·临床病理讨论·

Clinicopathological Conference

A 53 years old man with multiple organ failure

(The first case)

Case Presentation

Institute of Geriatric Cardiology, General Hospital of PLA

The patient is a man aged 53 yrs old. He had a history of hypertension for ten years, type-2 diabetes for 7 years, fatty liver, lacunar cerebral infarction and prostatic hypertrophy for many years. He had drunk large amounts of alcohol and smoked 50 – 60 cigarettes/day for more than 20 years. His parents, sister and son had diabetes.

The patient was first admitted to our hospital because of chest distress on Jul. 1997. The diagnoses were acute anterior myocardial infarction, old inferior myocardial infarction, heart failure and cardiogenic shock. His condition became stable and he was discharged after emergency treatment . A coronary arteriography examination showed that left descending anterior branch, circumflex artery and right coronary artery were stenotic on Oct. 1997. A stent was implanted in his left descending anterior branch.

The patient did not suffer chest distress and dyspnea until May 2000 when he was admitted to our hospital due to acute inferior myocardial infarction. On admission, his temperature was 36.8℃, the pulse rate was 72, the respiration rate was 20, and blood pressure was 120/75 mmHg(1 mmHg = 0.1333kPa). His general condition was bad with anemic face, diminished breath sound in both lungs, enlargement of cardiac dullness to left, and positive abdominal shift dull sound. Laboratory tests were performed (Tables 1 and 2). Hemorrhage of upper digestive tract occurred more than twice after admission. The final diagnoses were: multiple organ dysfunction syndrome (MODS), acute inferior myocardial infarction, old anterior myocardial infarction, 3rd-degree cardiac function, hypertension, cirrhosis of liver, esophageal varicosis, hepatic encephalopathy, ascites, hypersplenism, type-2 diabetes, diabetic nephropathy and pancytopenia. The patient recovered and was discharged after active treatment in our hospital.

The patient was admitted again because of pulmonary infection in Aug. 2001. His temperature was 37.1℃, the pulse rate, the respiration rate and the blood pressure were 76, 18 and 130/70 mmHg, respectively. His general condition was bad with anemia. Harsh breath sound and moist rales could be heard in both lungs. The border of cardiac dull enlarged to left. The rhythm was normal, and 2nd-degree of systolic murmur could be heard in second intercostal space. Abdomen was distended, and the periumbilical area was red in color but without tenderness. Liver could not be touched under the costal margin, where as the spleen could be touched about 4cm inferior to the costal margin. Abdominal shift dullness sound was positive. Both lower limbs were moderately edematous. Laboratory tests were performed (Tables 1 and 2). Cardiac ultrasonographic examination showed that the contraction amplitudes of the left ventricular postero-inferior wall, anterior wall and upper 1/3 of interventricular septum were decreased, the left atrium was enlarged, the valves had degenerative change and left ventricular function was damaged. Abdominal ultrasonography showed cirrhosis of liver, enlarged spleen, massive ascites, cholecystolithiasis and prostatic hypertrophy. The patient was treated with anti-infective drug, hypoglycemic agent, cardiac tonic, diuretic and so on. However, his condition was severe and he did not become better. The patient suddenly began to breath as sighing respiration at 23:50 on Oct. 29, 2001, and electrocardiogram showed ventricular fibrillation. He died at 1:35 a.m. on Oct. 30, 2001.

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Table 1 Values of hematologic examination

Variable	Aug. 1997	May 2000	Jan. 2001	Aug. 2001	Oct. 2001
Hemoglobin(g/L)	150	92	70	38	64
White-cell count(per L)	9.7×10^9	3.5×10^9	3.5×10^9	4.0×10^9	5.5×10^9
Differential count(%)					
Neutrophils	58	70	82	85	83
Lymphocytes	40	27	15	12	13
Platelet count(per L)	224×10^9	138×10^9	89×10^9	59×10^9	49×10^9

Table 2 Values of blood biochemistry

Variable	Jul. 1997	May. 2000	Jan. 2001	Aug. 2001	Oct. 2001
Urea nitrogen(mmol/L)	N	N	7.61	21.5	34.27
Creatinine(μmol/L)	N	N	158.3	296	374
Calcium(mmol/L)	N	N	2.28	2.06	2.07
Glucose(mmol/L)	17.36	10.46	12	7	7.01
Protein(g/dl)	N	N	N	N	N
Albumin	N	34.9	34.4	23.5	31.6
Potassium(mmol/L)	N	3.12	N	3.37	N
Sodium(mmol/L)	N	N	N	N	N
Chloride(mmol/L)	N	N	116	112	113.6
Carbon dioxide(mmol/L)	N	N	16.8	17	8.6
Magnesium	N	N	N	N	N
Aspartate aminotransferase(U/L)	N	N	N	N	N
Lactate dehydrogenase(U/L)	N	N	N	N	N
Alkaline phosphatase(U/L)	N	387.7	152.5	73	357.3

Report of X-ray examination (Prof. Cai Youquan)

A radiograph of the chest showed exudative inflammation at both lungs in Aug. 2001.

