Influence of TACE combined with radioactive seed radiotherapy on primary liver cancer patients' malignant biological indicators

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Objective: To analyze the influence of TACE combined with radioactive seed radiotherapy on primary liver cancer patients' malignant biological indicators. Methods: A total of 112 cases of primary liver cancer patients who received treatment in our hospital, Xijing Hospital and Tumor Hospital of Shaanxi Province were chosen as research subjects and divided into control group (TACE therapy alone) with 63 cases in it and observation group (TACE combined with radioactive seed radiotherapy) with 49 cases according to different treatment, and then the levels of malignant biological indicators after 2 months of treatment were compared between two groups. Results: Serum VEGF, FGF and MMP levels of observation group after treatment were significantly lower than those of control group; serum AFP-L3, GP73, Sb7-H3, AFU and CatS levels were significantly lower than those of control group; serum ICAM-1, ESM-1 and uPA levels were lower than those of control group. Conclusion: TACE combined with radioactive seed radiotherapy can effectively reduce primary liver cancer patients’ serum malignant biological indicator levels, decrease the degree of malignancy of cancer cells and slow disease progression, and is an ideal treatment.

1. Introduction

Primary liver cancer is a common malignant tumor in our country, the majority of patients has lost the best timing of radical surgery when diagnosed, palliative treatment is the main treatment, and most patients die of local recurrence or distant metastasis[1]. Transcatheter arterial chemoembolization (TACE) is currently the most common method of palliative treatment of liver cancer, curative effect is distinct but postoperative recurrence probability is extremely high, and the effect is questionable in prolonging survival time. Radioactive seed radiotherapy is a newly developed palliative treatment that relies on the x-rays and γ -rays released by 125I seeds to exert the killing effect on liver cancer cells[2]. In the research, the influence of TACE combined with radioactive seed radiotherapy on primary liver cancer patients’ malignant biological indicators was mainly analyzed, specifically concluded as follows.

2. Information and methods

2.1 Case selection

A total of 112 cases of primary liver cancer patients who received treatment in our hospital, Xijing Hospital and Tumor Hospital of Shaanxi Province from September 2010 to July 2014 were included in the research. The treatment they received was retrospectively analyzed and patients divided into control group 63 cases who received TACE therapy alone and observation group 49 cases who received TACE combined with radioactive seed radiotherapy.
Control group included 30 male cases and 33 female cases, they were 45-78 years old and the average was (69.82±7.83) years; observation group included 24 male cases and 25 female cases, they were 48-79 years old and the average was (68.97±7.61) years. Differences in gender, age, disease severity and other baseline information were without statistical significance between two groups (P>0.05).

2.2 Detection methods

2 months after treatment, 2 mL fasting peripheral venous blood was drawn from all included patients in the morning, centrifuged with 3 000 r/min and then placed in -20 °C refrigerator for use.

2.3 Treatment methods

Control group received TACE therapy alone, specifically as follows: femoral artery puncture to the tumor blood supply arteries via micro-catheter super-selection, slow perfusion of epirubicin 60 mg, cisplatin 60 mg and fluorouracil 1 000 mg, and finally injection of mixed iopiodin-epirubicin suspension (iodipin 10 mL and epirubicin 20 mg) 10 mL. When the tumor staining disappeared, embolization was terminated, and for part of the tumors with rich blood supply, gelatin sponge particles were used for embolization.

Observation group received TACE combined with radioactive seed radiotherapy, TACE method was the same as that of control group, and radioactive seed radiotherapy was as follows: 18 G puncture needle was locally punctured into the deepest tissue, radioactive seed was placed, then puncture needle was gradually withdrawn, and one seed was placed every 0.5 cm. The amount and measurement of implanted $^{125}$I seeds were calculated to ensure that the average energy of radioactive seeds was between 25-35 keV, the distance they could penetrate was 1.7 cm and the half-life was 59.6 d.

2.4 Observation indicators

Enzyme-linked immunosorbent assay was used to detect vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF) and matrix metalloproteinase (MMP) levels; liver cancer markers: alpha fetoprotein variant (AFP-L3), Golgi protein 73 (GP73), soluble B7-H3 (sB7-H3), α-L-fucosidase (AFU), cathepsin S (Cat S); intercellular adhesion molecule (ICAM-1), endothelial cell-specific molecule (ESM-1) and urokinase-type plasminogen activator (uPA).

