· 临床病理讨论 ·

Clinicopathological Conference

Oliguria and severe lower extremity edema 1 year after operation for gastric cancer with liver metastasis in an elderly patient

(the 29th case)

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Case presentation

On February 10, 2008, a 67-year-old man was admitted to our hospital for severe lower extremity edema. Three days before, he gradually developed oliguria (600-800ml/d) and pitting edema of lower extremities. The skin temperature and color of lower extremities showed no abnormality, and no fever, no palpitation, no lumbago or gross hematuria. The patient was admitted for further treatment. He had received selective transhepatic artery chemotherapy embolization and left gastric artery perfusion chemotherapy for 3 times successively and systemic venous chemotherapy for twice because of gastric cardiac carcinoma with multiple metastases in liver in April of last year. Reexamination of liver with MRI revealed reduction of some liver foci, but the primary cancer focus at cardia enlarged with bleeding tendency, so palliative proximal part gastrectomy was performed on September 27 of the same year. Postoperative pathological examination found moderately differentiated ulcer-type neuroendocrine carcinoma at lesser curvature of gastric cardia, invasion of carcinoma to whole layers of gastric wall, carcinoma nodules on serosa, metastatic carcinoma in lymph nodes of lesser curvature(1/12), but without carcinoma embolus in vessels. Two cycles of systemic chemotherapy were performed after operation. Afer chemotherapy, examinations such as B-mode ultrasonography and intensified CT indicated that the metastatic foci in liver increased and enlarged and metastatic foci appeared in lung on chest CT examination. Thereafter the treatment was mainly enhancing immunity, increasing nutritional support, alleviating suffering and prolonging life. He denied history of hepatitis, tuberculosis, hypertension, diabetes and coronary heart disease.

Physical examination on admission: the temperature was 37.0℃, the blood pressure 120/65mmHg, the pulse 72 beats/min, and the respiration 18/min. The patient was conscious. Sclera and skin had severe icterus, and several enlarged lymph nodes were palpable in the right supraclavicular fossa, hard in consistency, about 0.5cm×0.4cm in size, without tenderness, with obscure boundary, and were immovable. There were no rash or petechiae on skin, no liver palm and spider telangiectasia. The two pupils of the eyes were isocoria, capable of light reflex and light adaptation. The lips were not cyanotic, the neck was soft. There was no venous engorgement. Thyroid glands was not palpable, and there were no thrill. The chest and respiratory movement were symmetrical, and dull percussion note was found at the fourth intercostal space of the right medioclavicular line, and respiration sound was clear. The cardiac dullness was normal. The heart rate was 72/min. The rhythm was regular. The abdomen was slightly

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bulged. An old operation scar was seen at the abdominal wall. No gastrointestinal type and gastrointestinal peristaltic wave were seen, and there was no tenderness. Liver was palpable 6.0 cm under right costal margin. The spleen was not palpable. Shifting dullness was negative. What is more, severe pitting edema of both lower extremities and lumbosacral area was observed. The girth of left leg was 40cm, and the right one was 41cm. No other abnormities were found in this patient.

Laboratory examination disclosed the following findings: total protein 69g/L(55－80), albumin 35.8g/L(35－55), alanine aminotransferase (ALT) 108 U/L(0－40), aspartate aminotransferase(AST)194.6 U/L(0－40), total bilirubin (T-BIL)281.33 μmol/L(6.0－21), direct bilirubin(D-BIL) 226.54 μmol/L(1.7－6.8), γ-glutamyltranspeptidase(γ-GT)1402 U/L(0－52), alkaline phosphatase (ALP) 448 U/L(15－121), CEA 3.56μg/L(0－5). However, the serum level of blood urea nitrogen(BUN) was 5.72 mmol/L (2.8－7.2),and creatinine was 58.6 μmol/L(53－125). Electrocardiogram showed no abnormality. Echocardiogram findings: left ventricular ejection fraction was 68%. Heart size, shape and wall thickness were normal. Left ventricular contraction function was normal and pericardium had no abnormality. B-ultrasound findings: the liver volume was augmented, echo of liver was enhanced, and there were a lot of metastatic tumors in the liver(diameter from 0.9 to 6.0cm); bile duct and hepatic portal vein were not dilated, and there was no embolus in portal vein. Both kidneys and ureters were normal. Vascular ultrasound of both lower extremities showed no embolus in them.