A radiograph of the chest revealed chronic bronchitis on Jan. 9,2001.

A radiograph of the chest showed increased bronchovascular shadows besides chronic bronchitis on Jun. 19,2000.

A radiograph of the lower limb showed osteoporosis of right hip joint without necrosis on Jun. 19, 2000.

A radiograph of the knee joint only showed osteoporosis on Jun. 19,2000.

Clinical Discussion

Dr. Li Yufeng: The patient was admitted because of heart disease in 1997, and MODS was developed in 2001. I have some questions: ① as a 53-years-old male, what were the reasons that deteriorated his disease so fast? ② what was the cause of hepatocirrhosis? ③ what caused hemorrhage of the upper digestive tract? ④ what were the reasons of renal insufficiency?

Dr. Feng Bin: In my view, the patient's bad mental status was one of the major factors that caused his disease to deteriorate so fast. At the beginning, the patient would not like to see a doctor, would not like to communicate with other persons for some reasons. He used to refuse treatment after he was admitted to our hospital. Prof. Wang Shiwen and our medical staffs persuaded him patiently, and finally the patient trusted us. In a word, the psychological factor is an important factor for the development of the

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disease. We should do our best to cure the patient's diseases including his physical and psychological pain so that the patient would have full confidence to defeat all of his diseases.

Dr. Wang Shiwen : The patient refused any treatment when he was first admitted, but he cooperated with us finally after he received psychotherapy in our ward. Sometimes I chatted with him by myself.

Dr. Yan Muyang: I think the causes of hepatocirrhosis were : ① alcoholic cirrhosis due to consumption of alcohol for a long time; ②he had a history of hepatitis A and suspicious hepatitis B.

Dr. Xu Yaqin: What was the cause of hemorrhage of the upper digestive tract? In my opinion, hepatocirrhosis was the possible cause owing to long period of alcohol consumption, but there were no direct evidences, so we should consider other reasons which included the presence of disorders of esophagus and stomach, hematopathy and/or panhematopenia resulted from hemorrhage, gastrorrhagia induced by stress.

Dr. Zhang Xiaoying : The patient began to have renal dysfunction in 2000. The chronic renal dysfunction in decompensation stage was certainly diagnosed. The renal function could be affected by following diseases: ① seven years of diabetes mellitus; ② hypertension; ③ anemia; ④ infection and bleeding; ⑤ ischemic nephropathy.

The differences between diabetic nephropathy and hypertensive one include: protein in urine occurs earlier and progresses more rapidly in diabetes mellitus than in hypertension; the glomerular affection also occurs earlier than tubular affection in diabetic nephropathy; the hypertensive nephropathy usually lasts a longer period; the quantity of protein in urine is usually less in hypertensive nephropathy than in diabetic one. The patient had both diabetes mellitus and hypertension, so his renal dysfunction progressed rapidly.

Dr. Ye Ping: The patient had the following characteristics: ① long history of diabetes mellitus which hadn't been well controlled; ② hypertension; ③ heart failure; ④ renal failure; ⑤ hepatic dysfunction; ⑥ decrease in all blood counts. The diagnoses were: ① MODS with recurrent pneumonia which was the very common trigger for MODS in the elderly; ② multi-factorial heart failure induced by coronary artery disease, diabetic microangiopathy involving cardiac parasympathetic nerve as well as hypertension. Pneumonia aggravated the heart failure.

The cause of upper gastrointestinal hemorrhage left doubt. Although the esophageal-gastric varices caused by hepatocirrhosis would be the etiology. The patients just had tarry stool but no hematemesis. Other uncertain disease must exist, especially esophageal-gastric diseases.

Dr. Wang Jianchang from Geriatric Department of Air Force General Hospital: This patient had coronary angiography in the past. Was there any influence of contrast medium on renal function?

Dr. Zhang Xiaoying: In clinical aspect, almost 1/3 − 1/2 of the patients with coronary artery disease were concurrently found to have renal artery stenosis. On the other hand, profuse bleeding could induce ischemic renal failure.

