Effect of integrated surgery + radiotherapy + chemotherapy treatment on survival status and serum indexes in patients with gallbladder carcinoma

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ABSTRACT

Objective: To study the effect of integrated surgery + radiotherapy + chemotherapy treatment on the survival status and serum indexes in patients with gallbladder carcinoma. Methods: A total of 68 patients with gallbladder carcinoma were divided into observation group (received integrated surgery + radiotherapy + chemotherapy treatment) and control group (received surgery + radiotherapy) according to different treatments. Differences in the content of tumor markers, growth factors and adhesion molecules in serum as well as the median survival time and survival rate in 5 years of follow-up were compared between the two groups 1 month after treatment. Results: Tumor markers β2-MG, CA19-9, CA242, CA125, CA724, CEA and AFP content in serum of observation group after treatment were significantly lower than those of control group; growth factors VEGF, FGF, EGFR and HER2 content in serum were significantly lower than those of control group while IGFBP-2 and IGFBP-3 content were significantly higher than those of control group; adhesion molecules E-selectin, ICAM-1, VCAM-1 and sE-Cd content in serum were significantly lower than those of control group; the median survival time of 5-year follow-up as well as 1-, 3- and 5-year survival rate were significantly greater than those of control group. Conclusions: Integrated treatment of surgery + radiotherapy + chemotherapy can optimize the short-term and long-term curative effect in patients with gallbladder carcinoma.

1. Introduction

Gallbladder carcinoma is with extremely high malignancy, the mortality rate within 1 year after surgical treatment alone is as high as above 80%, and adding postoperative adjuvant treatment is the most important way to promote overall treatment effect[1,2]. Radiotherapy after surgery is more commonly used treatment at present, which prolongs patients’ survival time by killing the activity of residual tumor cells. Current study has found that some patients with gallbladder carcinoma are not sensitive to radiotherapy, so some scholars suggest adding the postoperative chemotherapy to the overall treatment plan, and integrated treatment of surgery + radiotherapy + chemotherapy was used to further enhance the therapeutic effect of the gallbladder carcinoma[3]. At present, the integrated treatment of gallbladder carcinoma is less covered by research reports, and there is no reliable judgment about its short-term and long-term curative effect after treatment. In the study, patients with gallbladder carcinoma in our hospital were selected as the research subjects, and the postoperative short-term serum indexes and long-term survival indexes of patients who received integrated treatment were studied in order to make clear the reliability of the integrated surgery + radiotherapy + chemotherapy treatment.

2. Materials and methods

2.1. General information
A total of 68 patients with gallbladder carcinoma treated in our hospital between April 2010 and April 2015 were included, and the inclusion criteria were: (1) were diagnosed with gallbladder carcinoma by pathology; (2) with expected survival time > 6 months; (3) with primary gallbladder carcinoma; (4) received systemic treatment for the first time; (5) patients signed informed consent. Exclusion criteria were: (1) with primary malignant tumor of other organs; (2) with liver and kidney dysfunction and couldn’t tolerate surgery trauma; (3) with severe blood coagulation dysfunction; (4) with severe acute infectious diseases; (5) with incomplete clinical data. 68 patients conformed to the inclusion criteria and were divided into control group (n=30) who received surgery + postoperative radiotherapy and observation group (n=38) who received integrated surgery + radiotherapy + chemotherapy treatment after the therapeutic regimen were retrospectively analyzed. Control group included 13 male cases and 17 female cases, they were 30-71 years old and (45.83±7.12) years old in average, 10 cases were with clinical IIA stage, 9 cases were with IIB stage, 6 cases were with IV A stage and 5 cases were with IV B stage; observation group included 20 male cases and 18 female cases, they were 32-73 years old and (47.69±7.55) years old in average, 13 cases were with clinical IIA stage, 10 cases were with IIB stage, 8 cases were with IV A stage and 7 cases were with IV B stage. The two groups of patients showed no significant difference in the distribution of gender, age and tumor staging (P>0.05) and could be subsequently compared.