After admission, the patient received the albumin supplement, diuretics and corresponding symptomatic treatment. The urine volume gradually returned to nomal (approximately 2500ml/d). But the jaundice was aggravated, and the edema of lumbosacral area and lower extremities was worsened progressively. On March 7, the patient appeared to be diuretic-resistant gradually with decrease in urine volume again. Laboratory examination disclosed the following findings: BUN 46.28 mmol/L,Cr 451.3 μmol/L, total protein 72.3g/L, albumin 35.9 g/L, T-BIL 1099.4 μmol/L, D-BIL 815.7 μmol/L, ALT 752.1 U/L, AST 1230.1 U/L, γ-GT 431.9 U/L, ALP 442.7 U/L. On March 10, hemafecia appeared, accompanied by slow shallow breathing. Blood gas analysis showed: pH 7.367 (7.35－7.45), PCO_2 29.0mmHg(35－45mmHg), PO_2 99.3mmHg(95-100mmHg), BE－7.9mmol/L (0±2.3mmol/L). After the treatment with correcting metabolic acidosis and haemostasis, the patient still had bad breath condition. Therefore, assisted respiration with tracheal intubation and respirator was used. Although the urine volume in 24h approximated 14ml, bedside hemofiltration could not be arranged because of the hemorrhage of alimentary tract. At 2:15 on March·13, heart rate and blood pressure of the patient began to decrease. Although epinephrin, atropine, lidocaine, dopamine and sodium bicarbonate were given to strengthen his heart, raise blood pressure, improve circulation and correct acidosis, the patient did not show any sign of resuscitation and died soon.

Discussion

Dr. WANG Jie: I will introduce the brief results of the patient's vascular ultrasonography. Hepatic portal vein was not dilated,and there was no embolus in it. The hepatic segment of inferior vena cave was narrowed obviously(diameter 2.3mm), while the inferior hepatic segment of inferior vena cave was dilated(diameter 25.2mm). The femoral veins and great saphenous veins were dilated with slow blood flow, there was no embolus in them.

Dr. CHANG Qing: The clinical characteristics of this case: (1) Elderly man of 67 years old, main clinical manifestations were lower extremity edema and oliguria. Short course of disease and fast progression of the disease; (2)He had history of cardiac cancer and the liver metastatic cancer. B ultrasound found that the volume of liver was augmented, and there were a lot of metastatic tumors in the liver(diameters from 0.9 to 6.0cm);

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(3) After admission, the patient received albumin supplement, diuretics and corresponding symptomatic treatment. The patient's urine volume in 24h increased initially, but the edema of lumbosacral area and lower extremities was worsened progressively. At last the patient appeared to be diuretic-resistant and developed multiple organ function failure leading to death. Many reasons can cause edema of lower extremity, the obstruction or thrombopoiesis of blood vessels may be the main reason for this patient.

Dr. CAI Changhao: The diagnosis of cardiac neuroendocrine carcinoma (NEC) and the metastatic liver cancer is clear. It was reported that the incidence rate of cardiac neuroendocrine tumor (NET) in gastrointestinal tract is high. Among NETs, the malignant ones are named NEC. NEC usually has poor prognosis with 8 months median survival time according to the report. The reason is that although it is sensitive to radiotherapy and chemotherapy, NEC is always with local or distant metastasis when clinically diagnosed. This patient received chemotherapy for many times after diagnosis, but as the tumor progressed, he died 11 months later. Edema of both lower extremities and lumbosacral area, as well as hypourocrinia emerged then. Urine volume was recovered after the treatment with diuretics, colloid supplement and so on, while edema of both lower extremities deteriorated. Similar cases were available in the past, which were finally diagnosed as obstruction of venous return by autopsy. The cardiac and renal functions of this patient were not apparently abnormal. Vascular ultrasound displayed that hepatic segment of inferior vena cava was obviously compressed, therefore the key reason of edema of this patient was obstruction of venous return. At the advanced stage of this case, large doses of diuretics was used with no response and hyperbilirubinemia occurred. Hemofiltration was not used because of advanced tumor. Finally, complications such as metabolic acidosis, respiratory failure, gastro-intestinal hemorrhage emerged.