Dr. Huang Jian: I'd like to give my points on the reasons of anemia. ① hypersplenism: all blood cells reduced with a normal marrow; ② the decrease in red blood cells and hepatic dysfunction were related to renal dysfunction. The decreased glomerular filtration rate (GFR) damaged the red blood cell function and caused reduction in its number. Hematopoietic growth factor erythropoietin also reduced in renal decompensation; ③ bleeding; ④ MODS also exacerbated anemia.

Dr. Zhou Jun from Xinjiang: The patient experienced hematuria, which maybe related to the damage of the hepatic and renal function. Could hemorrhage of the upper digestive tract cause hematuria?

Dr. Wang Shiwen: Hematuria could occur with hemorrhage of upper digestive tract , it is often related to the stress.

Dr. Yu Jiang from the General Hospital of the Armed Police : The patient was diagnosed with fatty liver in 1997, but he was found to have hepatocirrhosis 3 years later, which developed more quickly than usual. I want to know did he have viral hepatitis es-

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pecially hepatitis B. The laboratory findings showed that HBsAb, HbeAb and HbcAb were all positive, which represented the reproduction of hepatitis B virus.

Dr. Gao Jun from the 302nd Hospital: In the past, people thought that it means the reproduction of hepatitis B virus when HBsAb , HBeAb and HBcAb are all positive, but the opinions have changed. It is difficult to discover the reproduction of hepatitis B virus in this condition.

Dr. Liu Lixin : The following evidences support the diagnosis of the cirrhosis of liver: ① the patient drank large amounts of alcohol in the past 20 years, which can cause the chronic liver damage; ② he had suffered from hepatitis A and the laboratory findings showed that HBsAb, HBeAb and HBcAb were all positive which meant that he had experienced hepatitis B; ③ he had the hemorrhage of upper digestive tract and hydroperitoneum. Some evidences also showed that he had hypersplenism.

The renal function changed a lot at the end stage, SCr and BUN increased significantly. As Dr. Zhang has said that it is mostly related to the development of the renal disease, but I wonder if the patient has hepatorenal syndrome. It seems that there is certain relation between the changes of SCr , BUN and the severity of the hydroperitoneum. Did the patient have the prerenal factor to influence the renal function?

The patient had significant anemia, the causes of which may be manifold, such as hypersplenism, renal failure. He received various treatments including erythropoietin , vitamins, microelements, iron supplement and so on, but had little improvement. I think that the renal failure is not the most important cause of anemia.

Dr. Zhang Yun from the 304th Hospital : The patient had a history of left leg pain and also had hematuria. Did these symptoms relate to the renal disease, especially the possible embolism?

Dr. Ma Lu: The pain was of the joints, not the left leg .

Dr. Wang Yumei from the 304th Hospital: Since this patient was found to have MODS when he was only 53 years old, his illness should be happened on the basis of a longtime development. During this course, the viscera affected each other, therefore the failure of one organ was the results of multiple causes. MODS was also the results of interaction of different causes. It enlightens us that different aspects should be considered whenever we diagnose any disease.

Dr. Zheng Wei: I have several questions to ask: ① why did the heart remain less enlargement even if the patient had hypertension, diabetes mellitus and myocardial infarction for many years? ② was it enough to diagnose the hemorrhage of upper digestive tract according to the tarry stools? ③ how the sudden deterioration of the illness after a short time of amelioration before his death can be explained? ④ did the electrolyte disturbance exist when he was dying?

Dr. Yan Muyang: Ultrasound examination a month before he died showed that the kidney had shrunk, the echo was enhanced and the value of ejection fraction (EF) was 40%. We advised the patient to test the electrolytes when he had nasal bleeding, loose stools and oliguria, but he refused to do it, so we had little information about the electrolytes, maybe it was the underlying cause for ventricular fibrillation.

Dr. Guo Xiadong from Dept. of Radiology: The diagnosis of the MODS is sure, but the patient had a history of pneumonia and was bedridden, maybe the direct cause for his death was pulmonary embolism although the lung was negative from the X-ray. The magnetic resonance imaging (MRI) or enhanced CT scan could confirm the diagnosis.

Pathological Discussion

Dr. Yin Tong: Autopsy was carried out 63h after the death. The main pathological changes were found in the vital organs: heart, lung, liver and kidney.

Heart: From the gross appearance, the weight of the heart and the thickness of the left ventricular

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wall increased. The left anterior descending coronary artery was almost blocked totally and 50% – 75% of the left circumflex artery, 50% of the right coronary artery were blocked. Under the light microscope, there were many foci of old infarction scattered in at least 40% areas of the left ventricle.

