urinalysis: protein >3.0 g/L, red blood cells (RBC) 10 / high power field, white blood cells (WBC) 30 / high power field. He had received intravenous antibiotics for five days, but his symptoms were not ameliorated. Quantitative assessment for proteinuria: 3.01 g /d (urine volume 1700 ml). Blood biochemical tests: plasma protein 68.9 g/L, albumin 28.4 g/L, serum creatinine (Scr) 86 μmol/L. Since the onset of the illness, his body weight was not significantly reduced and his stool was not changed.

Past medical history: Stomach and duodenal ulcers were diagnosed by gastroscopy 2 years ago. Surgical repair of right indirect inguinal hernia was performed 8 months ago. He had no hypertension, coronary heart disease and diabetes, and no history of intravenous narcotic drugs.

Physical examination on admission: T 36.3℃, P 68 bpm, R 19/min, and BP 102/56 mmHg. Jaundice and skin petechia were not found. Superficial lymph nodes were not enlarged. There was a mild anemia. The jugular vein was markedly engorged during sitting. The respiratory sounds were clear, and moist rales were not heard at the bottoms of both lungs. Cardiac rhythm was regular, and a grade 2-3 systolic murmur was heard at the auscultation area of tricuspid valve. The abdomen was flat, soft, and had no tenderness. Liver was not palpable. Spleen boundary was expanded to 1 cm below costal margin. There was light pitting edema in both lower extremities. The nervous system had no abnormality.

At the 6:00 pm on the first day of hospitalization, the maximum body temperature was as high as 40.2 ℃, accompanied by shivering, and the blood culture of bacteria was performed at the time. At 10:00 pm on the second day, the peak body temperature was 39.4 ℃. Blood routine examination: WBC 12.4×10^9/L, neutrophils 88%; hemoglobin 103g/L, platelets 188×10^9/L. Urinalysis showed: protein 3.0 g/L, RBC > 50/high power field, WBC > 50/high power field. Microscopic examination of urine sediment: RBC was deformed. Quantitative assement for protein in

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urine: 5.4 g / d (urine volume 1890 ml). Blood tests: plasma total protein 65.0 g/L, albumin 27.1 g/L, Scr 113.0 μmol / L, urea 8.2 mmol / L, uric acid 376 μmol / L, creatinine clearance rate (Ccr) 52.8 ml / min, erythrocyte sedimentation rate 95 mm / h, C-reactive protein 14 mg/dl, serum complement C_3 18.8mg/dl, C_4 18.8mg/dl. Rheumatoid factor was positive. Hepatic function was normal. The levels of immunoglobulin: IgG, IgA and IgM were normal. The examinations of autoantibodies: anti-nuclear antibody, anti-dsDNA antibody, anti-RNP antibody, anti-Sm antibody, and anti-neutrophil cytoplasmic antibodies (ANCA) were negative. Electrocardiogram revealed no marked abnormality. Chest X-ray showed lung markings thickened, heart boundary enlarged. B-ultrasound showed that liver, gallbladder and pancreas were normal, spleen was enlarged, its length was 10.8 cm, thickness 4.2 cm, both kidneys were normal, the size of the left kidney was 11.3cm × 4.4cm × 5.2cm, and that of the right kidney was 10.2cm×3.8cm×4.5 cm. Echocardiography showed that there was a vegetation on the tricuspid valve, with a size of about 10mm×7mm, accompanied by severe tricuspid regurgitation and enlargement of the right ventricle, the ejection fraction was 60%. Retina examination revealed no abnormality. The blood culture of bacterium was Neisseria cinerea. The patient was firstly treated with linezolid, 600 mg, iv gtt, bid, for four weeks, then replaced by teicoplanin, 400 mg, iv gtt, qd, and levofloxacin, 200 mg, iv gtt, bid. On the third day of anti-infective treatment, his body temperature reduced to normal. On the fifth day, blood routine examination showed that WBC was restored to the normal range, hemoglobin was 96 g/L. There was a progressive decrease in hemoglobin. On March 2, hemoglobin decreased to the lowest level of 67 g / L. Bone marrow biopsy revealed that active proliferation of RBC series.