Dr. XU Shiping: The main features of pathological examination were as follows: Liver enlarged significantly to three times of its normal volume; there were tumor nodes of various sizes spreading all over the liver, and normal liver tissue could be hardly found; but the heart, both kidneys and ureters had no abnormality. Hepatic inferior vena cava was significantly surrounded and compressed by the tumor and the diameter of the vein was only 2 — 3mm, and the distal hepatic inferior vena cava was obviously dilated for compensation. There were metastatic tumors in lung, and 500ml of yellowish green ascitic fluid was found in abdominal cavity. Under optical microscope, plenty of cancer nests were observed in both lungs and liver parenchyma. Congestion in hepatic sinusoid was accompanied by multifocal hepatic necrosis with confluence. Cholestasis in some liver cells was also found, There was hyperplasia of fibrous tissue and infiltration of chronic inflammatory cells in portal area. Analysis of the causes of death: the patient with cardiac mass and hepatic metastasis was subjected to palliative operation. After the operation, more metastatic tumor nests were found in the liver. These nests became larger, compressed the inferior vena cava, and caused block of the venous return, resulting in ascites and edema, and consequent insufficiency of perfusion of the heart, kidney, and finally leading to multiple organ failure and death.

Dr. WU Benyan: I agree with the above opinions. The patient was admitted to our hospital for metastatic liver lesion discovered last April. Primary lesion and its origin were soon identified with the help of gastroscopy and liver biopsy. However, because of high malignancy of the poorly differentiated neuroendocrine carcinoma, widespread metastasis in the liver and the lungs soon occurred in spite of the treatment with chemotherapy for many times and local resection. At the advanced stage, severe edema of lower extremities as well as hyperbilirubinemia occurred. The reasons of the edema of lower extremity might be as follows: (1) Hepatogenic: multiple metastatic tumors in the liver caused decrease in normal hepatic tissues,

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which caused the liver function under a decompensated state, thus the hypoalbuminemia occurred and edema developed in the patient; (2) Nephrogenic: the impaired glomerular filtration and (or) tubular reabsorption caused inability of the kidney to excrete the fluid out of the body; (3) Cardiogenic: the congestion of systemic and pulmonary circulation in the patient caused by cardiac insufficiency resulted in the edema; (4) The edema also might be associated with the thrombosis of blood vessels of lower extremities, which caused block of venous return, leading to edema of lower extremities; (5) The edema might be caused by the obstruction of the portal vein or inferior vena cave due to compression by the tumor of liver, causing edema of lower extremities, lumbosacral region and scrotum. The diagnosis of the patient is clear. Although many times of chemotherapy were given to him preoperatively and postoperatively, there was no clinical amelioration. The metastatic tumors in the liver grew rapidly, severely impaired the liver function. There was no significant decrease in serum albumin after albumin supplement and plasma infusion. Although the total intake and output volume was in balance when the diuretic was used, the edema was aggravated instead. Therefore, we believe that liver dysfunction was not the main cause of the edema. The patient had no acute or chronic renal disease before, and the results of renal ultrasound examination and renal function assay also did not find abnormality of the kidney, the kidney function before edema was within the normal range and BUN and Cr did not rise until approaching his end. Therefore, nephrogenic edema may not be considered. Cardiac function of the patient was normal, thus the edema resulting from cardiogenic diseases was impossible. From the above analysis, we believe that the severe edema in this patient was associated with the obstruction of the inferior vena cava caused by compression of the increased volume of the liver. In this state, intravascular stenting in inferior vena cava can relieve the obstruction, but the growing tumor in the hard liver tissues would make it ineffective.

Finally, the autopsy results confirmed our clinical judgement: compression by tumor in liver caused obstructive jaundice, therefore, hyperbilirubinemia was another main factor leading to death of the patient.

