· 临床病理讨论 ·

Clinicopathological Conference

A 72-year-old woman with palpitation, short breath, oliguria, edema and melena

(The 22nd case)

Institute of Geriatric Cardiology, Chinese PLA General Hospital

Case presentation

The patient, a 72-year-old female, retired teacher, married, was admitted to the hospital because of palpitation and short breath after exertion for 40 years, oliguria and edema of lower limbs for 2 years and melena for 1 month. In 1966 the symptoms of palpitation and short breath after exertion occurred and were diagnosed as rheumatic heart disease. In 1997 she received valve replacement of aortic valve and bicuspid valve in Fuwai Hospital and then turned to be better and took warfarin as routine for anticoagulation. Two years ago palpitation and short breath were aggravated and tricuspid regurgitation was found. One year ago severe anemia (the lowest hemoglobin level was 42 g/L) was showed by laboratory examination. The cause of it was not identified at that time and was suspected as hemolytic anemia in Hematologic Department of Beijing University Hospital. The treatment with washed red blood cells was given monthly and hemoglobin could rise to 70－80g/L. Right pleural effusion and seroperitoneum occurred half a year ago and she received thoracentesis and abdominal paracentesis prior to admission. The pleural effusion was light red and peritoneal effusion was light yellow, both were transudate. One month ago stool was tarry like, 1 to 3 times a day. However, she did not undergo gastrointestinal endoscopy because of poor heart function. The patient was admitted for further treatment on December 22, 2006. She had no history of hypertension, coronary heart disease, diabetes, chronic bronchitis, asthma and drug hypersensitivity.

On physical examination, the temperature was 36.8℃, the blood pressure 120/80mmHg, the pulse 90 beats/min, and the respiration 20 /min. The patient was conscious and anemic. Skin had no rash and petechiae. No swelling of superficial lymph nodes was found, conjunctiva color was pale, pupils were equal in size, round and reactive to light. Jugular veins were engorged, trachea was centrally located, thyroids were not enlarged, lips showed no cyanosis and an old operation scar was seen at anterior chest wall. Respiratory movement of two lungs was symmetrical, and dull percussion note, weakened vocal fremitus and suppressed respiration sound were found at right lower lung. The heart was enlarged to both sides on percussion, heart rate was 90/min and regular, and systolic murmur of grade 3/6 at tricuspid area was detected on auscultation. The abdomen was inflated, no tender and no rebound tenderness were found. Liver was palpable 10cm under right costal margin. The spleen was not palpable. Shifting dullness was present. Bowel sounds were normal. Backbones and limbs had no abnormalities and tenderness. Both lower extremities and lumbosacral area had pitting edema. Arterial pulsation of both dorsum pedis was normal. Physiological reflexes

收稿日期:2007-04-02

作者单位:100853 北京市,解放军总医院老年心血管病研究所

作者简介:王新华,女,1974年1月生,山东省冠县人,在读博士研究生,主治医师。Tel:13241283506

existed, pathologic reflex was absent. Laboratory examinations: WBC 9.9×10^9/L, N 0.96, RBC 2.64×10^{12}/L, HB 75 g/L, PLT 194×10^9/L, INR 2.17, pro-BNP 2408 ng/L, TP 56.8 g/L, A 33.5 g/L, BUN 8.81 mmol/L, UA 613.0 μmol/L, Cr 87.6 μmol/L, TBil 24.7 μmol/L, DBil 10.0μmol/L, LDH 485U/L, Ca 1.94 mmol/L. Heart ultrasound found: ① left atrial diameter 71mm, right atrial diameter 54 mm, right ventricle diameter 44 mm, left ventricle diameter was normal; ② pulmonary arterial pressure 50mmHg; ③ severe tricuspid regurgitation and doubtful left atrial thrombus; ④ EF 54%. Chest X-ray: pulmonary congestion. Abdomen ultrasound: congestion of liver and ascites.

