· 临床病理讨论 ·
Clinicopathological Conference

An old male with dyspnea, edema of face and enlargement of multiple lymphnodes of neck

(The 20th case)

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Case presentation

A 74-year-old male was admitted to the hospital for edema of face for 1 week and dyspnea for 5 days.

One week before the admission, the patient developed edema of face and eyelids. Five days ago, he felt shortness of breath when lying down. In the following 2 days, he could not go to sleep. He was free from cough or expectoration, neither was chest distress . Since the onset of the disease, the patient was in low spirits, but with normal appetite and no fever and night sweat . He lost 3 kilograms in the last half year.

Past history: He reported a history of hyperalgia of left upper limb and lower limbs for 3 months, and a history of hypertension for 30 years, with peak blood pressure being 210/110 mmHg. Perindopril 4 mg qd was administrated for blood pressure control. He was diagnosed to have diabetes mellitus more than 10 years ago and took metformin 850 mg qd. He also suffered from cerebral lacunar infarction more than 10 years ago. Lumbar vertebral canal stenosis was diagnosed for 2 years. He smoked half box of cigarettes per day for 50 years. Exposure to radiation or toxicants was denied. No positive family history was found.

Physical examination: BP 150/65mmHg, P 94 bpm. Conscious but down in spirits. No pallor, slight cyanosis on lips. Non-pitting edema was found on his face, neck and upper limbs. Slight jugular vein distention as well as varicosity on chest wall were noticed. No mass in the thyroids. Several lymph nodes were palpable on the right side of the neck and the supraclavicular area, hard in character, about 1.5cm×0.5cm in size, without pain. Trachea was at central position. No chest deformity. Breath sounds were vesicular, harsh, with no dry or moist rales, neither pleural friction sound. Heart size was normal. Heart rate was regular, 94 bpm and no murmurs were heard. Peripheral blood vessels were normal. The abdomen was soft, without tenderness, rebound tenderness, or palpable masses. Shifting dullness negative. There was no edema on both lower extremities

Primary diagnosis: (1) enlargement of cervical lymphnodes; superior vena cava syndrome; (2) hypertention, grade 3, very high risk; (3)obstructive sleep apnea-hyponea syndrome; (4)old cerebral infarction; (5) diabetes mellitus,type 2 .

During the first one or two days after admission, some auxiliary tests were arranged for the patient, such as blood routine, urine and stool routine, biochemical examinations (including serum lipids, electrolytes, myocardial enzymes), blood sedimentation rate, blood coagulation function, blood gas analysis, blood markers of tumor, function of thyroid gland, HbA1c. All the above tests revealed no significant abnormalities. Both electrocardiogram and echocardiogram were normal. The abdominal ultrasonography was normal. Chest X

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ray showed that the upper mediastinum on the right side was widened, and its border showed lobulated shape and extended to lung field. Trachea below the level of T2 vertebral body was compressed and shifted to the left. The right diaphragm was uplifted. Ultrasonic imaging showed multiple enlarged lymphodes at both sides of the neck and subclavian area, and solid space-occupying lesion in the right upper mediastinum. No obvious abnormality was found in thyroid. Chest CT found multiple enlarged lymphnodes in the mediastinum. Lung cancer (mediastinum type) was considered. Superior vena cava was compressed by metastasis. Lymphoma could not be excluded. The result of bone marrow puncture examination was normal.

Clinical discussion

Dr Liu: The clinical characteristics of this case were as follows: (1) An old male patient suffered from the disease in a short time and the progress was fast. (2) He has history of hypertension, old cerebral infarction, diabetes mellitus and obstructive sleep apnea-hypopnea syndrome, but we didn't get his definite history of heart diseases. or pulmonary diseases. He smoked for a long time and lost 10 kg in body weight in the last 3 years. (3) At the moment, non-pitting edema of the face, neck and upper linbs, as well as increasing shortness of breath were the main symptoms. Varicosity on the chest wall and slight distention of bilateral jugular veins were noticed. Meanwhile, painless hard enlarged lymph nodes of about 1.5cm×0.5cm in size were palpable on the right side of neck and supraclavicular area; but no abnormal signs of heart, lung and abdomen were found. (4) The auxiliary examination showed multiple painless enlarged lymphnodes in both sides of the neck, widened mediastinum and space-occupying lesion in the right upper mediastinum. Tests for other organs' function, didn't find obvious abnormality.