(Translator: CHANG Qing)

老年男性胃癌肝转移术后尿少及双下肢重度浮肿1例

1 病例摘要

患者男性，67岁，主因“发现双下肢水肿3d”于2008年2月10日入院治疗。患者2008年2月7日出现双下肢水肿，为凹陷性，同时伴有尿量减少，600～800ml/d，无发热、心慌、气短、腰痛，无肉眼血尿，不伴有下肢皮温下降、皮肤颜色改变等其他不适。为进一步治疗收入院。患者去年4月因胃贲门癌伴肝脏多发转移，曾先后进行3次选择性肝动脉栓塞化疗及胃左动脉灌注化疗，2次行全身静脉化疗。复查肝脏MRI提示肝脏部分病灶缩小。但贲门处肿瘤原发病灶有所增大、且有出血倾向，遂于同年9月27日行姑息性近端胃切除术。术后病理为：胃贲门小弯侧溃疡型中等分化神经内分泌癌，癌组织侵及胃壁全层，浆膜面有癌结节，脉管内未见癌栓，小弯淋巴结见转移癌(1/12)。术后共进行2个周期的全身化疗，化疗后腹部B超及增强CT等检查均提示肝内转移病灶较前明显增多、增大，胸部CT见肺内出现转移病灶；此后治疗上以提高免疫力、增强营养支持、减轻痛苦、延长生命为主。否认肝炎、结核、高血压、糖尿病、冠心病病史。

入院时情况：体温：37.0℃，脉搏：72次/min，呼吸：18次/min，血压：120/65mmHg。神志清楚，皮肤、巩膜重度黄染，全身皮肤未见出血点、瘀斑、肝掌及蜘蛛痣。右锁骨上窝可触及多个0.5cm×0.4cm左右淋巴结，质硬，边界不清，无触痛，移动性差；眼睑无水肿，双侧瞳孔等大等圆，对光反射灵敏。口唇无紫绀，颈静脉无努张，颈软，甲状腺不大。两肺呼

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吸动度对称，双肺叩诊呈清音，肺肝浊音界位于右锁骨中线第4肋间，双肺呼吸音清晰，未闻及干湿性啰音。心率72次/min，律齐，腹略膨隆，未见胃肠型及胃肠蠕动波，腹正中可见手术瘢痕，愈合良好，腹软，全腹无压痛、反跳痛及肌紧张，肝肋下6.0cm可触及，质硬，无触痛，Murphy's征阴性，叩诊移动性浊音阴性，肝肾区无叩击痛，肠鸣音正常。脊柱及四肢无畸形，无压痛。双下肢、阴囊及腰骶部重度凹陷性水肿，左小腿最大周径为40cm，右侧为41cm，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、尿、便常规、电解质均在正常范围；血生化结果为：尿素氮(BUN)5.72 mmol/L，血肌酐(Cr)58.6 μmol/L，总蛋白69g/L(55～80)，白蛋白35.8g/L(35～55)，T-BIL 281.33 μmol/L(6.0～21)，直接胆红素(D-BIL)226.54 μmol/L(1.7～6.8)，丙氨酸转氨酶(ALT)108 U/L(0～40)，天冬氨酸转氨酶(AST)194.6 U/L(0～40)，γ-谷氨酰转肽酶(γ-GT)1402 U/L(0～52)，碱性磷酸酶(ALP)448 U/L(15～121)，癌胚抗原(CEA)3.56 μg/L(0～5)。心电图未见异常；超声心动图检查结果为：左室射血分数为68%，心脏大小形态正常，室壁厚度正常，左室整体收缩功能正常，心包未见异常；腹部B超：肝脏体积增大，实质回声弥漫性增强，肝左、右叶内显示许多直径0.9～6.0cm大小不等中高回声肿块，胆管、门脉不扩张，门脉内未见栓子，双肾、双侧输尿管及膀胱检查未见异常；行双下肢血管超声检查，显示血管内血流通畅，未见血栓形成。