The patient received a kidney biopsy on February 20. Immunofluorescence study of biopsy specimen showed that: IgG2+, IgA2+, IgM3+, $C_3$2 +, C_{1q}2 +, and fibrin associated antigen + were co-deposited as lumps or fine particles in the mesangial area and on the capillary wall. The examination of hepatitis B virus antigen was negative. Light microscopy showed that in six glomeruli in the biopsy specimen, glomerular endothelial cells and mesangial cells had diffuse proliferation, there was infiltration of a small number of leukocytes in the glomeruli, the immune complex was deposited beneath the endothelial cells and in the mesangial area, tubular epithelial cells had particulate and vacuolar degeneration, focal atrophy could be seen, there were protein casts and cellular casts, lymphocyte and monocyte infiltration in the interstitial tissue (Fig 1). Electron microscopy showed that glomerular endothelial cells had diffuse proliferation, mesangial matrix was widened, there was electron-dense deposit beneath endothelial cells and in the mesangial area, glomerular basement membrane was not significantly changed. The pathological diagnosis was endocapillary proliferative glomerulonephritis.

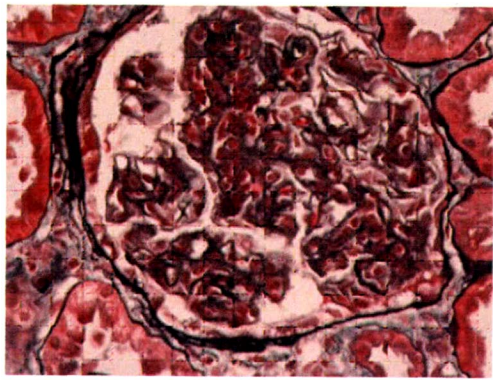

Fig 1 Endothelial cells and mesangial cells are diffuse proliferation in the glomerulus; immune complexes are deposited in the subendothelial cells and in the mesangial area; there is a small number of leukocytes infiltration, accompanied by karyorrhexis (PASM and MASSON staining)

In addition to the anti-infective treatment, the patient was also treated with other medications, such as ramipril 5 mg/d, valsartan 80 mg/d and Chinese medicine Bailing capsule 3.0g/d. No glucocorticoid hormone and immunosuppressive therapy were given. The condition of the kidney gradually

improved. On February 23, the level of C_3 rose to 58.0 mg / dl, C_4 to 27.0 mg / dl. On February 28, protein in 24h urine decreased to 1.3 g (urine volume 2520 ml); blood tests showed that plasma protein was 61 g / L, albumin was 31 g/L, the level of Scr returned to normal and Ccr was 95.4 ml/min.

The patient began to suffer from intermittent fever again on February 28, and his body temperature rose to 38.4℃, with chills. On March 13, the patient was moved to the division of heart surgery. On March 14, the highest body temperature reached 39.4℃. On March 20, the patient received tricuspid valve replacement operation. After the surgical treatment, his body temperature was restored to normal. Pathological study of tricuspid valve showed that there were fibrosis, calcification, degenerative necrosis, a small amount of WBC infiltration and mesothelial cell proliferation (Fig 2 and 3). On April 7, the patient recovered and was discharged. After two weeks, his urinalysis showed normal.

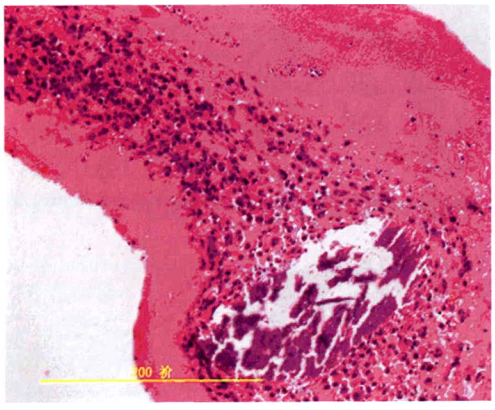

Fig 2 Tricuspid valve tissue fibrosis, calcification, degenerative necrosis; there is a large amount of leukocyte infiltration, and mesothelial cell proliferation (HE staining)