Dr Su: Superior vena cava syndrome (SVCS), caused by space-occupying lesion in right upper mediastinum was the most pronounced clinical manifestation in this case. SVCS is caused by complete or incomplete obstruction of superior vena cava because of various diseases. Its diagnosis mainly depends on the following typical manifestations: edema of face, neck and upper limbs; jugular vein engorgement; varicosity at chest wall or abdominal wall, accompanied by dyspnea, cough and chest pain. Chest X ray and CT examination can confirm the diagnosis. Tumors account for 97% of the causes of SVCS, while non-tumor diseases account for only 3%. Lung cancer and lymphoma are the most common causes of SVCS. In this case, we should take following diseases into account for differential diagnosis: (1) Lymphoma: the most common clinical presentation of lymphoma in adults is painless enlargement of lymph nodes, just like this patient, so lymphoma is highly suspected and we should perform lymph node biopsy as soon as possible. (2) Lung cancer: this patient have some risk factors for lung cancer, such as the old age, the male gender, and a long history of smoking. The mediastinum type of lung cancer in the upper right lobe is likely to invade superior vena cava. Cancer embolus might also be formed in superior vena cava. Lymphogenous metastasis of small cell lung cancer and adenocarcinoma to mediastinum will cause SVCS too. Therefove lung cancer can not be excluded in this case. (3) Other metastatic tumors: there were multiple painless enlarged lymph nodes in neck and mediastinum of the patient, so metastetic tumor should be cousidered, but there was no definite evidence of primary tumors from the results of various examinations of thoracic cavity and abdominal cavity, so this possibility is low.

Dr Zhao: I agree with Dr Su's consideration for the diagnosis, but we have to wait for several days until we get the result of lymph node biopsy. In the meantime, the patient's condition aggravated fast, especially compression of superior vena cava, esophagus and phrenic nerve. SVCS is divided into two types according to whether obstruction of brachiocephalic vein occurs . There will be severe high pressure in internal jugular veins if the brachiocephalic vein is blocked. In-

tracranial hypertension and cerebral edema are also common, which might cause death; so the obstruction should be relieved as soon as possible through chemotherapy or interventional treatment and necessary supportive treatment.

Dr Zhang: The space-occupying lesion in mediastinum of this old patient is growing rapidly, accompanied by enlargement of cervical and subaxillary multiple lymph nodes, dyspnea, symptoms of superior vena cava obstruction. Tumor is highly suspected, especially lymphoma. The patient's condition worsened rapidly, therefore the therapy might be delayed if we wait for the result of lymph node biopsy. It is necessary to consult with hematologists and to carry out chemotherapy as soon as possible.

Dr Ma: Lymphoma is highly suspected. The main characteristics of malignant lymphoma in senile patients are as follows: NHL is the most common type of lymphoma. Its progress is rapid and it is highly malignant. It is usually accompanied by many complications, and is more likely to be misdiagnosed. It was reported that NHL, especially diffused large B cell type, was the main type of lymphoma that caused SVCS. SVCS is tumor emergency and the aim of treatment is shrinking the tumor, relieving obstruction and restoring normal blood flow. For the sake of the severe condition of this old patient, chemotherapy should be given as soon as possible for relieving compression symptom and controlling the progress of patient's condition. Following therapy is recommended: (1) Losec 40 mg iv qd to prevent stress ulcer and hemorrhage of the digestive tract. (2) Chemotherapy with CHOP regimen: vindesine sulfate 4 mg iv d1; CTX 800mg iv d1; epirubicin 70 mg iv d1; methylprednisolone 120 mg iv qd d1-5. (3)5% sodium bicarbonate 250ml ivgtt to alkalize the urine and prevent acute tumor lysis syndrome. (4) Make sure that the patient excretes enough urine. Diuretic treatment is given if necessary. (5) Penicillin to prevent infection. CD 20 monocolonal antibody Mabthera should be used if B cell lymphoma is proved by immunohistochemical method. If it is a T cell lymphoma, we should consider changing to another therapeutic regimen after evaluation of the therapeutic effects.

