·临床病例讨论·

Clinicopathological Conference

A 77 year old man with pleural effusion and dyspnea after complete response of non-Hodgkin's lymphoma

(The twelfth case)

Case presentation

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The patient, male, 77 years old, was diagnosed to have non-Hodgkin's lymphoma(NHL) for 2 years and got chest distress and cough 5 days prior to the admission. In 2003, the patient was found to have left epididymis tubercle and left inguinal lump, accompanied with gross hematuria. After biopsy examination, NHL of diffuse large B-cell type, stage IV and CD20(+), was diagnosed. He accepted 8 courses of chemotherapy with CHOP and Mabtherapy treatment from 2003. After 2 cycles of therapy, the mass was deflated and gross hematuria disappeared, then he attained complete remission at last. He completed the last chemotherapy on June 11, 2004. From September 27, 2004, the patient developed chest distress, cough, a little and ropy sputum without fever, chest pain, night sweat, abdominal pain, diarrhea, urgency of urination, and odynuria. Two days later, low-grade fever appeared and the highest temperature was 37.3℃. From October 2, he began to have short breath on exertion, aggravation of cough and expectoration. The sputum increased in volume and was blood tinged. His past medical history included diabetes, laryngocarcinoma (postoperarion), prostate hypertrophy, etc.

The physical examination showed acute sick complexion. His temperature was 35.4℃. He was tachypneic, with a respiratory rate of 30 breaths per minute, but the pulse and blood pressure were normal. An enlarged lymph node as a soybean without tenderness was found in left iliac fossa. The breath sound diminished in the left middle and lower lung field and no rale was heard.

The laboratory examination showed that the white blood cell count was 10.3×10^9/L, hemoglobin 114 g/L, platelet 270×10^9/L, and neutrophile granulocyte 82%. ESR was 52 mm first hour. Blood biochemistry showed that only albumin was decreased and the others were nearly normal. X-ray examination showed left pulmonary atelectasis.

After considering the symptoms, signs and laboratory examinations, the diagnosis of atelectasis was made. The cause of left pulmonary atelectasis was unclear, was it pneumonia or other disease, such as NHL? After admission, anti-infection and supporting treatments such as antibiotics (sodium piperacillin, sodium cefoperazone tazobactam), expectorants, immunoglobulin and albumin were given. But the symptoms such as chest distress and dyspnea were aggravated progressively and temperature was increasing, with the highest being 38.4℃. The patient was obviously tachypneic, with the highest respiratory rate attaining 39 per minute. The other signs didn't change obviously. On October 5, ultrasound examination showed left pleural effusion and left pulmonary atelectasis. The symptoms still couldn't be relieved though thoracentesis and closed drainage were performed. Examination of pleural effusion showed that the red blood cell count was 362×10^6/L, white cells 4×10^6/L, protein 31.9 g/L, sugar 6.61 mmol/L and chloride 116.3 mmol/L. Tumor cell was not found in pleural fluid by repeated examination and tuberculosis test was negative.

The first clinical discussion

Doctor A (*Respiratory Department*): The clinical characteristics of this patient were advanced age, male, past history of NHL and laryngeal carcinoma. The patient

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now suffered from chest compression and shortness of breath with mild cough and a little sputum. We didn't find the obvious precipitating factor. We found the atelectasis in X-ray film (Fig 1a) and saw moderate volume of pleural effusion in left pleural cavity by ultrasonic examination. I believe that the compression by the fluid caused the atelectasis. The patient did not respond to antibiotics and supporting treatment. The pleural effusion was drained away more than 1500 ml everyday, but the symptoms were not relieved. According to all clinical characteristics, we can confirm the diagnosis of atelectasis and pleural effusion in the left side. Because of the high levels of body temprature and white blood cell count, the infection certainly exists. From the present examinations, it's hard to judge the nature of the pleural effusion, but according to the unfavorable response to the antibiotics, we should consider other pathogenesis. Although we didn't find the tumour cell in pleural effusion, yet for the NHL history, the possibility that there is infiltration of the lymphoma in pleura should be highly suspected. Now, in addition to active anti-infection treatment and continuing drainage, we ought to make particular examinations for the NHL.

