

## • 临床病理讨论 •

## Clinicopathological Conference

## An 85 year old man with widespread metastatic thyroid cancer

(The sixth case)

Case Presentation

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The patient began to have dysphagia after taking solid food in August 1998, accompanied with poor appetite, vomiting and fatigue. He could only take a little liquid food. His weight lost 5 kg within the recent half month.

He had the history of hypertension, coronary heart disease, myocardial infarction and right thyroid papillary carcinoma resection. Esophagus was normal on gastroscopy in March 1998.

On physical examination, the patient was malnourished with T 35.8°C and BP 105/60mmHg. Superficial lymph nodes were not palpable. There was a palpable hard mass 2 cm in diameter in the right thyroid gland area. The mass could move while swallowing. No rales could be heard in both lungs. The heart rhythm was normal. No abnormality was found on abdomen.

The chest radiograph revealed increased markings of both lungs, a pleural thickening along the right chest wall and blunt bilateral costophrenic angles. The chest CT showed knotty and patchy density in the posterior segment of superior lobe of left lung, medial segment of right middle lobe of lung and lateral basal segment of inferior lobe of right lung. The abdominal ultrasonographic examination showed an inhomogeneous low-level echo mass  $3.1 \times 3.0 \text{ cm}^2$  in size in the superior mid-abdomen, a strong echo mass  $2.2 \times 1.8 \text{ cm}^2$  in size in right adrenal gland, a cyst echo mass  $2.8 \times 2.8 \text{ cm}^2$  in size in right kidney and a cyst echo mass  $2.8 \times 2.8 \text{ cm}^2$  in size in left kidney. The abdomen CT showed a soft tissue dense mass in the root of mesentery reinforced slightly in contrast, a soft tissue dense mass protruding outward at the medial margin of right kidney reinforced slightly in contrast and a high density mass in the left kidney. Ultrasonography of

the thyroid gland revealed an inhomogeneous low-level echo mass  $2.6 \times 2.5 \text{ cm}^2$  in size in right lower cervical part, with plenty of blood supply. The CT scan showed a poorly demarcated soft tissue dense mass  $2 \times 3.5 \text{ cm}^2$  in size in the right thyroid gland area. Gastroscopy showed scattered erosion in gastric corpus and duodenum and normal esophagus. The stomach had little peristalsis. Histological examination of stomach showed a few abnormal cells with karyokinesis on biopsy. Immunohistochemistry revealed: vimentin(+), NSE(+), keratin(-).

Laboratory tests after admission showed: Hb 92 g/L, HCT 27.0%, PLT  $137 \times 10^9/\text{L}$ , WBC  $7.0 \times 10^9/\text{L}$ , N 0.80, ESR 65 mm/h, GPT 6.6 U/L, GOT 11.7 U/L, TP 59.9 g/L, ALB 38.3 g/L, TB 5.5  $\mu\text{mol/L}$ , DB 2.7  $\mu\text{mol/L}$ , GLU 4.58 mmol/L, BUN 7.58 mmol/L, Cr 126  $\mu\text{mol/L}$ , ALP 75.6 U/L, GGT 26.3 U/L, CK 64.3 U/L, LDH 215 U/L, K 3.89 mmol/L, Na 143.6 mmol/L, Cl 101.6 mmol/L, CEA 2.0 ng/ml, AFP <25 ng/ml, FT<sub>4</sub> 20.7 pmol/L(11.45-23.17), TT<sub>4</sub> 188.9 nmol/L(58.1-140.6), TSH <0.01 mU/L(0.35-5.50), FT<sub>3</sub> 7.7 pmol/L(3.5-6.5), TT<sub>3</sub> 3.6 nmol/L(0.92-2.37). Stool examination was normal.