After admission, the patient received diuretics, anticoagulants, blood transfusion, symptomatic and supportive therapy. The patient's condition improved and she was transferred to general ward on December 30, 2006. Dyspnea aggravation, oliguresis, acute left heart failure and type-2 respiratory failure occurred because of pulmonary infection. On January 6, blood gas analysis showed: pH 7.06, PO_2 69.8 mmHg, PCO_2 66.0 mmHg, AB 18.3 mmol/L, BE−10.3mmol/L. Heart beat and breath suddenly stopped at 17:35. The patient received cardiopulmonary resuscitation, intermittent administration of respiratory stimulant, adrenalin and bolus intravenous injection of sodium bicarbonate, tracheal intubation and respirator-assisted respiration immediately. The resuscitation was successful. Targocid and mepem were given for treating pulmonary infection. Urine volume increased to 2000 ml per day. Stool occult bloud was positive intermittently. On January 19, 2007 the respirator was removed successfully. Thoracentesis and chest drainage were given because of considerable pleural effusion. Bloody pleural effusion 600−700ml could be drawn every other day and tumor marker CA_{125} in it increased obviously. Chest X-ray did not find tumor. Computerized tomographic scanning could not be done because of the patient's poor condition. After removing the respirator, the patient's condition was stable for several days, but later dyspnea was aggravated and oliguria emerged. Blood routine examination showed total WBC count and neutrophils increased. Sputum culture showed stenotrophomonas maltophilia and ticarcillin was given according to susceptibility test. Diuretic was given every day. Dopamine and nitroprusside sodium were pumped into vein to improve heart function. Initially urine volume increased, but diuretic resistance appeared gradually. Dropsy became more serious day by day and extended to all over the body, and dilutional hyponatremia occurred. Warfarin dosage was adjusted to 1.5-3mg/day acconding to INR value, which fluctuated at 1.51−6.23. On January 22, gross hematuria appeared and INR was 4.87 at that time. On January 28, INR was 1.85 and urine routine examination still found the visual field full of RBC. On February 1, INR was 3.51, the gross hematuria disappeared and urine routine examination found RBC 7-10/HP. But urine volume decreased further. On February 3, urine volume was merely 300ml whole day and did not respond to diuretics. In the morning on February 4, the patient's BP decreased, heart rate decreased to zero. After cardiopulmonary resuscitation and respirator-assisted respiration, her heart-beat and BP recovered. But spontaneous breathing and consciousness did not return. The urine volume was 20ml whole day. Bloody liquid effused from oral cavity. The tracheoscopy found pneumonedema. Laboratory examinations: pH 7.318, PO_2 177.9mmHg, PCO_2 50.7 mmHg, BE−0.6 mmol/L, BUN 9.96 mmol/L, Cr 88 μmol/L, serum kalium 4.77 mmol/L, serum natrium 123.7 mmol/L, WBC 11.1×10^9/L, N 0.90, HB 60 g/L, RBC 2.14×10^{12}/L, PLT 251×10^9/L, INR 3.28, D-Dimer 4.68 mg/L. Continuous bedside hemofiltration by nephrology department was arranged in next day morning. However, at 8:40 on February 5, the patient's heart rate began to decrease, BP descended again and nasal cavity bleeding occurred. Dopamine, adnephrin, anisodamine, sodium bicarbonate were

given to raise BP, strengthen heart function, improve circulation and correct acidosis and continuous closed cardiac massage was applied. The patient did not show any sign of resuscitation and died at 9:43.

Clinical discussion

Dr. WANG Xinhua: The clinical characteristics of this case were as follows: ①rheumatic heart disease had existed for 40 years and 9 years ago replacement of aortic valve and bicuspid valve were given; ② warfarin for anticoagulant therapy was given for long time; ③ one year ago anemia was found and treated with blood transfusion intermittently; ④ the patient was admitted because of short breath, oliguria, edema and melena; ⑤after receiving diuretics, anti-infective, symptomatic and supportive treatment, the patient's condition was stable. Later on pulmonary infection induced acute exacerbation of congestive heart failure, stagnation of blood in lung, oxygen diffusion disorder, respiratory tract spasm, carbon dioxide retention, respiratory failure and acidosis. The functions of all organs further decreased on the basis of long-term stagnation of blood and hypoxia. The outstanding manifestation of kidney dysfunction was oliguria to anuria. According to the history of the patient, diagnosis of rheumatic heart disease and heart failure could be established. But the cause of anuresis was not clear. Referring to this patient, the choice of the right moment for hemofiltration in the cases of multi-organ failure needs to be studied and discussed further.