Cardiologist A: The patient is an old man. His ECG showed flat T wave and ischemic myocardium. At present, the main problems are high heart rate and short breath, both of them can cause arrhythmia. The changes of heart function should be the secondary changes. Because of the unknown pathogenesis, we may give him the Chinese traditional medicine "Xinkangpian" to improve the blood supply of the myocardium. Our urgent affair is to discover the pathogenesis and give him pertinent treatment.

Hematologist A: The patient has the history of NHL which was of highly malignant type and at stage ⅣB, so the prognosis should be the worst. Judged from the characteristics of the pleural effusion (slightly turbid with high protein content), the fluid is most likely to be the extravasate of blood. The low amount of cells in the pleural effusion may be related to the experimental method. We should exam the 24-hour effusion and choose the sediment in the lower layer. The difference of laboratorial technique may greatly influence the result. The result of protein examination was relatively more reliable. However, we can find some facts which don't support the infiltration of the lymphoma in pleura: ① The usual infiltration of the lymphoma in serous membrane cavity is symmetrical, hardly can we find the infiltration in single cavity; ② Although the patient completed his last chemotherapy three months ago, we examined him in detail three weeks ago and didn't find the evidence of relapse. He was in complete response at that time; ③ In the physical exam, we didn't find tumid superficial lymph nodes or mediastinal lymph nodes. Because the clinical treatment for NHL and tuberculous pleurisy is poles apart, in order to avoid the aggravation of the illness, it is better not to give any special treatment for NHL. We should do TB test and PPD test again and exam the pleural effusion everyday. At the same time, we should choose some more potent antibiotics for treatment of infection. After we find out the cause, we can give him effective etiological treatment.

Doctor A (*Digestive department*): Now, the patient is in critical ill: the amount of pleural effusion grows rapidly, the body temperature rises and the white blood cell count increases too. According to the negative result of TB test, basically we can exclude the diagnosis of TB. In order to give this patient better treatment, we advice to transfer him to hematological department.

Second clinical discussion

The patient was transferred to hematological department for further treatment on October 9, 2004. After that, dyspnea and high heart rate were not eased yet though most of his pleural effusion in left thoracic cavity had disappeared. On October 17, the patient got type-2 respiratory failure and had to receive endotracheal intubation through nasal cavity for mechanical respiration in order to save the life. Then the respiratory failure was eased, but the respiratory rate was still high (30-40/min). Pleural effusion test, blood examination, X-ray of

chest at bed and cardiogram were performed regularly.

Cardiologist B: The patient is clear-headed without any enlarged lymph node. The breath sounds are decreased in the lower posterior lung fields with dry rales audible in the upper lung fields. His heart rate is 91 to 100 beats per minute. All these may be the compensation of heart for a long period of anoxemia. I suggest that he needs a much potent anti-infection treatment and an ultrasound examination of heart in order to find if there is pericardial effusion and to define its quantity. If there is plenty pleural effusion in right thoracic cavity, puncture should be performed to release the fluid, large quantity of albumin should be infused (about 10 to 20 g per day), and diuretic should be given after albumin infusion and quantity of water intake should be limited to within 2500 ml per day.