Clinicopathological discussion

Dr. FANG Jing: The features of the patient were as follows (1) An old male patient of 61 years old fell into illness acutely. (2) Main clinical manifestation was intermittent high fever with chill lasting about half month, accompanied by edema for ten days. (3) The total number of peripheral

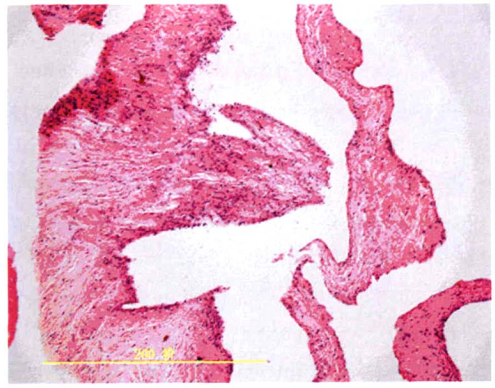

Fig 3 There is a large amount of leukocyte infiltration in endothelium, tricuspid valve tissue fibrosis, calcification, degenerative necrosis (HE staining)

blood WBC and neutrophils were increased. There was a mild anemia. (4) Hematuria, RBC > 50 / high power field, RBCs were deformed, protein in 24-h urine was 5.4 g. Blood biochemical tests showed serum albumin 27.1g/L. (5) Renal function was mildly declined. (6) Serum complement levels dropped significantly. (7) Echocardiography showed that there were vegetation on the tricuspid valve of about 10mm×7mm in size, severe tricuspid regurgitation, and enlargement of the right ventricle. (8) Blood culture of bacteria showed Neisseria cinerea. According to above clinical manifestations and examinations: firstly, subacute infective endocarditis was surely diagnosed, the pathology of tricuspid valve confirmed the diagnosis; secondly, the main manifestations of the kidney damage were hematuria, proteinuria, pyuria, hypoproteinemia, with plasma albumin <30.0 g/L, and mild kidney dysfunction, therefore, the diagnosis of acute nephritis syndrome and nephrotic syndrome were also established.

Dr. ZHENG Zhigang: The diagnosis of tricuspid infective endocarditis (IE) was clear. According to the severity and duration of the disease, the diagnosis of subacute IE was established. Echocardiography revealed a vegetation on the tricuspid valve. The tricuspid vegetation is apt to lead to pulmonary embolism, but in this patient, auscultation found $P_2 > A_2$, which might imply the possi-

bilily of presence of small emboli leading to pulmonary embolism, but further examination did not find the manifestations of pulmonary embolism. Blood culture of bacteria revealed Neisseria cinerea, and linezolid and teicoplanin were effective for the bacterium. The anti-infectious treatment should be used for 4—6 weeks or longer. There was a severe tricuspid valve insufficiency, and the right ventricle was enlarged. When the patient was in sitting position, his jugular vein was markedly engorged, indicating the presence of signs of right ventricle failure. This was the indication for the tricuspid valve replacement surgery. If the fever recurred, or blood culture of bacteria was persistently positive, or anti-infectious treatment was ineffective, tricuspid valve replacement surgery should be performed as soon as possible.

Dr. TAN Zhao: The kidney damage was pathologically diagnosed as endocapillary proliferative glomerulonephritis in the patient, and the clinical manifestation was nephrotic syndrome. If primary glomerulonephritis was the case, glucocorticoid hormone and (or) immunosuppressive drugs should be used. There was a small number of literature about IE related glomerulonephritis treated with glucocorticoid hormone and immunosuppressive drugs, but up to now, there was no common opinion on the glomerulonephritis treated with these medicines.

Dr. LIU Peng: The diagnosis of tricuspid IE was definite. After anti-infectious treatment for about 5 weeks, high fever reappeared in the patient, accompanied by chill, and the highest body temperature was 39.4 ℃. Echocardiography showed a vegetation on the tricuspid valve, severe tricuspid regurgitation, and right ventricle enlargement. These were signs of the right ventricle failure. Therefore, there was indication of tricuspid valve replacement operation for the patient.