Dr. XU Qiang: The diagnosis of the patient is clear. After admission she received diuretic, anti-inflammatory, symptomatic and supportive treatment, her condition improved for a time. Afterwards pulmonary infection was aggravated, respiratory failure appeared and resulted in breath and cardiac arrest. First rescue was successful. After removing the respirator, she had refractory asthma, diuretic was more and more ineffective and liquid was retained. Oliguria and anuresis occurred which aggravated heart failure. Breath and cardiac arrest emerged again. Cardiopulmonary resuscitation was successful, but brain recovery was unsuccessful. Rescue was ineffective and the patient died.

Dr. GAO Wei: The patient state of illness was protracted with multi-organ insufficiency. The patient's condition improved for a time. Then infection of lung was aggravated and breath and cardiac arrest appeared. The first rescue was successful. INR fluctuated significantly and hematuria appeared intermittently. Then anuresis appeared. I think that the causes of asthma is multifactorial. Cardiac insufficiency is the principal one, combined with pulmonary infection. Chest X-ray showed enlarged heart, and the pleural fluid was transudate, which indicates that heart failure is severe. The patient had edema of the whole body. After taking diuretic, urine volume increased initially, then diuretic was ineffective, and anuresis appeared. These factors aggravated heart failure and pulmonary infection could not be easily controlled. The patient died of respiratory failure and cardiac failure. The cause of anuresis may be as follows: ①haematuria repeatedly appeared and thrombosis may occur in collecting duct of kidney; ②blood stagnated in venous system and organs were in ischemia and hypoxia, so the function of glomerulus was influenced. Therapeutic measure for oliguria and choice of right moment for hemofiltration were worthy to be studied further.

Pathological discussion

Dr. LI Jiayue: The major pathological findings were as follows: ① rheumatic myocarditis; rheumatic valvular disease; ② mitral-aortic valve replacement; ③ aortic valvular mixed thrombus; ④aortic atherosclerosis with fibrous plaques; ⑤bilateral pulmonary emphysema, pulmonary edema, lung hemorrhage, acute and chronic inflammation of lung; ⑥bilateral pleural effusion (500ml at left

side, 200ml at right side); ⑦hemorrhagic ascites (about 1 500ml); ⑧congestive cirrhosis of liver; ⑨chronic congestion of all organs, especially the spleen and liver. From the pathological findings, we can consider that the cause of death was circulatory and respiratory failure as the result of pulmonary infection on the basis of chronic heart failure.

Dr. ZHAO Yusheng: I agree with the above opinions. Because of long-term rheumatic heart disease, enlarged heart and heart failure, pulmonary infection occurred repeatedly. The efficacy of diuretic was not good and there were pleural effusion and ascites, these were related to increase in venous pressure due to chronic heart failure. The patient suffered from heart disease of terminal stage and had respiratory muscle failure. After successful resuscitation at the first time and removing the respirator, carbon dioxide retention gradually appeared. In the case of metabolic and respiratory acidosis, hypoxia was aggravated and renal function was hard to improve, water and sodium retention were aggravated further, resulting in oliguria and anuria. Liver congestion resulted in congestive cirrhosis. Both heart failure and liver cirrhosis can cause profuse ascites. Autopsy showed that chordae tendineae of tricuspid valve thickened and the root of valve was calcified, but the valves did not thicken and fuse obviously. So obvious tricuspid regurgitation was mainly functional. There was mixed thrombus on the ventricular surface of aortic valve, so thrombo-embolism could not be ruled out, The thrombo-embolism is most commonly seen as cerebral embolism. Since cranial dissection was not done for the patient, so this possibility can not be fully ruled out. Erosion of gastric mucous membrane and dilatation of mucosal vessels could be seen under microscope. It is considered that this was stress erosion and hemorrhage resulting from hypoxia. Finally multi-organ failure(MOF) appeared. MOF was related to infection and hypoxia. Warfarin can increase the risk of hemorrhage. Furthermore, many factors can influence the effect of it. The dose of warfarin taken by the patient was not large, but INR fluctuated considerably. Hemorrhage coexisted with aortic valvular thrombus. Later on hemorrhage of many sites appeared and was considered to be related to warfarin and infection. Evidence of diagnosis of DIC was not enough, because of no thrombocytopenia. So the dose of warfarin should be individualized and closely monitored. Besides, CA_{125} increased but tumor was not found in this case. It is considered that increase in CA_{125} was related to nerve - endocrine activation and reflected aggravation of heart function. Previous study has demonstrated that there was relationship between heart function of heart failure patient and CA_{125}.