Doctor B (*Respiratory Department*): The pleural effusion of the patient decreased obviously and the high respiratory rate seems to be not correlated with pleural effusion. According to the chest radiography (Fig 1 b), there is a dark nodule with sharp edge arising from porta pulmonis in left upper lung field. Bronchoscopic examination should be used to find if there are blocks in small bronchi, then a biopsy should be performed to determine the pathological nature of the block. Bronchoscopic results showed that there were three bronchi aligning side by side and all of them were blocked almost completely by dark yellow substance, which were something like sputum and not the continuum of the bronchial wall. The branches of them were blocked by about 70%. The dark yellow substance was taken and sent to the pathological department for further examination. Then 0.9% NaCl solution was used to wash the blocked bronchi and all three bronchi were nearly opened completely 3 weeks later. According to the chest radiography (Fig 1c), the left nodular shadow almost disappeared completely, while the pleural effusion in right thoracic cavity appeared and this may be caused by the low albumin level of blood. At this time, high respiratory rate and heart rate were eased. Supportive care and anti-infection treatment should be maintained, then there may be a chance for the termination of artificial respiration. All in all, the present condition should be diagnosed as atelectasis due to sputum block, pneumonia with secondary pleural effusion.

Pathologist: The sample surface is dark yellow and the cross section is dark white. Its size is 0.1 cm × 0.2 cm. It is tough and do not has any tissue structure. There is only small quantity of epithelium in fibrinoid substance. It is considered as a sputum crust.

Diagnoses

Atelectasis due to sputum block, pneumonia with secondary pleural effusion.

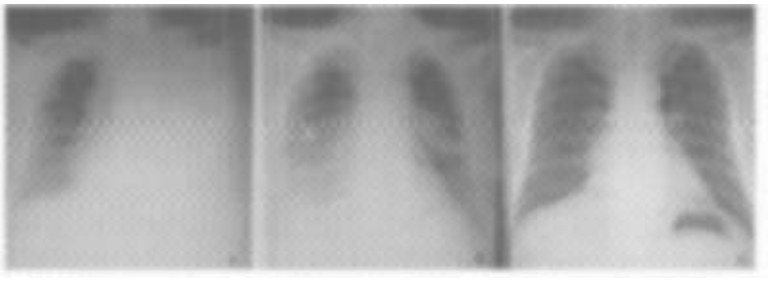

Fig 1. Changes of chest radiography before and after bronchial wash

a. Large amount of pleural effusion in left thoracic cavity; b. There is an irregular shaped node in the middle of left lung field after pleural drainage; c. The node in left thorax disappeared after bronchial wash and anti-infection treatment.

(Translator: LU Xuechun, FAN Hui, ZHU Hongli, et al)

淋巴瘤缓解后出现胸腔积液、呼吸困难1例

1 病历摘要

患者，男性，77岁，诊断为非霍奇金淋巴瘤2年，胸闷、咳嗽5 d。

病史：2003年初发现左侧附睾结节和左侧腹股沟包块伴肉眼血尿，活检及病理检查后诊断为非霍奇金淋巴瘤，弥漫大B细胞型，ⅣB期，CD20(+)。从2003年3月以来共完成了8次CHOP化疗联合美罗华治疗，2个疗程后包块缩小，肉眼血尿消失，达到完全缓解。末次化疗结束时间为2004年6月11日。2004年9月1日在本科全面评估后出院。2004年9月27日无明显诱因出现胸闷、咳嗽、咯痰，痰量不多，为白色泡沫样黏痰，当时无发热、胸痛、盗汗、腹痛、腹泻、尿急和尿痛。未予特殊处理。9月29日出现低热，最高体温37.3℃，不用药可自行恢复正常。10月2日开始有活动后胸闷气短，咳嗽咯痰加重，痰量增多并带有血丝，在解放军总医院急诊胸部X线胸片示左肺不张(图1a)。因其他科室床位紧张暂入消化科治疗。既往史：患者有糖尿病、喉癌术后及前列腺肥大等病史，目前病情稳定。

体格检查：体温35.4℃，心率74次/min，呼吸30次/min，血压135/60 mmHg。急性病容，全身皮肤黏膜无黄染、出血点，左髂窝可触及一个黄豆粒大小淋巴结，无压痛。呼吸急促，左侧第2肋以下呼吸音减弱，双肺未闻及干湿啰音。