Dr. CHEN Yipu: For an elderly patient with fever, anemia, large amount of proteinuria, edema, and hematuria, ANCA vasculitis should be considered firstly, but there were some evidences not supporting this diagnosis: (1) The patient had high fever accompanied by chills, and elevated blood WBC count, bacterial infection should be consider. (2) The patient of ANCA related vasculitis often has a large number of crescents or cellulose-like necrosis in the glomeruli and rarely presents such large amount WBC in urine. (3) The patient of ANCA related vasculitis usually has manifestations other than renal injury, such as hemoptysis, weight loss, joint and muscle pain, etc. All of these were absent in the patient. Echocardiography revealed a vegetation on the tricuspid valve, severe tricuspid regurgitation, and right ventricle enlargement, therefore, the patient with high fever should be suffered from IE. The large amount of WBC in the patient's urine might imply whether there were bacterial emboli in the kidneys, but tricuspid IE could not lead to the kidney embolism. The kidney damage of the patient was characterized by nephrotic syndrome, hematuria, urine RBC> 50 / high power field, mild decline of renal function and normal blood pressure, which might indicate that the pathological injury of the kidneys was proliferative glomerulonephritis. The pathogenesis of glomerulonephritis caused by IE is not yet entirely clear. There are some pathological types of the kidney damages induced by IE, whose accurate diagnosis relys on renal biopsy.

Dr. LI Wenge: With the ageing of human society, the prevalence of IE is significantly growing among the elderly population. In recent 10 years, the growing number of intervention therapy, such as endoscopy of vessels, stomach and intestine, and urinary tract, is the main cause for increase in IE. According to the Duke diagnostic criteria for IE, the manifestations for diagnosis are: (1) inflammatory lesion of tricuspid valve identified by pathological examination; (2) a vegetation on tricuspid valve, severe tricuspid regurgitation, and right ventricle enlargement revealed by echocardiography; (3) positive blood culture of bacteria. Therefore, the diagnosis of IE was sure in this patient. The kidney injury induced by IE mainly includes renal focal infarction, glomerulonephritis, acute interstitial nephritis and acute tubular necro-

sis. A few literature in recent years showed that IE could also be combined with ANCA-associated crescent glomerulonephritis, but the pathogenesis was not clear now. Some scholars suggest that the infective bacteria may have the same antigenic determinant with cytoplasmic antigen of neutrophiles, thus leading to the ANCA-associated crescent glomerulonephritis. The vegetation on tricuspid valve generally leads to pulmonary embolism and can not lead to focal kidney infarction. However, there were signs of kidney infarction in the patient, therefore, large numbe of WBC in the patient's urine might be aseptic WBC urine, which might mainly relate to endocapillary proliferative glomerulonephritis. Usually, acute glomerulonephritis occurs in young people. The main manifestation is acute nephritic syndrome, rarely nephrotic syndrome, and renal pathology is the type of capillary proliferative glomerulonephritis. Immunofluorescence examination can reveal that IgG and C_3 are the major components of granular immune deposits in glomeruli, rarely co-exist with IgA, IgM, and C_{1q} lumpy deposits. A lot of immune complex deposits in the glomeruli, and the manifestations of both acute nephritis syndrome and nephrotic syndrome in the patient suggested that the kidney damage caused by IE might have a great variety of manifestations. The IE-related glomerulonephritis might be induced by both the bacteria infection and the bacteria-mediated immune injury. There are a number of pathological types of glomerulonephritis caused by IE, including focal segmental glomerulonephritis, diffuse proliferative glomerulonephritis, and ANCA-associated crescent glomerulonephritis. In the focal segmental glomerulonephritis, endothelial cells or (and) mesangial cells have focal segmental proliferation in the glomeruli, and there is a small amount of leukocyte infiltration, GBM is generally normal. In the diffuse proliferative glomerulonephritis, endothelial cells and mesangial cells have diffuse proliferation in the glomeruli, usually there is a large number of neutrophil and monocyte infiltration, GBM can be thick or present double tracks, capillary loop has necrosis, and the cellular or cellular fibrous crescent occurs. Generally, the majority of the patients with IE-related glomerulonephritis have a good prognosis through active and effective anti-infectious treatment, the kidney damage is able to return to normal, even if there is a lot of crescents in the glomeruli. Few patients have been reported to receive glucocorticoid hormone and (or) immunosuppressive treatment. A small number of patients with kidney damage can develop to chronic renal insufficiency. After anti-infective treatment, the renal damages of the patient were progressively corrected, which further suggested that the endocapillary proliferative glomerulonephritis was caused by IE.