Diagnosis: Old myocardial infarction of left ventricle.

Lung: The weight of bilateral lungs increased. There was some pale secretion in the main bronchi. On squeezing, pink edema fluid effused from the section. Under the microscope, there was pale stained edema fluid. Erythrocytes and heart failure cells could be seen in the lung alveoli. In the alveolar walls, besides the dilated capillaries, there were hyperplasia of the collagen fibers and infiltration of the leucocytes.

Diagnosis: Edema and congestion of the lungs.

Liver: The liver was enlarged, but its surface was smooth. The color of the liver was from brown to red. In the cross section, there was no any nodular change. Microscopically, The hepatic lobules were regular and serious congestion could be seen in the hepatic sinusoids. Most of the hepatocytes near the central vein were necrotic(centrilobular necrosis) with the appearance of the so-called "nutmeg" liver. In the portal areas, infiltration of the lymphoytes and hyperplasia of the bile ducts were common.

Diagnosis:Chronic congestion of the liver.

Kidney: There were no apparent changes macroscopically. Under the microscope, atrophy of the renal corpuscles could be seen. In the glomeruli, there was accumulation of the amyloid material. Arteriolosclerosis could also be seen in some glomeruli.

Diagnosis: Hypertensive nephropathy and diabetic nephropathy.

Dr. Liu Aijun: The major pathological findings were: ① extensive old myocardial infarction with apex aneurysm; ② severe atherosclerosis: 3rd-degree and 4th clinical period for the aorta, 2nd to 4th clinical period for left anterior descending coronary artery; ③ hypertensive heart disease; ④ edema and congestion of the lungs; ⑤ diabetic nephropathy and hypertensive nephropathy; ⑥ indistinct chronic anemia; ⑦ severe congestion of the liver and fatty liver.

Except the changes of autolysis, there was no any obvious lesion in other organs.

From the aforementioned pathological changes, we can conclude that the death of the patient was caused by ventricular fibrillation as the result of extensive MODS.

Dr. Wang Shiwen: I propose a new medical term, *i.e.* multifactorial heart/renal failure, from this case, and we shall carry out statistic work on this disease. In treatment, we should consider the following aspects: ① it is most important to adjust metabolism and supply enough energy for successfully saving patients' life; ② the key is to solve the major problem. Pulmonary infection was this patient's major problem, so active treatment of pulmonary infection was the key for recovery of the patient; ③ pulmonary infection is often induced and is an important initiative factor of MODS in old patients; ④ correct use of medicines is also important.

1例53岁男性多器官衰竭

(第1例)

1 病例摘要

患者,男性,53岁,汉族,已婚,干部。有吸烟、饮酒史20年,高血压病史10年,2型糖尿病史7年,并有脂肪肝、腔隙性脑梗死、前列腺肥大等病史。1997年7月患急性前间壁心肌梗死、陈旧性下壁心肌梗死、心力衰竭、心源性休克,住解放军总医院老年心血管病研究所,经抢救病情稳定出院。同年10

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月作冠脉造影示 3 支血管病变、左室活动减弱、心尖部运动消失。左前降支植入支架。于 2000 年 5 月又因急性下壁心肌梗死入院，贫血貌，一般情况很差，心源性休克前期，肺部感染，腹水，全血细胞减少，血糖高。入院后多次出现柏油样便，血红蛋白(Hb)下降到 58g/L，红细胞(RBC)1.74×10^{12}/L，伴神志异常，诊断为 MOF，冠心病，急性下壁梗死、陈旧性前壁心肌梗死、心功能Ⅲ级，高血压病，肝硬化，食管静脉曲张，肝性脑病，腹水，脾功能亢进，2 型糖尿病，糖尿病性肾病，全血细胞减少。入院后经抢救，病情渐趋稳定出院。2001 年 8 月 13 日因肺部感染再次入院，贫血面容，体温 37.1℃，心率 76 次/min，律齐，双肺呼吸音粗，少量湿罗音，有腹水征，双下肢浮肿。化验：Hb 50g/L，RBC 1.69×10^{12}/L，血小板(PLT)65×10^{9}/L，白细胞(WBC)3.8×10^{9}/L、中性 0.835、淋巴 0.134，血肌酐 296μmol/L，尿素氮 22.64mmol/L，总蛋白 58g/L，白蛋白23.5g/L，总胆固醇 1.93mmol/L，尿红细胞满视野，尿蛋白 1.5g/L，尿糖 1000/L，超声心动(UCG)：左室下后壁、前壁、室间隔上 1/3 收缩运动减弱，左房扩大，左室功能受损。腹部超声：肝硬化，脾肿大，腹水(大量)，胆囊多发性结石，前列腺肥大。经积极治疗，病情仍危重，2001 年 10 月 29 日晚 23:50 突然出现叹气样呼吸，心电图示室颤，经抢救无效死亡。死亡原因：广泛陈旧性梗死，多器官功能衰竭导致室颤。