2.5 Statistical methods

SPSS 18.0 software was used to statistically analyze the data above, measurement data was by $t$ test and obtained results were considered to be statistically significant at the level of $P<0.05$.

3. Results

3.1 Serum VEGF, FGF and MMP levels

Tumor angiogenesis provides oxygen and nutrients to malignant cells, it is the foundation of further proliferation as well as invasion and metastasis of tumor cells, and many studies have confirmed that angiogenesis-related parameters are directly correlated with the malignant degree of tumors. VEGF, FGF and MMP are the currently clinical recognized factors directly related to angiogenesis, and in this study, detection of serum VEGF, FGF and MMP values of two groups after treatment showed that serum VEGF, FGF and MMP levels of observation group after treatment were significantly lower than those of control group ($P<0.05$), shown in Table 1.

3.2 Liver cancer marker molecules

The occurrence of liver cancer can cause abnormal secretion of a variety of factors at the same time and then result in the fluctuation of their serum levels, and joint detection of a variety of liver cancer marker molecules can increase the sensitivity and reliability of test results. In this study, the levels of serum AFP-L3, GP73, Sb7-H3, AFU, CatS and other markers of two groups with were detected after treatment, and the results showed that serum AFP-L3, GP73, Sb7-H3, AFU and CatS levels of observation group after treatment were significantly lower than those of control group ($P<0.05$), shown in Table 2.

3.3 Serum ICAM-1, ESM-1 and uPA levels

In patients with hepatocellular carcinoma, there are some factors.

### Table 1
Comparison of serum VEGF, FGF and MMP levels between two groups after treatment

<table>
<thead>
<tr>
<th>Groups</th>
<th>VEGF (ng/mL)</th>
<th>FGF (pg/L)</th>
<th>MMP (mg/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>aFGF</td>
<td>bFGF</td>
<td>MMP-2</td>
</tr>
<tr>
<td>Observation</td>
<td>19.21±2.35</td>
<td>6.29±0.83</td>
<td>7.25±0.83</td>
</tr>
<tr>
<td>Control</td>
<td>31.69±4.13</td>
<td>11.51±1.66</td>
<td>13.17±1.73</td>
</tr>
<tr>
<td>$t$</td>
<td>6.784</td>
<td>7.563</td>
<td>8.095</td>
</tr>
<tr>
<td>$P$</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>
that have necessary connection disease progression, also called illness-related factors. ICAM-1, ESM-1 and uPA are all recognized factors that play an important role in the development process of primary liver cancer, and their levels can indirectly reflect the disease severity and clinical effect, and at the same time, also have certain value in predicting long-term prognosis in patients. Specific testing showed that serum ICAM-1, ESM-1 and uPA levels of observation group after treatment were lower than those of control group \((P<0.05)\), shown in Table 3.

### Table 3
Comparison of serum ICAM-1, ESM-1 and uPA levels between two groups after treatment.

<table>
<thead>
<tr>
<th>Groups</th>
<th>ICAM-1 (ng/mL)</th>
<th>ESM-1 (ng/mL)</th>
<th>uPA (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>7.36±0.65</td>
<td>9.23±1.058</td>
<td>1173.54±242.76</td>
</tr>
<tr>
<td>Control</td>
<td>13.14±2.67</td>
<td>12.45±2.71</td>
<td>631.33±342.35</td>
</tr>
<tr>
<td>(t)</td>
<td>6.675</td>
<td>6.097</td>
<td>8.176</td>
</tr>
<tr>
<td>(P)</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

4. Discussion

Primary liver cancer is one of tumors with clinical high malignant degree, and it is with short duration, fast development and high case fatality rate. As the early clinical symptoms of liver cancer are not obvious and easy to be missed, the primary liver cancer patients that can actually accept surgical treatment only account for about 20%, and most have developed to middle-late stage when diagnosed and are unable to receive radical surgery[3]. There are many palliative treatment methods for primary liver cancer patients, including transcatheter arterial chemoembolization (TACE), percutaneous ethanol injection, \(^{125}\)I radiotherapy, radiofrequency ablation, etc. TACE is one of the most commonly used palliative treatment of primary liver cancer, and the vast majority of patients have rich arterial blood and are applicable to TACE treatment, which can effectively delay the tumor development and vascular invasion. But many studies have shown that TACE treatment alone is with high postoperative recurrence rate and directly affect the final survival of patients, and therefore, TACE combined with other palliative treatment is mostly adopted to enhance therapeutic effect[4,5].