(Translator: WANG Xinhua)

72岁老年女性心悸、气短、少尿、浮肿、黑便1例

1 病例摘要

患者女性，72岁，已婚。主因“劳力后心悸、气短40年，加重伴少尿、下肢浮肿2年，黑便1个月”于2006年12月22日入院。1966年因劳累后出现心慌、气短，就诊发现有“风湿性心脏病”，1997年于阜外医院行主动脉瓣、二尖瓣人工瓣膜置换术。术后症状明显好转，常规服用华法令抗凝治疗，近半年来剂量3mg 1次/d，国际标准化比值(international normalized ratio, INR) 2～2.5。2年前心慌气短加重，尿量减少，下肢浮肿，并逐渐加重，经检查发现“三尖瓣大量返流”。1年前查血常规发现贫血，血红蛋白最低仅有42 g/L，当时疑诊为“溶血性贫血”，给予每月输注一次洗涤红细胞，血红蛋白能上升至70～80g/L，曾于北京大学第一医院血液科诊治，未明确贫血原因。半年前发现右侧胸腔及腹腔积液。3d前行胸腔和腹腔穿刺，胸水呈淡红色，腹水呈淡黄色，均为漏出液，未查到抗酸杆菌。1个

月前发现大便呈黑柏油样，每天1～3次，因心功能差，未行胃肠内窥镜检查。为进一步诊治，以"风湿性心脏病 心衰"收入院。否认高血压、冠心病、糖尿病、慢性支气管炎、哮喘等病史，否认肝炎、结核、伤寒等传染病史。

入院时情况：体温36.8℃，脉搏90次/min，呼吸20次/ min，血压120/80mmHg。意识清楚，贫血貌，全身皮肤黏膜未见出血点、瘀斑，浅表淋巴结无肿大。睑结膜色淡，巩膜无黄染，双瞳孔等大同圆，对光反射存在。口唇无紫绀，耳鼻未见异常。气管居中，甲状腺无肿大，颈静脉怒张，胸前见陈旧手术疤痕，两肺呼吸运动对称，右侧肺部第五肋下叩诊浊音，语颤减低，双肺呼吸音粗，右下肺呼吸音消失。心前区无隆起，心界向两侧明显扩大，心率90次/ min，心律齐，三尖瓣听诊区可闻及3/6级收缩期吹风样杂音。腹膨隆，无压痛及反跳痛，肝肋下10cm，脾肋下未触及，移动性浊音阳性。脊柱及四肢无畸形，无变形及无压痛。双下肢及腰骶部可凹性水肿。双侧足背动脉搏动正常。生理反射存在，病理反射未引出。辅助检查：血常规：WBC 9.9×10^9/L，N 0.96，RBC 2.64×10^{12}/L，HB 75g/L，PLT 194×10^9/L；INR 2.17；pro-BNP 2408 ng/L。血生化：总蛋白56.8g/L，白蛋白33.5g/L，BUN 8.81 mmol/L，UA 613.0 μmol/L，Cr 87.6 μmol/L；TBil 24.7 μmol/L，DBil 10.0 μmol/L，LDH 485 U/L，Ca 1.94 mmol/L；便潜血弱阳性。心脏超声：(1)左房扩大，左房内径71mm；(2)右心扩大，右房内径54 mm，右室内径44 mm；左室大小正常，左室舒张末内径40 mm，收缩末内径29 mm，射血分数54%；(3)轻-中度肺动脉高压，估测肺动脉压50mmHg；(4)三尖瓣重度返流；(5)主肺动脉增宽，内径29mm；(6)可疑左房血栓。胸片：肺淤血，心影向两侧明显扩大。腹部B超：淤血肝，腹水。