入院后诊治经过：入院后给予补充白蛋白及加强利尿等治疗后尿量逐渐恢复正常，约2000～2500ml/d，但患者黄疸症状继续加重，双下肢、阴囊、腰骶部短期内发展为重度凹陷性水肿；2008年3月7日患者再次出现尿量减少，对利尿剂等均无反应，复查血生化：BUN 46.28mmol/L，Cr 451.3μmol/L，总蛋白72.3g/L，白蛋白35.9g/L，T-BIL 1099.4μmol/L，D-BIL 815.7μmol/L，ALT 752.1 U/L，AST 1230.1 U/L，γ-GT 431.9U/L，ALP 442.7U/L。3月10日患者出现便血，伴有呼吸浅慢，血气分析结果：pH 7.367，PCO_2 29.0mmHg，PO_2 99.3mmHg，BE －7.9mmol/L，积极给予纠正酸中毒、止血等处理后呼吸状态仍无改善，遂行经鼻气管插管术、呼吸机辅助呼吸；患者全天尿量为14ml。3月13日2:15患者血压、心率下降，给予肾上腺素、阿托品、利多卡因、多巴胺注射液、碳酸氢钠等药物强心、升压、改善循环、扩容、纠正酸中毒等治疗，抢救无效，临床死亡。

2 临床病理讨论

王节医师：简单介绍一下血管超声的情况：门脉不扩张，门脉内未见栓子，下腔静脉肝段明显变细，其内径约2.3mm(图1)，下腔静脉肝下段明显增粗，其内径约25.2mm，血流缓慢；双下肢股静脉各段、大隐静脉明显增粗，血流缓慢，未见血栓。可见下腔静脉肝段明显受增大的肝脏压迫。



图1 血管超声

常青医师：本病例特点：(1)老年男性，此次以双下肢水肿、尿少为主要表现，病程短，进展快；(2)既往有胃贲门癌伴肝内多发转移病史，腹部B超见肝脏体积明显增大，肝内布满直径0.9～6.0cm大小不等的转移灶；(3)入院后先后给予补充白蛋白、利尿等对症治疗，起初尿量明显增加，但双下肢水肿情况未得到控制，随着病情的进展，水肿逐渐加重，到了后期患者对大剂量的利尿剂也没有反应，最后出现了多器官功能衰竭导致患者死亡。引起下肢水肿的原因很多，结合患者病史及相关检查，考虑血管源性水肿可能性大。

蔡昌豪主任医师：患者胃贲门神经内分泌癌伴肝内多发转移诊断明确，神经内分泌肿瘤在胃肠道发生的几率比较高，恶性者称为神经内分泌癌，虽然对放化疗敏感，但由于神经内分泌癌发现时已多伴有局部或远处转移，因此治愈较难，有文献报道神经内分泌癌的中位生存期为8个月。该患者从发现到死亡共生存了11个月，期间经过多次局部及全身化疗，但肿瘤仍继续进展，后期出现了双下肢、腰骶部的水肿，同时伴有尿量减少，治疗上给予利尿、补充胶体等处理后尿量曾一度恢复，但双下肢水肿情况仍在继续加重。以往也曾有过类似的病例，最后尸检证实为下腔静脉受压导致血液回流受阻。该患者

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心肾功能均无明显异常，血管超声提示下腔静脉肝段明显受压，因此双下肢水肿的原因首先考虑为下肢静脉回流不畅所致。病程后期患者对大剂量利尿剂均无反应，同时伴有高胆红素血症，但因其为肿瘤晚期而无法进行血液滤过治疗，最后出现了代谢性酸中毒、呼吸衰竭、消化道出血等并发症。

徐世平副主任医师：病理解剖主要特点：肝脏明显肿大，体积是正常肝脏的3倍，肝内布满大小不等的肿瘤结节，几乎见不到正常的肝组织，但心脏、双侧肾脏、输尿管未见异常；下腔静脉肝段明显受肿瘤包绕、压迫，管腔直径仅为2～3mm，肝段远端的下腔静脉明显代偿性扩张（图2）；肺部发现转移灶，腹腔内可见500ml黄绿色积液。镜下双肺及肝实质内见多量癌巢分布，肝血窦淤血明显伴多灶性肝细胞坏死，互相融合，部分肝细胞淤胆，汇管区纤维组织增生伴慢性炎细胞浸润。死亡原因分析：患者原有贲门肿物伴肝内转移行贲门肿瘤姑息性切除，术后肝脏转移病灶增多、增大压迫下腔静脉，导致静脉回流不畅，引起腹水、水肿症状，继而引起心、肾等器官灌注不足，导致多器官功能衰竭死亡。