Intravenous nutrition support was given after admission. The patient's heart rate increased to 120-130 /min. The blood chemical examination showed: GPT 13 U/L, GOT 10 U/L, TB 6  $\mu\text{mol/L}$ , DB 2  $\mu\text{mol/L}$ , GLU 6.6 mmol/L, BUN 19 mmol/L, Amy 200 U/L, CK 95 U/L, CK-MB 12.3 U/L, K 4.6 mmol/L, Na 135 mmol/L, Cl 107 mmol/L, Ca 2.5 mmol/L. It was considered that it might be caused by hypovolemia, then volume expansion therapy was given. But the condition of the patient was not improved significantly. The temperature was 38.0°C with heart rate 140-150 /min and respiratory rate 40 /min. Moist rales could be heard in both

lungs. A chest radiograph showed increased markings of both lungs. The hematologic test, arterial blood gas and blood chemical values were: Hb 122 g/L, PLT  $124 \times 10^9$ /L, WBC  $21.6 \times 10^9$ /L, N 0.93, HCT 35.1%, pH 7.307,  $\text{PCO}_2$  24.8 mmHg,  $\text{HCO}_3^-$  12.0 mmol/L,  $\text{PO}_2$  106.4 mmHg,  $\text{SaO}_2$  97.1%, BE -11.9 mmol/L, GPT 21 U/L, GOT 60 U/L, GLU 10.6 mmol/L, BUN 24.7 mmol/L, ALP 72.8 U/L, GGT 35 U/L,

CK 366 U/L, CK-MB 46 U/L, LDH 733 U/L, K 3.89 mmol/L, Na 143.6 mmol/L, Cl 101.6 mmol/L, Amy 54 U/L. Electrocardiogram showed sinus rhythm without ST segment change. The patient might have pulmonary infection, uncompensated metabolic acidosis and acute myocardial infarction. The antibacterials, correction of acidosis and intravenous nitroglycerin were given. But the patient gradually got worse and died at 16:10 on September 5<sup>th</sup>.

## Clinical Discussion

*Dr. Sun Yufa:* According to the clinical signs, I thought the causes of death were as follows: ① Acute myocardial infarction. The patient had the history of coronary heart disease and myocardial infarction. Coronary artery was constricted. In spite of lacking typical elevation of the ST segment, acute myocardial infarction should be considered because of the increase in myocardial enzyme. However there might be other causes such as heart failure and infection. ② Pulmonary infection. The patient got a high fever, the white cells were so high, moist rales could be heard in both lungs and the markings of both lungs increased though the chest radiograph didn't show significant shadows. Pulmonary infection in the elderly might have atypical change on chest film. Pulmonary infection and acute myocardial infarction caused heart failure and death of the patient. ③ Malignant tumor. There were some masses in right kidney, right adrenal gland and posterior peritoneum. Gastroscopy showed scattered erosion in gastric corpus and duodenum. The stomach had little peristalsis. Histology showed a few abnormal cells with karyokinesis on biopsy. Immunohistochemistry revealed: vimentin (+), NSE (+). Primary neuroendocrine tumor of the stomach with metastasis to multiple organs should be considered. We still considered metastatic neuroendocrine tumor of the stomach. Patients with carcinomas usually died of complications such as embolism, massive hemorrhage, infection, etc. The patient might die of heart failure and respiratory failure caused by pulmonary infection.

*Dr. Wang Rong:* The definite diagnoses were acute myocardial infarction, pulmonary infection and

metabolic acidosis. As the patient had the history of thyroid papillary carcinoma, the mass in the right neck might be recurrent thyroid papillary carcinoma. The tubercles in lungs, the masses in right kidney, right adrenal gland and posterior peritoneum, and the lesion of stomach were metastatic carcinomas originated from thyroid papillary carcinoma. But the aged usually tended to have multiple primary carcinomas. So we should exclude the possibility that it was the malignant carcinoma originated from stomach or other organs accompanying thyroid papillary carcinoma.

*Dr. Jiao Fubin:* Gastroscopy showed scattered erosion in the stomach which had little peristalsis. Histology showed a few abnormal cells with karyokinesis on biopsy. The typical adenocarcinoma of stomach originated from epithelial tissue is of intraluminal growth. It is easy to get positive results on biopsy. However, there is another kind of carcinoma of stomach, which grows under mucosa and usually can not be seen. The characteristic of this carcinoma is poor compliance of stomach. We call it linitis plastica. So we suspected that the patient got this carcinoma. We should still exclude carcinoid of stomach because of positive vimentin and NSE.