入院后诊疗经过：入院后给予利尿、改善心功能、抗凝、输血、对症、支持等治疗，病情好转，于2006年12月30日转入普通病区。因肺部感染出现呼吸困难加重、尿少，于2007年1月5日晚发生急性左心衰，1月6日血气分析(吸氧浓度30%)：pH7.06，PO_2 69.8 mmHg，PCO_2 66.0 mmHg，AB 18.3mmol/L，BE－10.3mmol/L，示2型呼吸衰竭，代谢性酸中毒，当日17:35出现心跳呼吸骤停，给予持续胸外心脏按压，间断给予呼吸兴奋剂、肾上腺素、碳酸氢钠静脉推注，气管插管呼吸机辅助呼吸，约5 min患者心跳恢复，5h后神志转清，血压、心率、血氧饱和度均波动在正常范围内，复查血气基本正常。给予他格适联合美平抗炎，肺部感染好转，尿量开始增加，约2 000ml/d，便潜血间断阳性。于2007年1月19日成功脱机，并行胸腔穿刺抽液置管术，隔日可抽出600～700ml血性胸水，化验肿瘤标志物 CA_{125} 明显增高，胸片未发现肿瘤影像，因病情重未搬动患者行胸部CT检查。脱机后数日患者病情相对平稳，后来呼吸困难加重、喘息，尿量减少，血常规白细胞总数及中性分类增高，痰培养为嗜麦芽窄食单胞菌，根据药敏试验选用特美汀抗炎；每日应用利尿剂，静脉泵入多巴胺、硝普钠改善心功能，起初反应可，尿量增加，渐出现利尿剂抵抗，患者水肿逐日加重，至周身浮肿，稀释性低钠。根据INR值调整华法令剂量，1.5～3mg/ d，INR波动在1.51～6.23，最高一次为10.14。1月22日出现肉眼血尿，尿常规红细胞满视野，INR为4.87；1月28日INR为1.85，尿常规仍红细胞满视野；2月1日肉眼血尿消失，尿常规RBC 7～10/HP，INR 3.51。患者尿量进一步减少，2月3日全天尿量300ml，对利尿剂无反应。2月4日晨血压下降，心跳减慢直至停搏，给予心肺复苏，呼吸机辅助呼吸后心跳血压恢复，但患者意识未恢复，全天尿量仅20ml，口腔内有血性液体流出，气管镜检查示肺水肿。血气分析：pH 7.318，PO_2 177.9mmHg，PCO_2 50.7mmHg，BE－0.6mmol/L。血生化：BUN 9.96mmol/L，Cr 88μmol/L，钾4.77mmol/L，钠123.7mmol/L。血常规：WBC 11.1×10^9/L，N 0.90，HB 60g/L，RBC 2.14×10^{12}/L，PLT 251×10^9/L；INR 3.28。D-二聚体4.68 mg /L。联系肾科会诊做床旁血滤，肾科意见为患者心肺复苏后24h内血流动力学不稳定，不宜血滤，若情况许可考虑于次日晨行血滤。患者于2月5日晨8:40开始心率减慢，血压再次下降，鼻腔出血，给予多巴胺、肾上腺素、654-2注射液、碳酸氢钠等药物升压、强心、改善循环、扩容、纠酸等治疗，持续胸外心脏按压，抢救无效，患者临床死亡。

2 临床病理讨论

王新华主治医师：该病例特点包括：(1)风心病史40年，9年前行心脏主动脉瓣、二尖瓣人工瓣膜置换术；(2)长期服用华法令抗凝治疗；(3)1年前发现重度贫血，间断输血治疗；(4)此次因气短加重、尿

少浮肿、黑便入院；(5)入院后给予利尿、抗感染、对症支持等治疗，病情曾稳定好转，后来肺部感染诱发心衰急性加重，肺部淤血，氧气弥散障碍，气道痉挛，二氧化碳潴留，又出现呼吸衰竭，酸中毒，各脏器在长期淤血缺氧基础上功能进一步下降，肾脏突出表现为少尿，直至无尿。该患者风湿性心脏病、心衰诊断明确，但临终前无尿的原因不甚清楚。结合该病例，对多脏器功能衰竭患者血滤时机的选择问题值得进一步探讨。