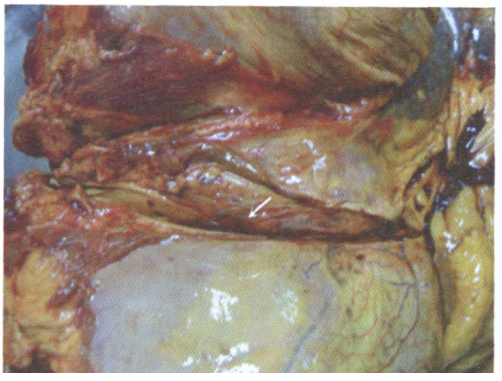


图2 尸检大体所见

吴本俨主任：同意以上分析意见。患者去年4月以发现肝内转移病灶为首发症状就诊，通过胃镜及肝穿刺活检等检查很快明确了肿瘤的原发病灶及肿瘤性质，但因中低分化的神经内分泌癌的恶性度较高，虽然经过多次化疗、局部手术切除，仍很快出现了肝、肺内的广泛转移。后期患者出现了双下肢重度水肿及高胆红素血症。导致下肢水肿的原因可能有以下几个方面：(1)肝源性：肝内多发转移肿瘤使正常肝组织的比例明显减少，继而引起肝功能失代偿，肝脏合成白蛋白减少形成低蛋白血症而引起水肿；(2)肾源性：肾小球滤过功能和(或)肾小管重吸收功能减低，导致肾脏无法将体内液体排出体外而引起全身水肿；(3)心源性：心功能不全致使体循环、肺循环淤血，血管内压力增高导致液体漏出至组织间隙引起水肿，以身体下垂部位为著；(4)下肢血管血栓形成，静脉回流障碍引起双下肢水肿；(5)下腔静脉或门静脉受肝脏肿瘤压迫，其所属回流静脉血液回流受阻而引起下肢、腰骶部及阴囊重度水肿。该患者胃贲门癌肝脏广泛转移诊断明确，术前、术后都进行了多次局部及全身化疗，但针对胃神经内分泌癌的化疗效果不佳，患者肝内转移病灶发展很快，肝功能逐渐衰竭，但在积极补充血浆、蛋白后患者血中的白蛋白水平始终未见明显降低，给予加强利尿后每天出入量基本平衡，然而水肿情况不仅未减轻反而继续加重，因此肝功能不全不是引起水肿的主要原因；肾源性水肿的患者既往多有急慢性肾脏病史，血BUN、Cr的升高，但该患者既往体健，腹部超声检查肾脏未见异常，水肿发生前肾功能始终在正常范围，直至临终时BUN、Cr才有所升高，因此肾源性水肿暂不考虑；该患者心功能正常，超声心动图及心电图均未提示有心功能不全的表现，心源性水肿的可能性很小；最后根据患者的病史，结合腹部超声、腹部CT及双下肢血管超声检查结果，首先考虑引起双下肢、阴囊、腰骶部重度水肿的原因为下腔静脉受明显增大的肝脏压迫而使下腔静脉回流受阻。在治疗上可以通过介入的方案在受压部位放置支架来减轻梗阻情况，但由于肿大的肝脏质地很硬，肝内肿瘤病灶在不断进展，因此效果不是很好，血管很快又会受压梗阻。患者病故后尸检所见使以前的临床判断得到证实。肝内肿瘤的压迫引起梗阻性黄疸，因此高胆红素血症也是导致患者死亡的另一个主要因素。

（参加讨论医师：王节、常青、蔡昌豪、徐世平、吴本俨）

（常青 整理）

万方数据