Clinical prognosis

After stent implantation in superior vena cava and the first chemotherapy with CHOP, the patient's symptoms were improved to a certain degree.

Five days after admission, lymph node biopsy confirmed the diagnosis: non-Hodgkin lymphoma (diffuse large B cell type). Immunohistochemistry showed: CD20++++, CD79α+, bcl-6-, CD10-, CD3-, CD45RO-.

Final diagnosis: (1) Non-Hodgkin lymphoma (diffuse large B cell type), immunohistochemistry: CD20++++; (2) Superior vena cava obstruction syndrome; (3) Hypertension, grade 3, very high risk; (4) Obstructive sleep apnea-hyponea syndrome; (5) Old cerebral infarction; (6) Diabetes mellitus (type 2).

Further treatment: (1) chemotherapy as CHOP + Mabthera with the interval of two weeks: vindesine sulfate 4 mg iv d1; CTX 1000mg iv d1; epirubicin 90 mg iv d1; methylprednisolone 100 mg iv qd d1-5 and Mabthera 600mg iv one day before beginning of chemotherapy. (2) Supportive treatment and heteropathy. (3) Control of blood glucose and blood pressure, protection of the heart.

After receiving chemotherapy for 6 cycles, the patient's symptoms such as edema and shortness of breath were alleviated to a great extent. Reexamination with chest CT revealed mediastinum and trachea were in the middle of the thoracic cavity, and enlarged lymph node was not found in mediastinum.

(Translators: Da Wa Ci Ren, Liu Lin)

老年男性颜面浮肿及憋气伴颈部多发淋巴结肿大

1 病例摘要

患者男性，74 岁。主因“颜面浮肿 1 周，憋气 5d”收入院。1 周前始出现面部肿胀感伴球结膜充血、水肿。5d 来平卧时憋气明显，继而不能平卧。不伴有咳嗽咯痰、胸闷胸痛等。自发病以来精神差，食欲可，无发热盗汗，二便无异常。近半年内体重下降 3 kg。左上肢、双下肢痛觉过敏 3 个月余。既往史：高血压 30 年，最高达 210/100mmHg，服用雅施达 4mg qd。阻塞性睡眠呼吸暂停低通气综合征 20 年。糖尿病 10 余年，服用格华止 850mg qd。腔隙性脑梗 10 余年。腰椎管狭窄 2 年。吸烟 50 年，每日 10 支。无射线及毒物接触史。无特殊家族史。查体：血压 150/65mmHg。心率 94 bpm。神志清，精神差。面部、颈部、双上肢非可凹性水肿。胸壁静脉曲张。双眼球结膜水肿。双侧颈静脉轻度充盈。双侧甲状腺未见肿大及结节。右颈前、颈后及右锁骨上区等处可及多个无痛性肿大淋巴结，质硬，大小约 1.5 cm×0.5cm。胸廓无畸形。双肺呼吸音粗，未及干湿性啰音，未及胸膜摩擦音。心界不大，心音有力，心率 94 次/min，未闻及瓣膜区杂音。外周血管征阴性。腹部阴性。双下肢无水肿。

入院初步诊断：(1)颈部淋巴结肿大、上腔静脉阻塞综合征；(2)高血压病 3 级，极高危；(3)阻塞性睡眠暂停低通气综合征；(4)陈旧性脑梗；(5)2 型糖尿病。

入院第 1～2 天内完善相关检查。血常规、尿常规、大便常规、血沉、凝血功能、肝功、肾功、血脂、电解质、心肌酶、血气分析、肿瘤标记物、甲状腺功能、糖化血红蛋白等检查未见明显异常。心电图大致正常。超声心动图：心内结构未见异常。胸片(图 1)：右上纵隔增宽，边缘呈分叶状改变，向肺野内突出。T2 椎体水平以下气管受压变窄且向左移位。右膈肌抬高。颈部 B 超：双侧颈部及锁骨下多发肿大淋巴结；右上纵隔区实性占位；甲状腺未见明显异常。腹部 B 超：未见明显异常。胸部 CT(图 2)：纵隔多发肿大淋巴结，考虑纵隔型肺癌？纵隔淋巴结转移可能性大并上腔静脉受累，不除外淋巴瘤。常规骨髓穿刺检查未见异常。