(Translator: LI Wenge)

老年感染性心内膜炎合并毛细血管内增生性肾小球肾炎1例

1 病例摘要

患者，男，61岁，北京市昌平区邓庄村农民。主因间断发热伴寒战半月，水肿10d于2008年1月25日入院。患者从2008年1月10日开始，在无明确诱因下出现发热，体温38.5℃，伴有寒战，发热每天出现1次或2次，无固定时间，持续约1～2h，出汗后可自行缓解，无盗汗，无咳嗽、咳痰、咯血、胸痛、胸闷、心悸，无尿频、尿痛、腰痛，尿色无异常，无皮疹、关节和肌肉酸痛，未予诊治，5d后发现眼睑和双踝关节周围水肿，就诊于北京大学人民医院，尿常规检查：蛋白＞3.0g/L，红细胞（RBC）10个/高倍视野，白细胞（WBC）30个/高倍视野，门诊给予静脉抗感染治疗，3d前查24h尿蛋白定量为3.01g（尿量1700ml），血浆总蛋白68.9g/L，白蛋白28.4g/L，血清肌酐（Scr）86μmol/L，以发热、水肿、蛋白尿原因待查入院诊治。患病以来，体重无明显减轻，大便无改变。

既往史：2年前因上腹部疼痛伴返酸，在昌平区中医院胃镜检查诊断为胃、十二指肠球部溃疡，服药

治疗2个月后治愈。8个月前在昌平区中医院进行右侧腹股沟斜疝修补术。无高血压、冠心病和糖尿病史。无静脉注射麻醉药物史。

入院查体：体温36.3℃，脉搏68次/min，呼吸19次/min，血压102/56mmHg，皮肤无黄染、出血点，表浅淋巴结未触及，轻度贫血貌，坐位时颈静脉怒张，双肺底未闻及干、湿啰音，心律齐，于胸骨左缘3～5肋间可闻及Ⅱ～Ⅲ级收缩期杂音，腹平软，无压痛，肝肋下未触及，脾肋下约1cm，无压痛，双下肢轻度水肿。神经系统查体未见异常。

在入院当日18：00时，体温高达40.2℃，伴有寒战，予抽血培养，次日22：00时体温最高达39.4℃。化验检查：血常规：WBC12.4×10^9/L，中性粒细胞占88%，血红蛋白103g/L，血小板188×10^9/L。尿常规：蛋白3.0g/L，RBC>50个/高倍视野，WBC>50个/高倍视野，尿RBC形态检查为畸形RBC。大便常规和潜血检查未见异常。24h尿蛋白定量5.4g(尿量1890ml)。血浆总蛋白65.0g/L，白蛋白27.1g/L，Scr 113.0μmol/L，尿素8.2mmol/L，尿酸376μmol/L，内生肌酐清除率(Ccr)52.8ml/min。血沉95mm/h，C-反应蛋白14mg/dl，血清补体$C_3$18.8mg/dl，$C_4$18.8mg/dl，类风湿因子阳性，肝功能和血脂未见异常。免疫球蛋白IgG、IgA和IgM水平正常，抗核抗体、抗dsDNA抗体、抗RNP抗体和抗Sm抗体，以及抗中性粒细胞胞浆抗体(anti-neutrophil cytoplasmic antibodies，ANCA)检查均阴性。心电图未见异常。胸部X线检查：双肺纹理稍粗，心影增大。B超检查：肝脏、胆囊和胰腺未见异常，脾大，长径10.8cm，厚度4.2cm，回声均匀，边缘钝，切迹明显，双肾实质回声均匀，左肾11.3cm×4.4cm×5.2cm，右肾10.2cm×3.8cm×4.5cm。超声心动图检查：三尖瓣前叶见赘生物，大小约10 mm×7mm，三尖瓣重度关闭不全，右心室扩大，射血分数60%。眼底检查未见异常。血培养结果为灰色奈色球菌。给予利奈唑烷600mg，静脉点滴，2次/d，治疗4周后改为替考拉宁400mg，静脉点滴，1次/d和甲磺酸左氧氟沙星200mg，静脉点滴，2次/d抗感染治疗。抗感染治疗3d后，患者体温恢复正常，5d后血常规检查：WBC恢复至正常范围，血红蛋白为96g/L，并且贫血出现进行性加重，至3月2日时，血红蛋白最低达67g/L，骨髓活检为RBC系增生活跃。