2.2. Treatment methods

The control group of patients received surgery + postoperative radiotherapy, specifically as follows: radical operation method for gallbladder carcinoma was the same as that in the literature, and patients received reverse intensity-modulated radiation therapy (IMRT) 1-3 months after operation. Patients were fixed by vacuum pad, scanning range was tracheal carina-the fifth lumbar vertebra, 3D reconstruction was conducted within the treatment planning system, and the clinical target volume, gallbladder carcinoma bed operation area, hilus lymph drainage area as well as superior mesenteric artery and retroperitoneal lymph drainage area were outlined. Planning target area externally expanded by 1cm on the basis of clinical target volume, and extended up and down (to the head and feet) by 1.5 cm. Observation group received integrated surgery + radiotherapy + chemotherapy treatment, surgery and radiotherapy methods were the same as those of control group, and the chemotherapy regimens were as follows: chemotherapy was synchronously performed after radiotherapy started, tegafur 1.0 and calcium folinate 0.2, intravenous injection, for six consecutive days, gemcitabine 0.6, injected on the first day and the fifth day of chemotherapy, monitoring white blood cell count, and giving ondansetron to stop vomiting as well as granulocyte colony-stimulating factor to improve the white blood cells.

2.3. Serum indexes

One month after treatment, 3 Ml of fasting peripheral venous blood was synchronously extracted from both groups of two groups, let stand at room temperature and centrifuged at 4 ℃ to get supernatant, and the specific detection indexes were as follows: (1) tumor markers: ELISA method was used to determine β 2 microglobulin (β 2-MG), carbohydrate antigen 19-9 (CA19-9), carbohydrate antigen 242 (CA242) carbohydrate antigen 125 (CA125), carbohydrate antigen 724 (CA724), carcinoembryonic antigen (CEA) and alphafetoprotein (AFP) content. (2) Growth factors: ELISA method was used to determine vascular endothelial growth factor (VEGF), basic fibroblast growth factor (FGF), epidermal growth factor receptor (EGFR), human epidermal growth factor receptor-2 (HER2), insulin-like growth factor-binding protein-2 (IGFBP-2) and insulin-like growth factor-binding protein (IGFBP-3). (3) Adhesion molecules: E-selectin, intercellular adhesion molecule-1 (ICAM-1), vascular intercellular adhesion molecule-1 (VCAM-1) and soluble E-cadherin (sE-Cd).

2.4. Survival conditions

The two groups of patients were followed up for 5 years, the median survival time as well as 1-, 3- and 5-year cumulative survival rate was recorded.

2.5. Statistical methods

Data obtained in the study was analyzed by SPSS23.0 software, measurement data comparison was by t test and P<0.05 indicated statistical significant differences.

3. Results

3.1. Tumor marker content

β 2-MG, CA19-9, CA242, CA125, CA724, CEA and AFP content in serum of observation group were significantly lower than those of control group (P<0.05), shown in Table 1.

3.2. Growth factor content

VEGF, FGF, EGFR and HER2 content in serum of observation...
group were significantly lower than those of control group while IGFBP-2 and IGFBP-3 content were significantly higher than those of control group (P<0.05), shown in Table 2.

3.3. Adhesion molecules

E-selectin, ICAM-1, VCAM-1 and sE-Cd content in serum of observation group were significantly lower than those of control group. Differences in adhesion molecules E-selectin, ICAM-1, VCAM-1 and sE-Cd in serum were statistically significant between two groups 1 month after treatment (P<0.05), shown in Table 3.

3.4. Survival

During 5 years of follow-up, comparison of the survival between two groups was as follows: the median survival time of observation group was (2.31±0.29) years, 1-year survival rate was 71.05% (27/38), 3-year survival rate was 28.95% (11/38) and 5-year survival rate was 15.79% (6/38); the median survival time of control group was (1.16±0.24) years, 1-year survival rate was 36.67% (11/30), 3-year survival rate was 20.0% (6/30) and 5-year survival rate was 3.33% (1/30). The median survival time as well as 1-, 3- and 5-year survival rate of observation group were significantly higher than those of control group (P<0.05).

