·临床病理讨论·

Clinicopathological Conference

An 85 year old woman with paroxysmal precordial pain and chest compression

(the eleventh case)

Case presentation

Institute of Geriatric Cardiology, Chinese PLA General Hospital

The patient, female, 85 years old, was admitted to the hospital because of paroxysmal precordial pain and chest compression for 7days with aggravation for 13 hours.

The patient suffered from precordial pain and chest compression during sleep, which persisted for 20 minutes or so and were relieved by taking through sucking the Chinese drug "Suxiaojiuxinwan" and "Fufangdanshendiwan". The above symptoms occurred 3 to 5 times every day without intensive treatment and got more severe as bursting pain at 22:00 on December 29, 2003. The pain radiated to the left shoulder accompanied with perspiration and pallor of face. The bursting pain had persisted for 3 hours without remission before the patient was admitted on emergency on Dec 29, 2002. Because ECG of the patient indicated that ST segment decreased by 0.2 - 0.3 mV in leads Ⅱ, Ⅲ, aVF and 0.3 - 0.5 mV in V1-V6 leads, meanwhile T wave was inverted in V1-V6, the patient was diagnosed as coronary heart disease, acute non-ST-segment elevating myocardial infarction.

The past history consisted of acute myocardial infarction in 1993 (the location was unknown), hypertension for 40 years, cerebral embolism in 1986 and 1998 respectively.

Physical examination: The temperature was 36.5℃, pulse was 70 per minute, and blood pressure was 110/62 mmHg. The patint was conscious with chest deformity. Chest percussion found hyperresonance. The respiratory sound was clear. Neither dry nor moist rales were heard in both lungs . The heart rate was 70 beats per minute, cardiac rhythm was regular and a grade 3 /6 systolic murmur was heard at auscultation area of aortic and mitral valves. No positive sign except the liver enlargement was found in abdominal examination. There was no peripheral edema at lower extremities. ECG demonstrated sinus rhythm, ST segment decreased by 0.2 - 0.3 mV in leads Ⅱ, Ⅲ, AVF and 0.3 - 0.5 in leads V1-V6 and T wave was inverted in V1-V6. Myocardial enzyme examination showed that CK-MB was 21U/L and troponin cTnI 0.385 ng/ml. Examination on Jan 2, 2003 found that CK was 934. 2U/L , LDH1127. 5U/L, cTnI 35.2 ng/ml and AST 719 mmol/L.

The patient got angina at 9:00 on January 1st and received accelerated dropping of isosorbide mononitrate. At 17: 40 the precordial pain occurred again without remission followed by continuous dropping of blood pressure, speeding up of heart beat, moist rales over both lungs and cyanosis. ECG indicated elevation of ST segment by 0. 1 mV in lead aVR in addition to the existing ST-T change in other leads. Arterial gas analysis suggested metabolic acidosis and hypoxemia. At 19: 45 the patient was in light coma with heart rate 37 beats per minute, blood pressure 64/43 mmHg, and breath rate 12 per minute. Treatment with coramine, atropine, dopamine and 654-2 intravenous injection and sodium bicarbonate intravenons drip was given. At 20:05 tracheal intubation through mouth, respirator for assisting respiration, dopamine for maintaining blood pressure and IABP implantation were given. At 0: 55, the patient became conscious, the blood pressure was stable under maintenance treatment with sodium nitroprusside and dopamine, acidosis was corrected and electrolytes were normal. Afterward, the patient's condition was still critical and the myocardial enzymes rose progressively. At 16: 45 on January 1st, the temperature elevated to 39.2℃ and ECG showed paroxysmal ventricular tachycardia followed by ventricular escape beat rhythm, tachpnea, pallor of face and cyanosis of lips, the peripheral blood pressure could not be measured, moist

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rales could be heard at both lung bases, ECG showed paroxysmal ventricular escape beat rhythm and paroxysmal ventricular tachycardia. All emergency treatments failed. At 18:40, the patients had no autonomous respiration, no electrocardiac activity and finally died.