2 临床与病理讨论

刘兆平医师：该病例的特点如下：(1)老年男性，病程短进展快；(2)既往有高血压、陈旧性脑梗、阻塞性睡眠呼吸暂停低通气综合征、2 型糖尿病、长期吸烟史等，但无明确心肺腹部疾病，近 3 年内不明原因消瘦 10kg；(3)此次以颜面部及双上肢区浮肿伴进行性憋气为主要表现；同时查体可见胸壁静脉曲张，双侧颈静脉轻度充盈。右颈前、颈后及右锁骨上区等处可及多个无痛性肿大淋巴结，质硬，大小约为 1.5 cm×0.5cm。心肺腹部未见异常体征；(4)辅助检查：颈部多发无痛性淋巴结肿大，纵隔增宽，纵隔占位性病变；其余脏器功能基本正常。

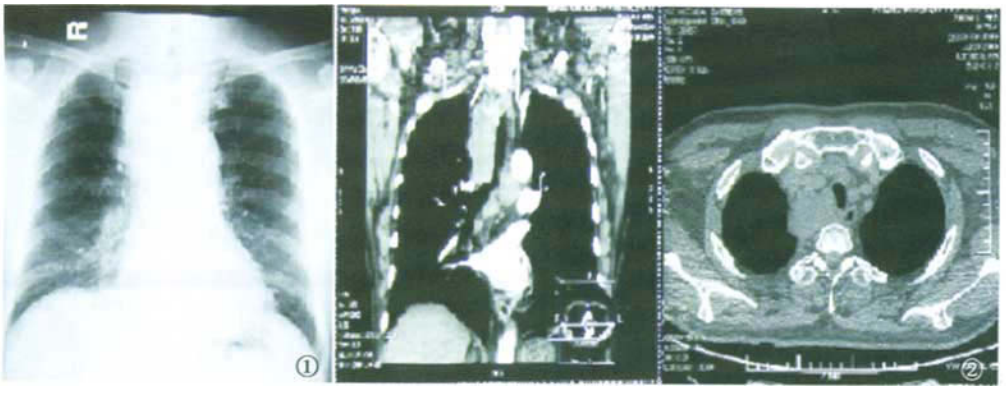

图 1 治疗前胸片

图 2 治疗前胸部 CT

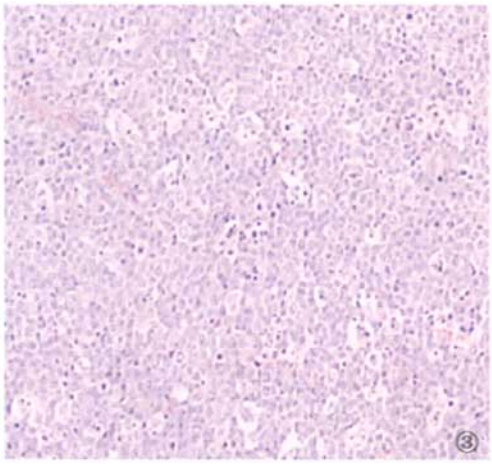

图3 治疗前淋巴结活检(HE,×20)

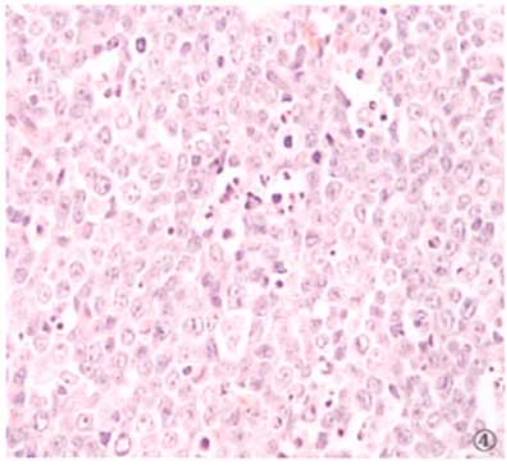

图4 治疗前淋巴结活检(HE,×40)

