

Clinicopathological Conference (the 54th case)

Postoperative treatment for an octogenarian early gastric cancer patient who had undergone radical gastric resection

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Case presentation

An 82-year-old male patient was admitted to our department due to “intermittent upper abdominal discomfort for 20 years and post-operation of distal gastrectomy of early gastric cancer for more than one month”. Since 1987, the patient presented with intermittent upper abdominal discomfort, receiving upper GI endoscopic examination, and based on pathological biopsy specimen, was diagnosed as chronic atrophic antral gastritis. In June 2004, upper GI endoscopy and pathology examination indicated mild to moderate dysplasia accompanied with intestinal metaplasia. Two months later, the following-up endoscopic examination and biopsy demonstrated tubular adenoma which followed resection by APC. In May 2011, endoscopic examination showed a type IIb+c lesion less than 2cm on the greater curvature of the antrum, the pathological diagnosis was poorly differentiated adenocarcinoma mixed with signet ring cell carcinoma. Preoperative imaging studies including chest and abdominal CT scans found no evidence of distant metastasis or local infiltration. The operative procedure was distal gastrectomy with lymph node exploration and 5,6 station dissection, and Billroth-I method reconstruction. No macroscopic metastasis was visually seen in the lymph nodes, liver or peritoneum. The macroscopic findings of the resected specimen were an irregular shaped ulcerative lesion 16×10×3 mm in size on the anterior wall of the gastric antrum. The pathologic findings showed poorly differentiated adenocarcinoma which had invaded to the deep submucosa of the stomach. Microscopic margin and all three dissected lymph nodes were negative. The result of an over-expression assessment of Her-1 and Her-2 is negative, but the VEGF was positive, Ki-67 +40% and TopIIa +20%.

The patient had a history of coronary heart disease for more than 30 years, chronic bronchitis for 20 years. He was diagnosed type 2 diabetes 24 years ago; the blood glucose was well controlled with oral metformin and acarbose.

Physical examination and laboratory test after admission: He was well developed and moderately nourished. No superficial lymph node enlargements were found. Pulmonary sounds were clear and symme-

trical, No wheezes. No rales. HR:72/min. Heart sounds were strong and no splitting. Cardiac rhythm was regular. No pathological murmurs. Abdomen was soft. Gastrointestinal type or peristalses were not seen. There was a vertical scar in the middle of abdomen, no tenderness or rebound tenderness. Live and spleen were not palpable. Shifting dullness was negative.

Blood routine test: PLT $155 \times 10^9/L$, RBC $3.9 \times 10^{12}/L$, Hb115g/L, WBC $5.35 \times 10^9/L$, N 0.59, L 0.34. Kidney and liver function tests were normal. Pre-operation serum CEA fluctuated between 5.24 and 5.74μg/l. Fecal occult blood test was negative. C¹³-Urease breath test was negative. EGC is normal. Abdominal ultrasound showed gallbladder polyps and prostatic hyperplasia with calcification. The enteral nutrition feeding tube was removed after careful diet transition. Whether or not the patient would receive adjuvant chemotherapy was discussed in our department.

DISCUSSION

Dr. Huang Haili: According to pre-operative imaging findings and post-operative histopathological results, the patient's TNM stage was T1N0M0 (stage IA). The prognosis for a curatively resected early gastric cancer is generally good, and post-operative chemotherapy was not indicated in EGC patients who underwent R0 resection. However, limited by patient's age and basic condition, only D0 lymph node (station 5,6) dissection was performed, and only three lymph nodes were recovered in the surgical specimen. As we know that the lymph node metastasis from SM-EGC is about 20%. Patients with type C and an undifferentiated histological type may have even higher risk of lymph node metastasis. A recent study further divided T1b stage to SM1, SM2, SM3, with the probability of lymph node metastases at 10%, 19%, 33% respectively. The patient's SM3 T stage and elevated serum CEA level also increased the risk of lymph node metastasis. On the other hand, pre-operative detection of perigastric lymph node metastasis through CT and US is difficult due to their limited sensitivity (ranges from 56%–78%), and sensitivity and accuracy of intraoperative assessment of lymph node metastasis for EGC is 55.6%–73.2% and 76.4%–91.9% respectively, so we could not surely exclude metastasis lymph node at

other perigastric stations based on our evidence. According to NCCN Gastric Cancer Guidelines, it is recommended that curative gastric resection should include the regional lymphatic with a goal of examining at least 15, or greater, lymph nodes for accurate staging. Therefore, the prognosis of this patient will be determined by the possibility of lymph node metastasis. In summary, because of the deficiency of lymph node dissection and the patient's high expectation of prognosis, the individual treatment should be considered. If the patient has an aggressive attitude to post-operative treatment, adjuvant chemotherapy, such as Xeloda, may be an appropriate choice.