Clinical discussion

Dr. Zhang Wenli: According to the symptoms, physical signs, ECG and myocardial enzyme of the patient, the diagnosis of "coronary heart disease, acute non-ST segment elevating myocardial infarction" was clear. Since the patient suffered from extension of infarction again in a short period, some factors such as the disturbances of metabolism, electrolytes and acid-base balance might play roles in the worsening of his condition. Generally, the aged is less vulnerable to penetrating myocardial infarction than the youngers, but the fact that the patient developed cardiogenic shock and significnat increasing of cardiac enxymes suggested that the infarction lesion had penetrated the whole wall. Serious consideration should be taken for the choice of interventional therapy for this kind of patients, because the atherosclerotic lesions in the elderly are extensive and so fragile and sensitive that even a light stimulation might lead to a severe cardiac event.

Dr. Gao Wei: The prognosis is bad when the aged patients suffer from non-ST segment elevating MI. Usually, cardiogenic shock happens when the area of infarction is over 40% of the myocardium, so I estimate that the area of infarction of this patient was extensive. That was why the patient inevitably experienced cardiogenic shock, multiple organ failure and final death in such a short time despite the active treatment with drugs and IABP implantation.

Dr. Gao Lei: The extension of infarction probably had something to do with the following factors: constipation, spasm of coronary artery, and some other factors. Non-ST elevating MI in the elderly often indicates that the lesions are extensive and IABP should be implanted to improve the perfusion of important organs.

Dr. Tian Jinwen: I agree with the present diagnosis of "acute non-ST-segment elevating MI". Considering that the features of ST segment elevation in aVR lead as well as extensive depression in precordial leads and irreversable dropping of blood pressure, infarction in right ventricle was highly suspected.

Dr. Yan Muyang: The mortality would rise to 70% - 80% when acute coronary syndrome in the elderly leads to cardiogenic shock. According to the ECG findings, I think the coronary aterial lesions were extensive. It was the collateral circulation that supplied the oxygen for the myocardium, but its ability of compensation was not enough. Any stimulation, such as infection and sympathetic stress, might cause severe cardiac event. Assistant instruments, IABP and respirator should be used in time, moreover, emergency interventional therapy targeting at the culprit arteries is also crucial because it can improve prognosis.

Dr. Zhao Huaibing: Infarction extension is the state of *in situ* worsening of ongoing MI. Since the old female patient experienced extensive subendocardial MI, cardiac dysfunction, slow flow of blood stream and irritable state of coronary artery as well as vascular spasm might cause infarction extension. Furthermore, a grade-3 systolic murmur was heard at auscultation area of mitral valves. If it was verified to be a new sign, papillary muscle dysfunction after MI should be highly suspected. In my opinion, interventional therapy should be given as soon as possible.

Dr Cheng Rui: The inconsistency in the early stage between significant depression of ST segment and minor changes of myocardial injury indicators suggested that the myocardial infarction was local, while the following changes of myocardial injury indicators suggested infarction extension. In my opinion, ischemic reperfusion injury and endothelial dysfunction might take part in the pathogenesis of infarction extension. Considering that the acute coronary artery syndrome in the elderly mostly has extensive lesions and leads to obvious coronary stenosis, antiplatelet therapy instead of thrombolysis is strongly recommended.

Dr. Zhao Yusheng: The clinical characteristics of this case were advanced age, female, past history of hypertension, cerebral embolism, and old myocardial infarction. The patient suffered from unstable angina, unpenetrating MI, postinfarction angina and infarction extension. Attention should be paid to the following points: Firstly, ST segment elevation in aVR lead accompanied with extensive ST segment depression in leads of anterior wall and inferior wall always suggests a severe occlusive lesion in left main coronary arteries or somewhere else, which always leads to poor prognosis. Secondly, according to the pathophysiological character of non-ST segment elevation myocardial infarction in the elderly, thrombolysis is not recommended. Retrospective and prospective studies showed that thrombolysis for this kind of cases would increase the mortality, while interventional therapy would rescue more myocardium and seems to be more beneficial to the elderly than to the young. Finally, the thrombus in coronary artery in the elderly is mainly caused by platelet aggregation, so it is important to reinforce the anti-coagulation therapy. Platelet aggregation inhibitor and statins can obviously improve the prognosis.