实验室检查：白细胞10.3×10^9/L，中性粒细胞0.82，血红蛋白114 g/L，血小板270×10^9/L，血钠135 mmol/L，血钾3.7 mmol/L，血氯110 mmol/L，肌酐89.5 μmol/L，尿素氮7.76 mmol/L，总蛋白56.5 g/L，白蛋白29.6 g/L，天冬氨酸氨基转移酶18 U/L，丙氨酸氨基转移酶3 U/L。血沉52 mm/h。X线胸片示左肺不张。

入科诊断：(1)左肺不张原因待查：肺炎？(2)非霍奇金淋巴瘤ⅣB期，弥漫大B细胞型；(3)2型糖尿病；(4)喉癌术后；(5)前列腺肥大。

诊治经过：入科后给予抗生素(哌拉西林、头孢哌酮钠/他唑巴坦钠)、祛痰、免疫球蛋白及白蛋白等抗感染及支持治疗，但胸闷、呼吸困难等症状逐渐加重，体温逐渐升高，最高达38.4℃；呼吸频率增快，最快达39次/min，其他体征与入院时相比无明显变化。10月5日动脉血气分析：pH 7.388，PO_2 78.4 mmHg，PCO_2 31.4 mmHg，SO_2 95.1%，BE-5.3 mmol/L，HCO_3^- 18.5 mmol/L。左侧超声检查提示左侧胸腔中等量积液，左下肺不张。10月5日进行胸腔穿刺，胸腔闭式引流，可引出清亮胸水，每日量在1500 ml左右，胸水检查：积液呈黄色，透明度微混，红细胞数362×10^6/L，白细胞数4×10^6/L，糖6.61 mmol/L，蛋白31.9 g/L，氯化物116.3 mmol/L，多次复查未见肿瘤细胞，胸水培养无细菌生长，结明三项均为阴性。虽经胸腔闭式引流持续开放，胸闷、呼吸急促等症状仍不能缓解。

2 第一次临床病例讨论

呼吸科医师A：该患者有以下特点：(1)老年男性；(2)既往非霍奇金淋巴瘤及喉癌病史，目前为治疗后；(3)本次起病无明显诱因，以胸闷气短为主要表现，虽有咳嗽、咯痰但程度较轻；(4)胸片有左肺不张，超声检查提示左侧胸腔中等量积液，考虑肺不张为胸腔积液压迫引起；(5)抗感染及支持治疗效果不佳；(6)虽然每日胸腔积液引流量在1500 ml左右，但胸闷、呼吸急促不能缓解。从上述临床特点来看，左肺胸腔积液，左肺不张诊断明确。至于病因，从体温和外周血象白细胞偏高来看感染肯定存在，从目前的检查来看胸水性质难以判定，但两种抗生素不能使症状缓解，应考虑同时有其他致病因素存在。患者有淋巴瘤病史，虽然胸水多次检查未见肿瘤细胞，但不能除外淋巴瘤胸膜浸润，因胸水检查瘤细胞敏感度比较低。目前在积极抗感染和继续进行胸腔闭式引流的情况下，应重点针对淋巴瘤进行检查和治疗。

心内科医师A：患者年龄较大，心电图提示T波低平、心肌缺血。目前的主要症状是呼吸急促，心率过快，二者可导致心肌缺氧，引起心律失常。心功能的变化应该是一个继发性改变，在目前病因未明的情况下，可给予欣康片以改善心肌供血。目前当务之急是查找病因，针对病因进行治疗。