Radioactive seed radiotherapy is the emerging treatment that implants the radioactive seed iodine in liver cancer lesions to kill residual or recurrent cancer cells[6]. Radioactive seed iodine 125 can launch X-rays and \(\gamma\)-rays, X rays can induce the generation of oxygen free radicals, thus killing tumor cells, and the ionization effect of \(\gamma\)-rays can make DNA double-strand of tumor cells break and then apoptosis. Radioactive seed iodine 125 has longer decaying period and can play a role for a long time after implanted in tumors, and at the same time, its characteristic of conformal radiotherapy avoids the damage to normal liver tissue around the tumor[7,8]. Radioactive seed radiotherapy combined with TACE treatment is considered to be the best way to treat middle-late liver cancer at present, but clinical relevant reports on its practical application are still less, TACE combined with radioactive seed radiotherapy was used as observation group object in the research, and the influence of combined therapy on malignant biological indicators of liver cancer cells was mainly analyzed.

Vascular endothelial growth factor (VEGF) is a vascular endothelial cell-specificity of heparin-binding growth factor, its level increases significantly when malignant tumors exist, it can induce tumor angiogenesis, and it is an indispensable ingredient of tumor growth, invasion and metastasis. Fibroblast growth factor (FGF) contains two subtypes, aFGF and bFGF, and both can promote the migration and proliferation of vascular endothelial cells and have the effect of promoting angiogenesis[9]. Matrix metalloproteinase (MMP) has many subtypes, MMP-2 and MMP-9 are two subtypes playing a major role, MMP-2 main degrades collagen type \(\|\) component in basement membrane, and MMP-9 can decompose extracellular matrix basement membrane, and at the same time has synergistic effect on VEGF[10]. Above research results showed that serum VEGF, FGF and MMP levels of observation group after treatment were significantly lower than those of control group \((P<0.05)\), indicating the positive role of TACE combined with radioactive seed radiotherapy in inhibiting tumor cell proliferation.

In the malignant transformation of liver cancer cells, the expression of a variety of proteins in cells will also change, so the changes of the levels of clinical serum liver cancer active molecules can be used to determine liver disease[11]. Alpha fetoprotein variant (AFP-L3) is produced when the sugar chain structure of AFP molecules has heterogeneity change, and its sensitivity is higher than AFP; Golgi protein 73 (GP73) is mainly expressed in bile duct epithelium and rarely exists in liver cells in normal state, and its level increase sharply in cases of liver cell canceration; soluble B7-H3 (sB7-H3) is a costimulatory molecule of B7 family that is highly expressed in liver cancer, lung cancer and other malignant tumor cells; \(-\)-fucosidase (AFU) belongs to the lysosomal acid proteolytic enzyme,
cathepsin S (Cat S) is proteolytic enzyme containing cysteine group, and both can be abundantly expressed in liver cancer cells[12,13]. Above research results showed that serum liver cancer marker molecules AFP-L3, GP73, Sb7-H3, AFU and CatS levels of observation group after treatment were significantly lower than those of control group ($P<0.05$), indicating that after combined treatment, liver cancer active molecule levels significantly decreased and liver cancer viabiliy was reduced.

Intercellular adhesion molecule (ICAM-1) is rarely expressed in normal tissues, ICAM-1 in serum is mostly from tumor cells, and its level can directly reflecting the presence and metastasis of tumor; endothelial cell-specific molecule (ESM-1) can be combined with liver cancer cell growth factor through glycan chain to affect tumor angiogenesis, ESM-1 expression is little in normal tissue, it is known that ESM-1 is massively expressed in a variety of cancer tissues, and it can be used as one of the important indexes to judge prognosis[14]. Urokinase-type plasminogen activator (uPA) can activate the fibrinolytic enzyme system and promote the degradation of extracellular matrix basement membrane, and can promote tumor cell penetration of normal tissue barrier as well as infiltration and metastasis[15]. Above research results showed that serum ICAM-1, ESM-1 and uPA levels of observation group after treatment were lower than those of control group ($P<0.05$), indicating that combined treatment could effectively reduce tumor cell invasion ability and the malignant degree of tumor.

Based on above discussion, it is concluded as follows: TACE combined with radioactive seed radiotherapy can effectively kill tumor cells and contain malignant biological behavior of tumor cells, and it has positive significance in controlling the illness of patients with primary liver cancer.

References