苏加林医师:此次突出表现为纵隔占位性病变所致上腔静脉阻塞综合征(superior vena cava syndrome, SVCS)。SVCS是由各种不同病因引起的完全性或不完全性上腔静脉阻塞,导致血液回流受阻造成的临床症候群。SVCS的诊断主要靠典型的临床表现:颜面、颈部及上肢区充血水肿,颈静脉怒张,胸壁和(或)腹壁静脉曲张,伴有呼吸困难、咳嗽、胸痛等;胸片及胸部CT等影像学检查可确诊。SVCS的病因中肿瘤因素占97%,非肿瘤因素占3%,肺癌与恶性淋巴瘤为最常见病因。本例病因诊断考虑如下:(1)淋巴瘤:成人淋巴瘤最常见的临床表现是无痛性淋巴结肿大。与本患者表现相似,应高度怀疑淋巴瘤。应尽快行淋巴结活检取得病理诊断。(2)肺癌:患者老年男性,有长期吸烟史,为肺癌的高危人群。右上肺叶的纵隔型肺癌,最易侵犯上腔静脉或引起上腔静脉内癌栓形成,肺小细胞癌、腺癌常有纵隔淋巴结转移,也常为恶性SVCS的病因。故此诊断不能除外。(3)其他转移瘤:患者颈部及纵隔内可见多处无痛性淋巴结肿大,应考虑到转移瘤。但患者胸腹腔内未见明确原发肿瘤。故此可能性较小。

赵锋医师:同意苏加林医师的诊断考虑。但等到病理确诊尚需时日,而患者病情进展较快,包括上腔静脉、食道、膈神经受压症状明显。SVCS根据伴或不伴无名静脉梗阻分成两型,伴有无名静脉梗阻者颈内静脉高压严重,此型的直接致死原因常为颅内高压、脑水肿。因此需尽快通过化疗或介入治疗解除压迫症状,加强支持治疗。

张树基教授:患者老年男性,纵隔肿物增长迅速伴有颈部及腋下淋巴结肿大,呼吸困难,上腔静脉阻塞表现。肿瘤可能性大,特别是淋巴瘤。患者病情进展快,若等病理回报诊断明确后再行治疗可能会延误病情。建议尽快请血液科专家会诊,尽早进行化疗。

马明信教授:高度怀疑淋巴瘤。而且老年恶性淋巴瘤以非霍奇金淋巴瘤多见,进展快,恶性度高,合并症多,误诊率高等。有文献报道,引起SVCS的恶性淋巴瘤中以非何杰金淋巴瘤为主,且大部分为弥漫大B细胞型。SCVS属肿瘤急症,SVCS的治疗目标是缩小肿块,缓解阻塞,恢复正常的静脉血流。鉴于患者高龄,肿瘤压迫症状进展迅速,应尽快行化疗,缓解压迫症状,并控制病情发展。建议如下方案治疗:(1)洛赛克40mg iv qd预防应激性溃疡及消化道出血;(2)CHOP方案化疗:希艾克(硫酸长春地辛)4mg iv d1;环磷酰胺800mg iv d 1;表柔比星70mg d 1;甲泼尼龙120mg d 1~5冲击治疗;(3)5%碳酸氢钠250ml缓慢静滴,碱化尿液,预防溶瘤综合征的出现;(4)保证足够的尿量,必要时利尿;(5)青霉素预防感染。若免疫组化为B细胞来源可考虑加用CD20单克隆抗体美罗华治疗;若为T细胞来源则应评价化疗效果后决定是否更改方案。