Dr. Wu Daohong: We've investigated 301 poorly differentiated type EGC patients who underwent radical surgery from September 1983 to July 2010 in our hospital, focusing on which clinicopathological factors will influence the prognosis. These poorly differentiated histological types included adenocarcinoma, mucinous adenocarcinoma and signet-ring cell carcinoma. The lymph nodes were examined in 294 cases, of which 56 cases were histologically diagnosed as lymph node metastasis. Univariate analysis revealed that tumor size (diameter >1.5cm), depth of invasion, lymphovascular invasion and P16 over expression were associated with regional lymph node metastases. Multivariate analysis indicated that the tumor size (diameter >1.5cm), the deep of invasion (to the submucosa), and the lymphovascular invasion were independent risk factors for lymph node metastases. The stratified analysis showed that when the tumor

ranged from 1.5 to 3.0cm and invaded to the submucosa without lymphovascular invasion, the rate of lymph node metastasis was 19.0% (12/63). Based on our studies and although the number of dissection lymph node was less than 15, the risk of lymph node metastasis in this patient was considered low. Taking into account patient's age and comorbid diseases, I suggest close follow-up rather than adjuvant chemotherapy.

Professor Wu Benyan: The diagnosis of this patient was clear, EGC with T1N0M0 (IA stage). Although we are concerned about lymph node metastasis due to insufficient numbers of lymph node dissection, the adverse effects of chemotherapy, including myelosuppression, gastrointestinal distress, cardiotoxicity, which often are more obvious in elderly patients, should also be taken into consideration. Based on NCCN Guidelines and our experiences, pN0 EGC patients who received R0 resection will not benefit from post-operative chemotherapy. In my opinion, the appropriate post-operative treatment for this patient is close observation and follow-up.

After discussion among our department and full communication with the patient, the follow-up strategy was taken. In December 2011, the patient came back to our department for surveillance, routine physical examination and imaging study, including chest CT, abdominal CT scans and endoscope. We found no evidence of local relapse and metastasis. So far, the patient was still under surveillance.

(Translator: SU Binbin)

老年胃癌 1 例根治术后的治疗选择

1 病例摘要

现病史: 患者男性, 82 岁, 主因“间断上腹部不适 20 余年, 胃窦早癌根治术后 1 月余”于 2011 年 7 月 18 日入院。患者自 1987 年起出现上腹部不适, 多次胃镜检查提示胃窦慢性萎缩性胃炎。2004 年 6 月胃镜示: 胃窦幽门型黏膜腺体轻-中度不典型增生伴肠化; 2 月后复查胃镜示: 胃窦幽门型黏膜慢性炎症伴管状腺瘤形成, 少数腺体中度不典型增生。1 月后行胃窦息肉氩气刀切除术, 术后病理示: 管状腺瘤。2011 年 5 月胃镜示: 胃窦大弯中部 2 cm × 1.5 cm 不规则糜烂灶 (图 1), 活检病理示: 胃窦低分化腺癌及印戒细胞癌。术前评估: 肺部 CT、腹部 CT、超声 (图 2) 未见转移证据。2011 年 6 月行“远端胃癌根治术, 空肠造瘘术”, 术后病理示: 胃窦大弯侧溃疡型低分化腺癌, 1.6 cm × 1 cm × 0.3 cm 范围, 肿瘤浸润胃黏膜下层, 切缘阴性, 大弯侧淋巴结未见转

移 (0/3); 免疫组织化学检测: Her-1 (-); Ki-67 + 40%, Top a + 20%, Her-2 (+), VEGF (+), 患者为进一步诊治由普外科转入老年消化科。

既往病史: 冠心病病史 30 余年, 慢性支气管炎病史 20 余年, 上述病情平稳; 1988 年诊断“2 型糖尿病”, 目前口服二甲双胍、阿卡波糖治疗, 血糖控制尚可。

入院查体: 皮肤巩膜无黄染, 浅表淋巴结未触及肿大, 双肺呼吸音清晰, 未闻明显干湿啰音。心率 72 次/min, 节律齐, 各瓣膜听诊区未闻及杂音。腹部饱满, 上腹部正中切口长约 15 cm 的术后瘢痕, 腹中部留置空肠营养管, 周围无明显渗出, 腹软, 全腹无压痛、反跳痛, 未触及包块, 肝脾肋下未及, 移动性浊音阴性。

诊疗经过: 入院后检查: 血常规: PLT $155 \times 10^9/L$, RBC $3.9 \times 10^{12}/L$, Hb 115g/L, WBC $5.35 \times 10^9/L$, N: 0.59; 血生化检查: 肝、肾功能指标未见异