2 临床讨论

本例罹患高血压、2 型糖尿病、冠心病多年。于 1997 年出现急性前间壁心肌梗死，并发心衰及心源性休克。治疗好转后作冠脉造影证实有 3 支血管病变，于左前降支植入支架。2000 年又发生急性下壁心肌梗死，并发腹水及全血细胞减少、肺部感染、多次柏油样便，经救治好转。2001 年 8 月因肺部感染再次住院。有全血细胞减少、腹水、血尿、低蛋白血症、肾功能不全、左室功能障碍(LVEF 40%)、MOF。2 个月后一日深夜突发性室颤死亡。① 患者有多年高血压及糖尿病史，且糖尿病未获良好控制，有严重冠心病，曾多次发生心肌梗死、伴左室功能不全、心力衰竭、肾功能衰竭、肝功能障碍，故 MOF 的诊断可以成立。患者曾有肺部感染的反复发作，肺部感染是 MODS 的触发因素，在老年人尤其常见。② 患者的心力衰竭除由严重冠心病所致外，与高血压性心脏病及糖尿病性微血管病变亦有关系，因而可以称为多因性心力衰竭。③ 腹部 B 超提示有肝硬化，临床上有腹水、脾大、低蛋白血症、全血细胞减少，其原因可能为酒精性肝硬化，因患者有长期大量饮酒史，亦不能排除慢性乙型肝炎演变所致。④ 慢性肾衰、失代偿期，其原因可能为：糖尿病性肾病及高血压性肾损害联合作用所致。前者一旦发生蛋白尿，病情进展较快，对肾小球的影响早于对肾小管的影响。后者则发展较慢，尿蛋白少于前者。由于患者既有糖尿病性肾病，又有高血压性肾损害，故其肾功能不全发展快速。此外，感染及出血亦加重了肾功能的恶化。⑤ 上消化道出血，其原因可能为肝硬化引起食管静脉曲张出血所致，但缺乏直接证据。其他原因亦不能排除，如食管及胃本身疾患、血液病、凝血机制障碍、心脏应激引起胃粘膜糜烂出血等。

临床诊断：冠心病、陈旧性广泛心肌梗死、2 型糖尿病、糖尿病性肾病、高血压、高血压性心脏病、高血压性肾损害、腔隙性脑梗死、胆结石、肝硬化、肝功能衰竭、全血细胞减少、慢性肾衰、左室功能不全、心力衰竭、消化道出血、肺部感染、MOF、室颤、心因性猝死。

(参加讨论医师有：李玉峰、冯斌、晏沐阳、徐雅琴、张晓英、叶平、黄容、刘立新、蔡友权、张平、王士雯等)

3 病理讨论(尹彤、刘爱君医师)

尸体解剖主要检查了心、肺、肝、肾等重要脏器，其他脏器除自溶性改变外，未见其他显著变化。

主要病理改变：① 陈旧性广泛心肌梗死，前侧壁、心尖部室壁瘤。② 严重的动脉粥样硬化：主动脉 3 级，临床 4 期，前降支 2～4 期；③ 高血压性心脏病：左室壁厚 1.6cm；④ 肺淤血，局部有肺水肿；⑤ 糖尿病性肾病、高血压性肾病；⑥ 慢性贫血不明显；⑦ 重度肝淤血、脂肪肝。

死亡原因：猝死(MODS，广泛心肌梗死基础上发生室颤导致死亡)。

王士雯院士：通过这个病例，我提出一个新名词：多病因心衰，多病因肾衰(multifactorial heart/renal failure)，今后我们将统计这些疾病。在治疗上主要从以下几方面注意：① 代谢调节，能量补充，这对抢救的成功至关重要；② 抓主要矛盾，该患者以肺部感染为其主要矛盾，治疗肺部感染对整体病情的改观十分关键；③ 老年人发病多从感冒、呼吸道感染开始，进一步启动 MODS，因此，肺部感染是 MODS 的启动因素之一；④ 合理用药，随时调整营养。

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