3 临床转归

经过上腔静脉支架植入术及第一次CHOP方案化疗后,患者压迫症状有所好转。

入院第5天病理报告(图3,图4):右颈部淋巴结活检病理:非霍奇金淋巴瘤(弥漫大B细胞型)。免疫组化(图5,图6):CD20+++、CD79α+、

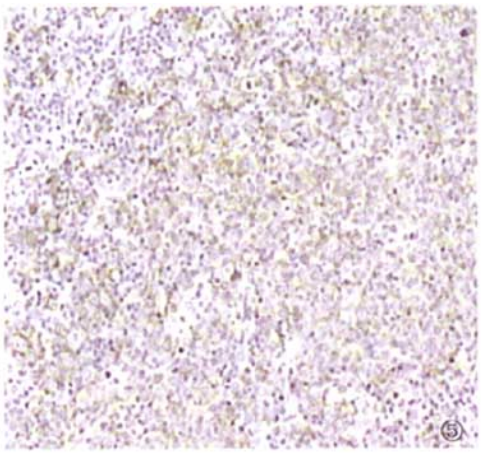

图5 治疗前淋巴结活检免疫组化 CD20+(×20)

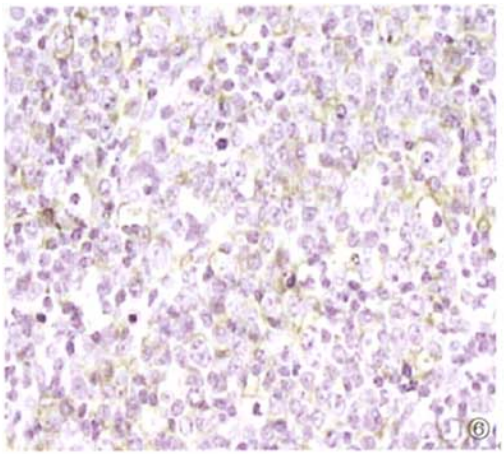

图6 治疗前淋巴结活检免疫组化 CD20+(×40)

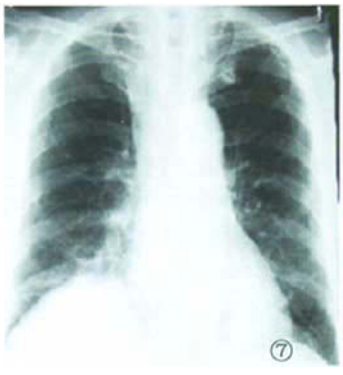

图7 治疗后胸片

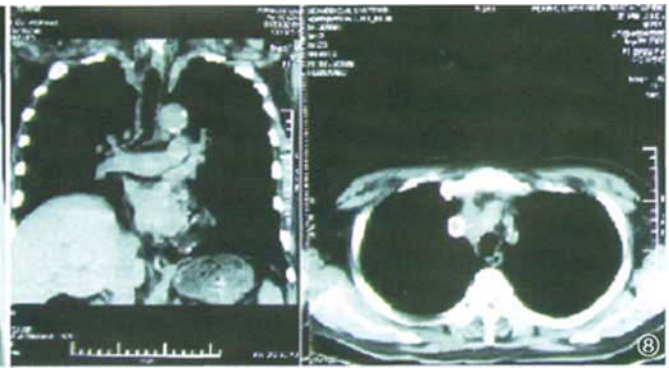

图8 治疗后胸部 CT

bcl-6-、CD10-、CD3-、CD45RO-。

明确诊断:(1)非霍奇金淋巴瘤(弥漫大B细胞型),免疫组化:CD20++++;(2)上腔静脉阻塞综合征;(3)高血压病3级,极高危;(4)阻塞性睡眠暂停低通气综合征;(5)陈旧性脑梗;(6)2型糖尿病。

进一步治疗:(1)每隔2周左右按CHOP+美罗华方案化疗(希艾克 4mg iv d 1;环磷酰胺 1000mg iv d 1;表柔比星 90mg d 1;泼尼松 100mg d 1～5;并于化疗开始前1 d应用美罗华 600mg 静点);(2)加强支持治疗;(3)控制血糖、血压、保护心脏等治疗。连续化疗6周后,患者颜面及双上肢区浮肿消退、憋气缓解,复查胸片(图7)及胸部CT(图8):纵隔气管居中,纵隔未见肿大淋巴结。

(整理者:达娃次仁)