*Dr. Shao Yong:* The patient's death was attributed to complex factors. The patient could have lower respiratory tract infection because of fever, increased white cells and increased markings. When lower respiratory tract had focal inflammation in the elderly, chest film could be atypical. Heart failure resulting from infection caused increase in heart rate. Hemoglobin and hematocrit before death in comparison with those on admission increased obviously, which might

be due to hypovolemia. In addition to infection, uncompensated metabolic acidosis aggravated the process. Because the patient had the history of myocardial infarction and increased myocardial enzyme, local myocardial infarction should be considered in spite of atypical clinical symptoms and electrocardiogram. Surely, heart failure, shock and infection could cause myocardial enzyme too. The patient had the history of thyroid papillary carcinoma resection. Ultrasound and CT revealed the recurrence of thyroid carcinoma, which pressed esophagus to cause dysphagia. The histological type of previous thyroid carcinoma was papillary carcinoma. This type of malignant carcinoma belongs to low grade and its progression is slow. The patients have normal duration of life if the membrane of carcinoma is intact after resection without metastasis. If vessels are invaded, the 10 year survival rate

is 30%. In this patient, gastroscopy showed scattered erosion in the stomach and duodenum. Peristalsis of gastric corpus was poor. Histology of stomach showed abnormal cells. Carcinoma under mucosa should be considered such as in situ carcinoma. This kind of carcinoma commonly invades and grows under mucosa. Gastroscopy might show normal mucosa. It is not easy to get positive histological results. Deep dig-out biopsy could improve positive rate. Carcinoid of stomach should be excluded because of positive NSE. Because the lesion of stomach and duodenum was so widespread, we should consider metastatic carcinoma besides primary carcinoma of stomach. The masses of right kidney, right adrenal gland and posterior peritoneum tended to be metastatic carcinoma, and they needed to be confirmed by histology.

## Pathological Discussion

*Dr. Shi Huaiyin:* The pathological diagnoses were as follows:

(1) Recurrent thyroid carcinoma after resection,  $3.4 \times 2.8 \times 2.0 \text{ cm}^3$  in size. The histological types were as follows: ① typical papillary carcinoma; ② follicle isoforms of papillary carcinoma; ③ undifferentiated carcinoma. Parathyroid gland and skeletal muscles beside thyroid gland were infiltrated, accompanied by bleeding and necrosis. The metastatic organs were as follows: ① heart: there were diffused metastatic nodes. The biggest node in left ventricle was 4 cm in diameter. All layers of both ventricles were infiltrated by carcinoma cells, accompanied by bleeding and necrosis. The volume of bloody fluid in pericardium was 350 ml; ② adrenal glands: the biggest node in right adrenal gland was  $4 \times 3 \times 3 \text{ cm}^3$  in size and that in left adrenal gland was 0.5 cm in diameter, accompanied by bleeding and necrosis; ③ kidney: the biggest node in right kidney was  $4.8 \times 4 \times 3 \text{ cm}^3$  in size. The major metastatic carcinomas were in renal corpuscles; ④ pancreas: the mass was  $2.4 \times 2.0 \times 1.8 \text{ cm}^3$  in size; ⑤ both lungs: there were diffused metastatic nodes in lungs, and some tissues of carcinoma could be seen in arteries; ⑥ diges-

tive tract: metastatic carcinomas infiltrated digestive tract from serous membrane to submucosa. The biggest node in stomach was 0.6 cm in diameter. The node on Treitz ligament was  $4 \times 3.5 \times 3.2 \text{ cm}^3$  in size; ⑦ lymph nodes: the nodes on abdominal wall, diaphragm and abdominal aorta were about 0.5 cm in diameter.

(2) Stasis of blood and edema of both lungs.

(3) Cyst of 1.2 cm in diameter in inferior pole of left kidney, accompanied by bleeding.

(4) Atherosclerosis. ① Aorta atherosclerosis, compound lesion phase. ② Coronary atherosclerosis, fibrous plaque phase. Anterior descending branch and right coronary artery belonged to grade 3 and left circumflex branch to grade 2.

(5) Focal bleeding and necrosis around central vein of liver.

The pathological cause of death should be extensive metastasis of carcinoma which caused serious damage of multiple organs and systems.

*Dr. Li Xianghong:* Thyroid papillary carcinoma is low-grade malignant tumor, which grows slowly. This type of carcinoma in the elderly usually tends to combine with undifferentiated carcinoma which is

high-grade malignant tumor. It has strong invasiveness and is apt to metastasize, as was confirmed by autopsy. Invasion of carcinoma to myocardium leads to increase in myocardial enzyme but not acute myocardial infarction. The reason of scattered erosion in

gastrointestinal tract was that invasion of metastatic carcinoma to submucosa and muscular layer caused necrosis of mucosa.