Pathological Discussion

The main autopsy diagnosis: atherosclerosis, coronary atherosclerotic heart disease, acute myocardial infarction, cardiac apex, which involved anterior wall, lateral wall and inferior wall of left ventricle, papillary muscles of posterior wall of left ventricle, interventricular septum as well as right ventricle. There were many old infarction foci at cardiac apex anterior wall, lateral wall and inferior wall. The infarction was located in the inner 1/3 of cardiac ventricular wall (subendocardial infarction), at cardiac apex and anterior wall with local infarct penetrating the whole wall (transmural myocardial infarction).

The stenosis degree at the starting part, middle part and distal part of the left anterior descending coronary artery was 50% - 70%, 60% - 90% and 20% - 40% respectively, that of the starting part and distal part of left circumflex branch of coronary artery was 40% - 60% and 30% respectively, and that of the starting part, middle part and distal part of the right coronary artery was 50% - 80%, 30% - 60% and 20% respectively. The aortic atherosclerosis belonged to grade-Ⅳ and was in the process of compound lesion. Atherosclerosis of cerebral arteries belonged to grade Ⅰ-Ⅱ. There were old cerebral infarction at bilateral basal nuclei, edema and emphysema in both lungs, collapse of upper lobe of left lung and lower lobe of right lung, edema of lower lobe of right lung, local obstructive organized pneumonia at middle lobe of right lung. Hydrothorax was found: 150 ml in left pleural cavity and 400 ml in right. There were many foci of erosion and hemorrhage in gastric mucosa, congestion in most of the organs (stomach, intestine, liver, spleen, adrenals and kidneys), erosion of lower segment of esophagus accompanied with large amount of chronic inflammatory cell infiltration, colloid adenoma of 0.8 cm in diameter in right lobe of thyroid gland.

(Translator: Zhang Yi, Ma Jing)

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阵发性心前区疼痛、胸闷一例

1 病历摘要

患者,女性,85岁,主因发作性心前区疼痛、胸闷7 d,加重13 h于2002年12月30日入院。患者缘于2002年12月23日夜间睡眠无明显诱因出现心前区疼痛,胸闷,范围巴掌大小,持续20 min不

等，含服“速效救心丸、复方丹参滴丸”后缓解。上述症状一天发作3～5次，未曾就诊。2002年12月29日22:00患者无明显诱因再次出现心前区疼痛，性质较前剧烈，呈撕裂样，向左侧肩部放散，伴大汗，面色苍白，无恶心呕吐，持续3 h不缓解，急呼120送至解放军总医院急诊科，行心电图检查示Ⅱ、Ⅲ、aVF导联ST段水平下移0.2～0.3 mV，V1-6 ST段水平下移0.3～0.5 mV不等，T波倒置，急诊以“冠心病、急性非ST抬高性心肌梗死”收住院。

既往1993年曾患急性心肌梗死（部位不详），40年高血压病史，1986年和1998年2次患脑血栓病。

体格检查：体温36.5℃，心率70次/min，呼吸18次/min，血压110/62 mmHg，神清，胸廓畸形，双肺叩诊呈过清音，听诊呼吸音清晰，未闻及干湿啰音，心率70次/min，律齐，心尖部及主动脉瓣听诊区可闻及3/6级收缩期杂音，腹平软，无压痛，肝脏肋下2.0 cm，脾肋下未及，全腹叩诊呈鼓音，双下肢不肿。辅助检查：心电图：窦性心律，Ⅱ、Ⅲ、aVF导联ST段水平下移0.2～0.3 mV，V1-6 ST段水平下移0.3～0.5 mV不等，T波倒置。心肌酶：CK-MB 21 U/L，肌钙蛋白0.385 ng/ml。住院后给予吸氧、扩冠、抗凝等治疗，2003年1月2日CK 934.2 U/L、LDH 1127.5 U/L、肌钙蛋白35.2 ng/ml、AST 719 mmol/L。