常;癌胚抗原 (carcino-embryonic antigen, CEA) 波动在 $5.24 \sim 5.74 \mu\text{g/L}$, 粪便潜血阴性; 13C 呼气试验 (-), 便幽门螺杆菌抗原阴性; 腹部超声示: 胆囊壁胆固醇性息肉, 前列腺增生伴钙化; 心电图示: 窦性心律。

逐步过渡饮食顺利, 2 周后拔除空肠营养管。就患者是否需要术后辅助化疗讨论如下。

2 临床讨论

黄海力主治医师: 根据术前影像学表现及术后病理诊断, 该胃癌患者 TNM 分期为 T1N0M0, A 期。按照指南 T1 期胃癌患者淋巴结转移概率低, 通常能够根治性切除, 不需要辅助化疗。但该患者特殊之处在于术者顾忌到其高龄及基础疾病等因素, 术中经过探查后仅清扫了第 5、6 组淋巴结, 术后病理仅检出 3 枚淋巴结, 均为阴性, 所以该患者属于 D0 切除。该结果远未达到美国国立综合癌症网络 (National Comprehensive Cancer Network, NCCN) 指南建议的胃癌根治术淋巴结清扫范围和至少检出 15 枚淋巴结的个数。虽然术中探查了其余部位淋巴结, 未发现转移证据, 但文献报道术中探查淋巴结是否转移敏感性仅在 $55.6\% \sim 73.2\%$, 准确性在 $76.4\% \sim 91.0\%$ 之间, 因此该患者其余 N1 乃至 N3 站淋巴结是否存在转移仍存疑虑。所以, 该患者关键在于判断淋巴结转移的可能性。文献报道, 早期胃癌淋巴结转移主要与肿瘤大小、侵犯深度及脉管癌栓、术前 CEA 水平等有关。T1b 淋巴结转移概率为 $20\% \sim 25\%$, 但 T1b 可进一步分为 SM1, SM2, SM3, 淋巴结转移概率分别为 $10\%, 19\%, 33\%$ 。根据术内镜超声检查及病理判断, 该患者胃癌侵犯 SM3, 加之术前 CEA 升高, 病理为低分化、印戒细胞癌, 因此转移概率可能还要高些。综上所述, 该患者应该个体化考虑术后的治疗, 患者思虑较重, 若愿望积极, 可以适当考虑口服卡培他滨 (商品名: 希罗

达) 辅助化疗, 并定期随诊。

吴道宏副主任医师: 我们曾总结过解放军总医院从 1983 年 9 月至 2010 年 7 月分化不良型早期胃癌 301 例, 其均为根治性切除术。其中分化不良包括低分化腺癌、黏液腺癌、印戒细胞癌 3 种病理类型。其中 294 例术后找到淋巴结, 56 例有区域淋巴结转移, 占 $19\% (56/294)$; 7 例术后标本未找到淋巴结。通过单因素分析我们发现, 肿瘤大小 (直径 $> 1.5 \text{ cm}$)、浸润深度、淋巴管癌栓、P16 表达与区域淋巴结转移相关; 多因素回归分析提示, 肿瘤直径 $> 1.5 \text{ cm}$ 、浸润至黏膜下层、淋巴管癌栓为淋巴结转移独立危险因子; 分层分析显示, 肿瘤直径 $1.5 \sim 3.0 \text{ cm}$ 、无淋巴管癌栓的黏膜下层癌淋巴结转移率为 $19.0\% (12/63)$ 。该患者肿瘤直径 1.6 cm 、浸润黏膜下层、无淋巴管癌栓, 尽管淋巴结清扫个数不足 15 个, 但本身淋巴结转移的风险小, 考虑到患者高龄, 基础疾病多, 因此可暂不考虑辅助化疗, 给予密切随访。

吴本俨主任医师: 该患者胃癌的术后病理分期为 T1N0M0 (IA 期), 不需要辅助化疗。该患者的特殊性在于, 术后标本淋巴结检出数少, 担心存在转移淋巴结残留的问题。但另一方面, 高龄患者化疗耐受能力弱, 化疗副反应, 如骨髓抑制、消化道反应、心脏毒性等问题往往比较明显, 因此化疗更应趋于谨慎。综合指南及我们的经验, 该患者术后辅助化疗可能无法获益, 应采取更为密切随访的策略。

经全科谈论并与患者充分沟通后, 对患者采取随访策略。该患者于 2011 年 12 月回我科复诊, 常规查体及胸、腹部 CT 及胃镜均未见肿瘤复发证据。目前给予继续随访。

(参与讨论医师: 苏斌斌, 黄海力, 吴道宏, 吴本俨)

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