(Translators WU Daohong, WU Benyan)

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## 1 例 85 岁男性甲状腺癌广泛转移

### 1 病历摘要

患者,男性,85 岁。主诉因进食梗噎、食欲减退半月于 1998 年 8 月 19 日入院。患者既往有高血压病、冠心病、心肌梗死,曾行右侧甲状腺乳头状癌切除术。入院查体发现甲状腺右叶区可扪及 2 cm 质硬包块。胸部 CT:双肺可见结节状、点状、斑片状高密度影。腹部 CT:右肾内侧缘实质可见突向外的软组织块影,左肾内可见圆形的高密度结节影,腹膜后肠系膜根部可见块状软组织密度影。增强扫描右肾病灶均匀轻度强化,左肾内病灶未见明显强化影,腹膜后肠系膜根部软组织块影轻度强化。胃镜:胃体、十二指肠见散在疣状糜烂灶,活检病理:胃粘膜慢性炎症改变,幽门螺杆菌(*Helicobacter pylori*, HP)感染(++) ,伴溃疡形成,溃疡底部固有膜有小片异型细胞,核分裂相可见;免疫组化结果:波形蛋白(vimentin)(+)、非特异性酯酶(nonspecific esterase, NSE)(+)、角蛋白(keratin)(-)。甲状腺 B 超:右下颈部可见 2.6 cm×2.5 cm 大小不均匀低回声肿块,其内部血供异常丰富。8 月 20 日化验检查血常规:Hb 92 g/L, HCT 27.0%, PLT  $137 \times 10^9$ /L, WBC  $7.0 \times 10^9$ /L, N 0.80;肝肾功能、电解质正常。9 月 3 日晚患者心率增快、120-130 次/min,烦躁,肌酸激酶(creatinine kinase, CK)95 U/L,心肌型肌酸激酶同工酶(MB isoenzyme of creatine kinase, CK-MB)12.3 U/L。考虑可能为血容量不足所致,予以扩容治疗后,心率仍快。9 月 4 日患者体温 39.0℃、心率 140-150 次/min、呼吸 40 次/min,双肺有较多湿啰音,胸部 X 片:双肺纹理增粗。血常规:Hb 122 g/L, WBC  $21.6 \times 10^9$ /L, N 0.93, HCT 35.1%;血气分析:pH 7.307, PCO<sub>2</sub> 24.8 mmHg(1 mmHg=0.1333 kPa), HCO<sub>3</sub><sup>-</sup> 12.0 mmol/L, PO<sub>2</sub> 106.4 mmHg, SaO<sub>2</sub> 97.1%, BE -11.9 mmol/L。血生化

检查:CK 366 U/L, CK-MB 46 U/L, 乳酸脱氢酶(lactate dehydrogenase, LDH)733 U/L;心电图为窦性心律,ST 段无明显改变。考虑患者可能存在急性心肌梗死,并发肺部感染、失代偿性代谢性酸中毒,予以扩冠、抗感染、纠正水电酸碱失衡治疗,但患者病情逐渐恶化,于 9 月 5 日 16:10 死亡。

### 2 临床与病理讨论

该患者死亡原因可能由多发因素所致。患者有发热、白细胞升高,胸部 X 片提示肺纹理增加,可能存在下呼吸道感染,因为老年人下呼吸道小灶性炎症有时在胸片上没有典型表现。感染诱发心功能不全致心率增快。另外,患者血红蛋白、红细胞比容后期较入院时明显升高,结合发热、呼吸快、心率快,考虑存在血容量不足,加之感染,导致失代偿性代谢性酸中毒,加剧了病情的发展。患者出现心肌酶升高,虽然临床症状、心电图不支持,但患者既往有心肌梗死病史,不能除外小灶性心肌梗死。当然,心肌酶升高还可继发于心功能不全、休克、感染。患者既往有甲状腺癌病史,B 超、CT 提示甲状腺癌复发,因此,患者进食哽咽是肿瘤压迫食管所致。胃镜检查发现胃、十二指肠多发疣状糜烂灶,胃体蠕动少,病理发现异型细胞,需要考虑粘膜下肿瘤,特别是胃硬癌,其特点是粘膜下潜行浸润生长,而胃粘膜可无异常表现,常常不容易获得阳性病理结果,采用深挖式活检可提高阳性率。由于免疫组化 NSE 阳性,还需除外胃类癌。该患者胃、十二指肠病灶广泛,除考虑原发于胃的肿瘤,还需考虑来源于甲状腺的转移癌。腹膜后、右肾、右肾上腺肿块多考虑为肿瘤转移,但肿瘤性质还需病理证实。