患者1月1日9:00出现心绞痛发作，加快爱倍滴速后症状缓解，17:40再次出现心前区疼痛，较上午剧烈，持续不缓解，血压进行性下降，心率增快，查口唇紫绀，双肺闻及湿性啰音及哮鸣音，心电图aVR导联ST段抬高0.1 mV，余导联ST-T改变较前无明显变化（图1），动脉血气分析示低氧血症并

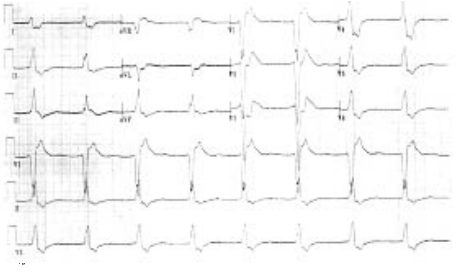

图1 心电图表现

注：窦性心率，aVR导联ST段抬高0.1 mV，Ⅱ、Ⅲ aVF导联ST段水平下移0.2～0.3 mV，V1－6 ST段水平下移0.3～0.5 mV不等，T波倒置

代谢性酸中毒19:45出现浅昏迷，心率37次/min，血压64/43 mmHg，呼吸12次/min，给予尼克刹米、阿托品、多巴胺及654-2静推，碳酸氢钠静滴等治疗，20:05给予经口气管插管，呼吸机辅助呼吸，多巴胺维持血压，急诊置入主动脉内球囊行主动脉内球囊反搏治疗，0:55患者意识清楚，血压在硝普钠和多巴胺维持下较稳定，代酸纠正，电解质正常。后病情仍较危重，心肌酶进行性升高，2004年1月2日患者于16:45体温39.2°C，心电示波短阵发性室性心动过速，随后出现室性逸搏心律。呼吸急促，外周血压测不到，面色苍白，口唇紫绀，双肺底部可闻及湿啰音，心电示波阵发性室性逸搏心律，阵发性室性心动过速，经抢救无效，18:40患者无自主呼吸，无心电活动，临床死亡。

2 临床病理讨论

尸体解剖主要所见：动脉粥样硬化症，冠状动脉粥样硬化性心脏病，广泛性急性心肌梗死，累及心尖、左室前壁、侧壁、下壁、左室后壁乳头肌、室间隔、右室；多灶性陈旧性心肌梗死，主要累及心尖、前壁及下壁，并可见于上述发生急性心肌梗死的部位。梗死范围主要为心室壁内层1/3（心内膜下），心尖及前壁局部达全层（透壁性梗死）。左冠脉前降支起始部、中间段、远端狭窄程度分别为50%～70%、60%～90%、20%～40%（图2）；左旋支起始部、远端

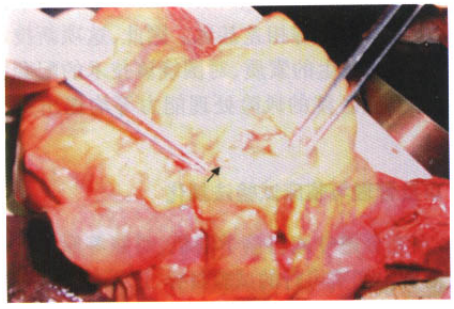

图2 冠状动脉尸检结果

注：左冠状动脉管壁僵硬，管腔狭窄呈同心圆性，狭窄程度约为85%～95%

狭窄程度分别为40%～60%、30%；右冠脉起始部、中间段、远端狭窄程度分别为：50%～80%、30%～60%、20%，主动脉粥样硬化Ⅳ级，复合病变期；脑动脉粥样硬化Ⅰ－Ⅱ级。双侧基底节区陈旧性腔隙性脑梗死。双侧肺淤血、肺气肿；左肺上叶、右肺下叶肺萎陷；右肺下叶轻度肺水肿；右肺中叶局部阻塞性