患者于2月20日进行了肾穿刺活检，免疫荧光检查：免疫球蛋白IgG2+，IgA2+，IgM3+，$C_3$2+，C_{1q}2+，纤维蛋白相关抗原+，呈团块状沉积在肾小球系膜区，或细颗粒状沉积在毛细血管壁，乙型肝炎病毒抗原检查阴性；光镜检查：可见6个肾小球，内皮细胞和系膜细胞呈弥漫性增生，可见少量WBC浸润，内皮细胞下和系膜区可见嗜复红蛋白沉积，肾小管上皮细胞可见空泡和颗粒变性，灶状萎缩，可见细胞和蛋白管型，肾间质可见灶状淋巴细胞和单核细胞浸润(图1)；电镜检查：肾小球内皮细胞弥漫增生，系膜基质增宽，内皮细胞下和系膜区可见电子致密物，基底膜未见明显改变；病理诊断为毛细血管增生性肾小球肾炎。

患者住院期间，除给予抗感染治疗外，还给予了雷米普利5mg/d、缬沙坦80mg/d，以及中成药百令胶囊1.0g，3次/d等药物治疗，未给予任何糖皮质激素和免疫抑制剂治疗，肾脏病变逐渐好转，2月23日血清补体水平升至$C_3$58.0mg/dl，$C_4$27.0mg/dl，2月28日24h尿蛋白减少至1.3g(尿量2520ml)，血浆总蛋白为61g/L，白蛋白为31g/L，肾功能恢复正常，Ccr为95.4ml/min。

患者于2月28日再次出现间断发热，体温最高达38.4℃，伴有畏寒，3月13日转入心脏外科，3月14日体温最高达39.4℃，伴寒战，患者于20日进行三尖瓣置换术，术后体温正常。三尖瓣病理检查：瓣膜组织纤维化、钙化，伴有退变性坏死，可见急性炎症细胞浸润和间皮细胞增生(图2，3)，于4月7日康复出院。出院2周后随访，尿常规检查蛋白阴性，WBC阴性，RBC阴性。

2 临床病理讨论

方静医师：患者病例特点是：(1)男性，61岁；(2)急性发病，主要表现为间断高热伴寒战约半月、水肿10d；(3)外周血WBC总数和中性粒细胞数均增加，伴有轻度贫血；(4)尿中RBC>50个/高倍视野，RBC形态检查为畸形RBC，尿中WBC>50个/高倍视野，24h尿蛋白定量5.4g，血浆白蛋白27.1g/L；(5)肾功能出现短暂性轻度减退；(6)血清补体水平显著下降；(7)超声心动图检查三尖瓣前叶见赘生物，并伴三尖瓣重度关闭不全，右心室扩大；(8)血培养结果为灰色奈色球菌。根据上述临床表现和检查结果，首先，患者诊断亚急性感染性心内膜炎(infectious endocarditis，IE)成立，患者三尖瓣置换术后瓣膜病理检查也证实了该诊断。其次，肾脏损害主要表现为血尿，尿中同时存在大量WBC，以及大量蛋白尿，血浆白蛋白<30.0g/L，并出现短暂性肾功能减退，因此，该患者诊断急性肾炎综合征和肾病综合征也成立。

郑知刚医师：诊断三尖瓣IE明确，根据病情程度和病程进展情况，诊断为亚急性IE。患者超声心动图检查三尖瓣前叶见赘生物，三尖瓣赘生物易发生肺栓塞，该患者听诊$P_2>A_2$，不除外已有小栓子导致肺栓塞的可能。眼底检查尚未发现栓塞表现。血培养结果为灰色奈色球菌，对利奈唑烷、替考拉宁等抗生素敏感，抗感染治疗应在4～6周或以上。患者三尖瓣重度关闭不全，说明三尖瓣破坏重，血液返流量大，已有右心室扩大，坐位时颈静脉怒张明显，表明已存在右心衰竭的迹象，建议择期进行三尖瓣置换手术。如果患者再次出现发热，或血细菌培养阳性，说明抗感染治疗效果欠佳，则应尽早进行三尖瓣置换手术。