许强主治医师：患者诊断明确，入院后给予利尿、抗炎、对症支持等治疗，病情曾好转，后来感染加重，出现呼吸衰竭，致心跳呼吸骤停，复苏成功。脱机后喘息反复发作，后来利尿剂效果也越来越差，液体潴留，尿少、尿闭，反过来又加重心衰，再次出现心跳呼吸骤停，虽心肺复苏成功，但脑复苏未成功，抢救无效死亡。

高伟副主任医师：患者病情迁延，老年多脏器功能不全，病情曾一度好转，后来感染加重，出现呼吸心跳骤停，成功复苏，并成功脱机。服用华法令，凝血指标 INR 波动较大，间断出现血尿，后来出现尿闭。患者喘息的原因考虑是多因素的，心功能不全是主要因素，合并肺部感染。胸片示心脏大，胸水化验为漏出液，提示心衰重。周身浮肿，给予利尿剂，起初尿量增加，后来对利尿剂反应差，出现了尿闭，又加重心衰，肺部感染不易控制，最终呼吸衰竭、心力衰竭而死亡。分析尿闭原因：(1)反复血尿是否有肾脏集合管系统的血栓形成；(2)患者静脉系统淤血，器官缺血缺氧，影响肾小球的功能。针对尿少采取的措施，血滤时机的选择，值得进一步探讨。

李佳月医师报告病理诊断：(1)风湿性心脏病；(2)主动脉瓣和二尖瓣人工瓣膜置换术后；(3)主动脉瓣混合血栓；(4)主动脉粥样硬化纤维斑块期；(5)双侧肺气肿，轻度肺水肿、肺出血、肺急慢性炎；(6)双侧胸腔积液：左侧约 500ml，右侧约 200ml；(7)血性腹水，约 1 500ml；(8)淤血性肝硬化；(9)全身脏器慢性淤血，以脾、肝等脏器为著。患者的死亡原因：慢性心衰基础上肺部感染造成循环呼吸衰竭死亡。

赵玉生主任：同意以上分析意见。患者长期风湿性心脏病，心脏明显扩大，心衰，肺部感染容易反复发生，利尿效果差，同时有胸水、腹水，原因与慢性心衰静脉压增高有关。患者心脏病终末期，存在呼吸肌的衰竭，第一次复苏成功并顺利脱机后又逐渐出现二氧化碳潴流，代谢性酸中毒加呼吸性酸中毒状态下缺氧加重，肾功能难以改善，水钠潴留亦进一步加重，逐渐出现少尿、无尿。肝淤血最后导致淤血性肝硬化，心衰及肝硬化都可以造成死者的大量腹水。尸检病理见三尖瓣腱索增粗，瓣膜根部钙化，但瓣膜增厚融合不明显，患者生前三尖瓣返流明显，应主要源于功能性返流。主动脉瓣心室面出现混合血栓，不排除血栓脱落造成血栓栓塞，而血栓栓塞以脑栓塞最为常见，死者未做头颅解剖，不能完全排除这种可能。胃内见血样内容物，镜下只见胃黏膜糜烂，黏膜血管扩张，结合病史考虑为缺氧造成的应激性糜烂出血。最后出现多脏器功能衰竭，原因与感染、缺氧有关。华法令会增加出血风险，且该药易受多种因素的影响，该患者在华法令剂量并不大的情况下，INR 值变化较大。在该患者，出血与主动脉瓣血栓情况并存，后来出现多部位出血，考虑与华法令和感染有关。弥漫性血管内凝血诊断依据不足，因患者血小板不低。所以华法令的使用剂量应个体化，严密监测。另外，该患者 CA_{125} 升高，CA_{125} 是卵巢癌的肿瘤指标，病理未发现肿瘤，考虑其升高与心衰时神经、内分泌激活有关，反映了心功能的恶化。已有研究证实了心衰患者心功能与 CA_{125} 的关系。

（参加讨论医师：王新华、许强、高伟、李佳月、赵玉生）

（王新华 整理）