血液科医师A：病史不重复。患者有淋巴瘤病史，分型属于恶性度较高预后较差的类型且分期较晚，属预后最差的ⅣB。弥漫大B细胞淋巴瘤病程

中可以有结外浸润,包括浆膜腔。从目前胸腔积液微混,蛋白偏高的性质来看,血性渗出液的可能性大。至于胸水细胞数量偏低可能与实验室检查方法有关,所送检的胸水应该是全部24 h的引流液,检查时应该取下层沉淀液进行细胞学检查,检查手法的差异对结果影响很大,而蛋白检查的结果相对更为可靠。但以下几点不支持淋巴瘤浆膜腔浸润:(1)一般淋巴瘤浆膜腔浸润呈对称性,很少有单个浆膜腔受累;(2)尽管末次化疗时间已有3个月余,但3周前曾在本科进行全面复查,当时一般状况好,淋巴瘤的各项指标均正常,为完全缓解状态,如出现淋巴瘤胸膜腔浸润,从发病的时间上不符;(3)目前患者浅表淋巴结和腹膜后等淋巴结均无肿大,这也与淋巴瘤复发不符。因结核性胸膜炎和淋巴瘤在治疗上存在矛盾,在胸水病因未明之前不宜进行抗淋巴瘤治疗,以免加重病情。目前应继续胸水送检,复查结明三项和PPD试验,在积极排查结核性胸膜炎的同时,继续给予抗感染治疗,但在抗生素的选择上应加强。病因明确后进行病因治疗。

消化科医师:患者目前病情危重,胸水发展迅速,体温升高,外周血白细胞升高,结明三项阴性来看,基本可以排除结核病的可能。目前在我科继续治疗已不适宜,建议转入血液专科进行治疗。

3 进一步诊治及第二次临床病例讨论

2004年10月9日患者转入血液科继续治疗,左侧胸腔积液虽然大部分消失,但白蛋白严重偏低,呼吸困难和心率偏快仍不能缓解,10月17日患者出现2型呼吸衰竭后给予经鼻气管插管呼吸机辅助呼吸,虽呼吸衰竭得以纠正,但呼吸频率仍偏快,介于30~40次/min之间,定期进行胸水、血液、床旁胸片和心电图检查。

心内科医师B:患者神志清楚,全身浅表淋巴结无肿大,两上肺可闻及干啰音,两下肺呼吸音明显减弱。心率波动于91~100次/min之间。考虑心功能不全是由于心脏长期缺氧所致。建议:尽快控制肺部感染,行床旁超声检查,明确心包有无积液和积液量,若右侧胸腔积液量较多应进行穿刺引流,大量补充白蛋白,每日应在10~20 g,输白蛋白后给予大量利尿剂,严格控制每日液体入量在2500 ml以内。

呼吸科医师B:目前患者的胸水明显减少,呼吸频率加快的原因与胸水关系不大。从胸水消退后的胸片上看,左上肺有一结节影(图1b),且有一起自肺门边缘锐利的不规则影,不能除外支气管堵塞。应在呼吸机辅助呼吸和抗感染治疗同时进行床旁气管镜检查,以明确支气管堵塞性质。从支气管镜的检查来看,左上肺叶后段3个品字型分布支气管几乎完全被黄色质韧物质堵塞,该物质与气管壁在解剖结构上不连续,可能为痰痂,其下一级支气管开口约70%被堵塞,用活检钳钳夹堵塞物送检,经每周一次的庆大霉素生理盐水溶液反复冲洗,3周后堵塞的支气管已完全通畅。从胸片上(图1c)看,左胸球状阴影基本消失,但右侧出现胸腔积液,考虑为低蛋白血症继发而来,患者呼吸急促和心率偏快症状缓解,继续给予强有力的支持和抗感染治疗,患者有望脱机。因此,患者目前的诊断应为痰痂堵塞性肺不张,肺炎继发胸腔积液。

病理科医师:送检的物质为灰黄色固体,切面为灰白色,大小约0.1 cm×0.2 cm,质韧,病理检查未见组织结构,仅在纤维素样渗出物中含有少量脱落的上皮细胞成分,考虑为痰痂。

4 最后诊断

痰痂堵塞性左肺不张,肺部感染继发胸腔积液。

(卢学春,范辉,朱宏丽等整理)