谭昭医师：患者肾活检诊断为毛细血管内增生性肾小球肾炎，临床表现为肾病综合征，若为原发性肾小球肾炎，则应使用糖皮质激素和(或)免疫抑制剂治疗，该患者肾炎与亚急性IE相关，但也有少数文献报告，IE导致的肾小球肾炎有应用糖皮质激素联合环磷酰胺治疗的病例，是否在充分抗感染治疗后肾脏损害仍无明显好转的情况下才使用，目前尚无统一认识。

刘鹏医师：患者三尖瓣IE明确，经过抗感染治疗约5周后又出现间断发热，体温最高达39.4℃，三尖瓣存在赘生物，并且三尖瓣重度关闭不全、右心扩大，以及有右心衰竭表现，具备手术清除感染灶和进行三尖瓣置换术的指征。

谌贻璞医师：患者为老年男性，主要表现发热、贫血，并出现大量蛋白尿、水肿，以及血尿，首先应考虑ANCA相关性小血管炎的可能性，但不支持本病的是：(1)患者发热伴有寒战，外周血WBC升高，应考虑细菌性感染；(2)ANCA相关性小血管炎即使肾小球出现大量新月体以及纤维素样坏死，尿中可出现较多WBC，但罕见象该患者这样，尿中有如此之多的WBC，WBC>50个/高倍视野；(3)ANCA相关性小血管炎常出现肾损害以外的表现，如咯血、体重下降、关节和肌肉疼痛等，该患者上述症状和体征缺如。患者超声心动图检查发现三尖瓣前叶见赘生物，并伴有三尖瓣重度关闭不全、右心室扩大，因此，患者高热的病因为IE。患者尿中存在大量WBC，是否由细菌栓子引起的肾脏局灶脓肿所致，应高度警惕，但该患者仅发现右心瓣膜病变，难以解释由细菌栓子直接损伤肾脏所致。此外，患者肾脏损害表现为大量蛋白尿，低蛋白血症，出现肾病综合征，血尿也突出，尿中RBC>50个/高倍视野，并曾出现肾功能轻度减退，但无高血压，病理类型可能为细胞增殖性肾小球肾炎。IE导致的肾小球肾炎发病机制目前还不完全清楚，文献报告可能主要与细菌损伤及其感染所诱发的免疫功能异常有关，肾脏损害的病理类型有多种，确诊需要靠肾穿刺活检。

李文歌医师：伴随着人类社会的老龄化，以及老年人心脏瓣膜的退行性变和钙化的增多，老年人已成为IE的多发人群，IE的患病年龄，也有日益增大的趋势，此外，无器质性心脏病的患者也明显增加，这可能与近10余年来临床上日益增多的心血管创伤性检查和介入治疗、各种血管、胃肠道和泌尿生殖系统的内镜检查，以及长期中心静脉留置导管等有关。根据IE的Duke诊断标准，该患者三尖瓣赘生物病理学检查存在活动性心内膜炎症，超声心动图检查发现三尖瓣不仅有赘生物，并存在重度血液返流，以及患者发病过程中存在高热、血培养细菌阳性和肾小球肾炎等，因此，该患者诊断IE肯定。IE导致的肾脏损害主要包括肾脏局灶梗塞、肾小球肾炎，以及急性间质性肾炎和急性肾小管坏死，近年来的文献报告，IE也可合并ANCA相关的新月体肾炎，发病机制尚不清楚，有学者提出，某些感染的细菌可能与中性粒细胞胞浆具有相同的抗原决定簇，从而导致了ANCA相关的新月体肾炎。该患者IE病灶主要在右心，一般容易导致肺栓塞，若感染灶在左心或主动脉瓣，才易导致肾脏梗塞发生，该患者临床上也未发现有肾脏局灶梗塞的表现，因此，患者尿中出现的大量WBC可能为无菌性WBC尿，可能主要与毛细血管内增生性肾小球肾炎有关。就一般情况而言，感染导致的急性肾小球肾炎多发生于青少年，临床上主要表现为急性肾炎综合征，肾病综合征较少见，肾脏病理类型是毛细血管内增生性肾小球肾炎，肾小球免疫荧光检查可见以免疫球蛋白IgG和补体C_3为主的颗粒状沉积，罕见同时出现IgA、IgM、C_{1q}等多种免疫球蛋白和补体成分呈团块状沉积。该患者为老年，临床表现既存在急性肾炎综合征，也存在肾病综合征，肾小球中有多种免疫球蛋白和补体成分沉积，提示IE导致的肾脏损害临床表现多样化，肾炎的发病主要与细菌感染介导的免疫损伤有关。IE导致的肾小球肾炎，病理类型有多种，轻者通常为局灶节段性肾小球肾炎，主要是节段性内皮细胞、系膜细胞增生，少量中性粒细胞和单核细胞浸润，肾小球基底膜正常；重者为弥漫增生性肾炎，大量内皮细胞、系膜细胞增生，大量中性粒细胞和单核细胞浸润，肾小球基底膜可出现双轨，可伴有毛细血管袢坏死，以及细胞性或细胞纤维性新月体，多数患者预后良好，经过积极有效的抗感染治疗后，肾脏损