机化性肺炎。双侧胸腔积液:左胸腔 150 ml,右胸腔 400 ml,胃黏膜多灶糜烂伴出血:胃内见咖啡色液体 200 ml,全身多脏器(胃肠、肝、脾、肾上腺、肾)显著淤血;食道下段黏膜糜烂伴多量慢性炎细胞浸润;甲状腺右叶胶样腺瘤,直径 0.8 cm。

结合病理检查及临床病史,认为本例患者死因明确,系由于在陈旧性心肌梗死的基础上发生广泛急性心内膜下心肌梗死及局部透壁性心肌梗死,导致心源性休克,心功能衰竭死亡。

分析本病例特点为:(1)老年女性,起病急,病情进展迅速。(2)既往有高血压、陈旧性心肌梗死及脑血栓病史。(3)入院后先后发生不稳定性心绞痛,非透壁性心肌梗死,梗塞后心绞痛,梗塞延展,继而出现心源性休克,泵衰竭,最终死亡。由于心源性休克多在心肌梗死后发生在心肌坏死范围超过 40% 时,故推断该患者心内膜下心肌梗死累及范围较大,血管病变较广泛,心肌供血主要依靠侧支循环,代偿能力较差,因此,虽然经过积极的扩冠、抗凝、IABP 植入等治疗,仍然引发严重的心血管事件。

老年患者发生非 ST 段抬高型心肌梗死时,预后较年轻人差。许多因素如情绪应激、冠脉痉挛、便秘以及酸碱失衡、电解质紊乱等都可导致梗塞延展,此类患者应尽早选择介入治疗,重建血管,挽救存活的心肌,可明显改善预后。同时 IABP、呼吸机的时机选择恰当及时也可避免严重心性事件的发生。在诊断方面,若心电图显示下壁、前壁导联广泛的 ST 段压低、T 波倒置,同时存在 aVR 导联 ST 段抬高,多提示左主干病变或左主干等同病变,若及时尽早干预可明显改善预后。另本病例的冠脉病变特点也提示老年人冠脉病变多为硬斑块造成固定的严重狭窄,即使小血栓形成也可造成管腔的完全闭塞,同时累及范围较大,这些病理生理特点决定了此类患者不宜行溶栓治疗。回顾性和前瞻性研究结果都显示这些患者溶栓治疗可能会增加死亡率,但尽早行介入治疗则可以尽可能地挽救存活的心肌。而且老年人血管腔内的血栓多为白血栓,因此尤其要加强抗凝治疗,应用血小板聚集的抑制剂和他汀类药物可明显改善预后。

(马晶,赵玉生整理)

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度不一,使得移植后效果、效果维持的时间、不良反应及最终的预后等相差甚远。因此,这项新技术的开展对临床医生的素质、对围绕该技术的配套医疗技术及实施医院的风险处理能力等均提出更高要求。

3 审批管理与临床试验法规化

在充分遵守流行病学随机、对照等原则的基础上,需确定切实可行的试验目标、选择合理的试验方法、招募有代表性的受试者、确立试验结果的评价指标、选用已充分验证的评价工具、决定最佳的治疗时间和随访期限、计算试验所需的样本量、规定数据处理原则、试验方案的实施,还要考察是否严格执行临床试验研究的伦理原则等,每一环节都与试验结果的可靠性息息相关。需要强调的是,训练有素的研究人员和临床医生对操作过程、围移植期和随访情况的详细记录是十分必要的,人们可及时根据反馈信息对操作进行分析和改进,促进干细胞移植基础与临床研究的发展。

由于干细胞工程产品的"个体化、鲜活性、体内再生"等特征,与普通药物或一般体细胞治疗和基因治疗不同,但在体外进行处理过程中仍将接触器皿、培养基、血清、细胞因子、化学试剂、分离液等等,也存在病原体污染、热源等风险,也应有严格的操作标准,除注重此领域相关的伦理法规外,同样也需获得国家药品食品监督管理局(SFDA)的批准(不经体外处理的治疗方案除外)。同时,还应制定相关的临床准入条件、标准和管理办法,与"产品"报批结合,各有侧重,相辅相成,最终使"合法"产品应用于"准入"医院。