4. Discussion

Gallbladder carcinoma has extremely high malignant degree and its latent pathogenesis causes that most patients have missed the best opportunity of early treatment. At present, study has found the clinically diagnosed patients with gallbladder carcinoma are mostly at III-IV stage, and surgical treatment alone is of little significance in prolonging the survival time of patients[4]. Radiotherapy after gallbladder carcinoma surgery is the common way to consolidate treatment effect and kill residual tumor cells, and relevant statistics show that patients with gallbladder carcinoma receive surgery combined with radiotherapy, the median survival time is about 1 year, and the recurrence occurs within 1-3 years after treatment[5,6]. How to further prolong the survival time and improve the lifetime of patients with gallbladder carcinoma is the clinical focus, some scholars recommend adding postoperative chemotherapy to form the integration of surgery + radiotherapy + chemotherapy, but there is still little research about the clinical application effect of the therapy. In the study, patients with gallbladder carcinoma who received surgical treatment in our hospital were selected as the research subjects, and the effect of the integrated treatment on serum indexes and 5-year survival was mainly elaborated.

Biological indexes in serum can objectively reflect the biological and pathological process of tumor and due to the lack of specific indexes for early diagnosis of gallbladder carcinoma, the combined detection of multiple tumor markers can improve the accuracy and specificity of detection results[7-9]. β-2-MG, CA19-9, CA242, CA125, CA724, CEA and AFP are the tumor markers that are currently discovered to be highly expressed in hepatobiliary system[10,11]. Their detection in the study showed that β-2-MG, CA19-9, CA242, CA125, CA724, CEA and AFP content in serum of observation group were lower 1 month after treatment, indicating that integrated treatment is more effective on killing tumor cells and containing tumor activity, and lays the foundation for the optimization of patients’ long-term treatment prognosis.

The gallbladder carcinoma invasion and metastasis greatly depend on angiogenesis, and the content of serum growth factors will directly determine the tumor cell invasion[12]. In the study, the levels of VEGF, basic FGF, EGFR, HER2, IGFBP-2, IGFBP-3 and other common growth factors were tested, and it was found that VEGF, FGF, EGFR and HER2 content in serum of observation group were lower while IGFBP-2 and IGFBP-3 content were higher after treatment. VEGF is the known factor with the strongest ability to promote angiogenesis, and FGF has the dual roles of promoting angiogenesis as well as tumor cell proliferation and division. Research has found that EGFR and HER2 levels are associated with the development of gastric cancer, and were lower in normal human body[13]. IGFBP-2 and IGFBP-3 can be combined with IGF-1 and suppress its function, and they have the effect of inhibiting tumor cell proliferation[14]. The above research results show that after integrated treatment, the tumor angiogenesis and proliferation activity in patients with gallbladder carcinoma are both reduced, which is the intuitive sign of effective treatment. In addition to growth factors,
adhesion molecules are also the key to affect the tumor cell invasion and metastasis, the levels of various adhesion factors are extremely low in the body under physiological conditions, but when tumors occur, all kinds of adhesion factors are massively expressed and mediate tumor metastasis[15-17]. In the study, the levels of four adhesion factors E-selectin, ICAM-1, VCAM-1 and sE-Cd in patients with gallbladder carcinoma were detected after treatment, and it was found that E-selectin, ICAM-1, VCAM-1 and sE-Cd content in serum of observation group were lower, indicating that the integrated treatment can reduce the tumor invasion in patients.

It has been found in the assessment of short-term curative effect in patients with gallbladder carcinoma that the integrated treatment can significantly inhibit the malignant degree of tumor cells. In order to further clarify the long-term curative effect of the treatment, the included patients were followed up for 5 years in the study, and it was found that the median survival time as well as 1-, 3- and 5-year survival rate of observation group were higher after treatment, indicating that integrated surgery + radiotherapy + chemotherapy treatment also has outstanding effect on optimizing the long-term survival rate of patients with gallbladder carcinoma. To sum up, it is concluded as follows: integrated treatment of surgery + radiotherapy + chemotherapy can optimize the short-term and long-term curative effect in patients with gallbladder carcinoma.

References