害多能恢复正常，即使伴有较多新月体的肾小球肾炎，预后也较好，极少有应用糖皮质激素和(或)免疫抑制剂治疗的报告，但也有少数患者肾脏损害衍变为慢性肾功能不全。该患者肾活检病理类型为毛细血管内增生性肾小球肾炎，病理类型与临床表现符合，经过抗感染治疗后，肾脏损害也较快恢复，这一点也与IE所导致的肾炎相吻合。

(参加讨论医师：李文歌、方静、谭昭、郑知刚、刘鹏、谌贻璞)

(李文歌 整理)

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仍然是现阶段效果最好的房颤非药物措施之一，但其适应证较窄，目前主要适用于一些需要外科手术治疗，且同时合并房颤的器质性心脏病患者，特别是伴有巨大左心房的持续性房颤患者。

综上所述，在房颤的非药物治疗领域，导管消融治疗之外的治疗措施多存在效果不确切或者适应证较窄等不足，因此难以成为房颤治疗的主流措施。

4 展望

新的抗心律失常药物仍在不断开发，研发方向将是具有心房特异性(致室性心律失常发生率低)和抗心律失常机制靶点的广泛性(提高有效性)的新一代药物。安全、有效、服用方便不需监测凝血的抗凝药物也是药物治疗的发展方向。但是药物的研发、临床试验、临床应用周期长，在可以预见的将来，导管消融无疑是最有可能彻底攻克房颤的治疗措施。

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细胞因子通过合成分泌的相互调节、受体表达的相互调控、生物学效应的相互影响而构成一个极为复杂的细胞因子及受体网络，共同参与心力衰竭的发展，细胞因子对心力衰竭的检测和病情预后有重要的价值。

参考文献

[1] Deswal A, Petersen NJ, Feldman AM, et al. Cytokines and cytokine receptors in advanced heart failure: an analysis of the cytokine database from the Vesnarinone Trial(VEST). Circulation, 2001, 103: 2055-2059.

[2] Cesari M, Penninx BW, Newman AB. Inflammatory markers and onset of cardiovascular events: results from the Health ABC study. Circulation, 2003, 108: 2317-2322.

[3] Stumpf C, Lehner C, Yilmaz A. Decrease of serum levels of the anti-inflammatory cytokine interleukin-10 in patients with advanced chronic heart failure. Clin Sci (Lond), 2003, 105: 45-50.

[4] Yamaoka M, Yamaguchi S, Okuyama M. Anti-inflammatory cytokine profile in human heart failure behavior of interleukin-10 in association with tumor necrosis factor-alpha. Jpn Circ J, 1999, 63: 951-956.

·启 事·

因本刊来稿较多，为缩短论文的刊出周期，和增大每期的信息量。因此，自2008年第7卷第3期起，每期页码由原80页增加至96页。订价暂时不变。

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