病理诊断:甲状腺癌术后复发,组织学类型:①典型乳头状癌;②滤泡亚型乳头状癌;③未分化癌。浸润至甲状旁腺、甲状腺周围骨骼肌组织,并转移至

心脏、肾脏、胰腺、肺、消化道、腹壁、膈肌。双肺淤血、水肿。死亡原因:由于肿瘤广泛转移,造成多脏器严重损伤。心、肺受累引起患者心功能衰竭、肺水肿,最后多器官功能衰竭、死亡。

(参加讨论医师:孙玉发,王蓉,缴富斌,邵勇,石怀银,李向红)

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## · 经验交流 ·

# 连续性肾脏替代疗法在老年多器官功能衰竭治疗中的应用

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连续性肾脏替代疗法(continuous renal replacement therapy, CRRT)自 1997 年开始应用于临床以来,日益显示出在救治多器官功能不全综合征(multiple organ dysfunction syndrome, MODS),特别是老年多器官功能衰竭(multiple organ failure in the elderly, MOFE)时的优势。

## 1 临床资料

1.1 一般资料 选择于 1999 年 6 月至 2002 年 3 月在本医院进行 CRRT 治疗、符合 MOFE 诊断标准的患者 15 例,其中男性 12 例,女性 3 例,年龄 64~85 岁,平均 75.8 岁。15 例患者全部有心、肾功能衰竭及肺感染或呼吸衰竭。其中 5 例伴发神经系统功能损伤,11 例用升压药维持血压,4 例机械通气。

1.2 治疗方法 15 例患者均采用日间 8~12 h CRRT, 10~270 h 不等,每例平均 55.3 h,其中连续性静-静脉血液滤过(CVVHF)750 h,连续性静-静脉血液透析滤过(CVVHDF)80 h。仪器使用 prismaTM 机器、M 60 管路和滤器(面积 0.6m<sup>2</sup>,AN 69 膜);血管通路为股静脉双腔内置管;血液流速 100~150 ml/min;置换液采用前稀释法,置换液、透析液均为碳酸氢盐,速度均为 1 500~2 500 ml/h,置换液每次平均为 16 L;15 例患者均有不同程度出血倾向,故采用低分子肝素“速避凝”抗凝,首剂 0.1~0.4 ml,4~8 h 追加 0.4 ml,均抗凝有效。

1.3 结果 4 例患者死亡;3 例治疗后心血管、神经系统趋于稳定转为间歇性血液透析(intermittent

hemodialysis, IHD)治疗;其余 8 例均不同程度延长了存活时间,最长 1 例延长了 60 d。

## 2 讨论

MOFE 不同于 MODS,王士雯将其定义为老年人(>60 岁)在器官老化和患有多种慢性疾病基础上,由某种诱因激发,在短小时内出现两个或两个以上器官序贯或同时发生衰竭。MOFE 死亡率非常高,有报道≥3 个器官衰竭的 MOFE 患者的病死率几乎达 100%。

与传统的 IHD 相比,CRRT 对血流动力学影响小,具有持续、缓慢、稳定的特点,用于重症患者更安全、耐受性更好。CRRT 清除了多余的容量负荷,使酸中毒和电解质紊乱得到纠正;心肌抑制因子被清除,使患者心功能得到改善;同时减轻了肺水肿和胸腔积液,使肺部感染易于控制,患者的通气功能得到改善。AN 69 膜可清除部分中分子炎症介质和血管活性物质。有研究发现 MOFE 患者血浆中 IL-1、IL-6 和 TNF 水平显著高于健康老年人,而病死组又显著高于存活组,且与器官衰竭数目呈显著正相关。

发生 MOFE 的患者往往存在多种基础疾病、营养不良及消化功能障碍,全身抵抗力极差。CRRT 可以充分调控液体平衡,接受胃肠外营养所需的剂量,避免了 IHD 对液体的限制,使患者得到充分的营养和足够的热量。对此类患者,CRRT 能圆满替代肾功能,而且也能显著改善其他器官功能,延长生存期。

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