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Clinical evaluation of Radio Frequency Ablation(RFA)in the treatment of Gestational trophoblastic tumor(GTT)

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Abstract

Objective: To discuss the feasibility and therapeutic efficacy of the three types of treatment methods for Gestational trophoblastic tumor(GTT).

Methods : 72 patients diagnosed as GTT were selected and divided into three groups according to different treatment styles including single chemotherapy (group A), Total hysterectomy combined with chemotherapy (group B), and Radio Frequency Ablation (RFA) combined with chemotherapy (group C) .The curative effects of three groups were evaluated according to the blood HCG levels and remission of metastasis. **Result:** The curative effect

rates of the three groups from A to C were respectively 93.3%, 93.3%,100% . there was no significant differences between three groups ($P > 0.05$). the remission rate of GTT has statistical significance at different stages ($P < 0.05$), but the differences has no statistical significance among the groups of different ages,and different types. the course frequency of chemotherapy in group A and B was significantly shorter than group C ($p < 0.05$).

Conclusion: GTT is mainly treated by chemotherapy. Patients suffering from GTT can get satisfactory treatment by Total hysterectomy or RFA combined with chemotherapy. RFA combined with chemotherapy is the best choice for the younger patients who has fertility requirements

Keywords: Gestational Trophoblastic Tumor; Treatment; Radio Frequency Ablation (RFA)

The GTT including Choriocarcinoma and invasive hydatidiform mole which originated from placental villi , which seriously affects the life quality and threats human's mental and physical health ^[1]. Generally, choriocarcinoma and invasive hydatidiform mole can be radically cured through chemotherapy alone, but some patients are prone to be drug resistant to chemotherapy medicines ^[2-4].

In clinic Hysterectomy is performed shorten the time span of chemotherapy, but patients will lose their fertility abilities ^[5]. RFA is a kind of hyper-thermal damage technology which developed recently, and becomes a new targeted therapeutic method in gynecology ^[6]. People proposed some questions such as: Is it possible for treating primary uterine lesions by making completely absorbed through some targeted therapies without a hysterectomy? The paper mainly discusses the feasibility and therapeutic efficacy of RFA to GGT by comparing the three types of treatment methods , and there are the reports.

1 Material and Methods

1.1 General Materials

We selected the patients who diagnosed with choriocarcinoma and invasive hydatidiform mole in our hospital from July 2011 to October 2012. Among them 23 cases were diagnosed as choriocarcinoma, in which 11 cases were secondary to hydatidiform mole, 6 cases were secondary to artificial abortion, one case was secondary to ectopic pregnancy, and 5 cases of term birth; All cases were staged according to FIGO standard, and no more patients with stage IV. Metastasis lesions were diagnosed by color ultrasound, chest radiograph, chest and abdominal CT, and head MRI, etc. Almost all patients were given chemotherapy 2-3 courses, after then divided in to three groups According to patient's age, with or without fertility requirements, the lesion size and the depth of muscular invasion, blood HCG level before treating, with or without metastasis and so on.

1.2 Therapy Methods

Group A: chemotherapy alone, consisting of 31 cases , aged 23-36 years, with mean age of 33 years. It was consisted of 4-8 treatment courses.and the average course of treatment was 5.9 courses; 5-fluorouracil(Fu) combined with ActinomycinD (ACID) chemotherapy or EMA-CO Were used for chemotherapy According to prognostic scoring chemotherapy plan. Nearly all Patients from another two groups were given 1-2 courses of chemotherapy before operation, and also were given continuous chemotherapy 2-4 times after operation. During the chemotherapy, symptomatic treatment by increasing white blood cell and protecting gastric mucosa were given if the patients had happened drug toxicities such as myelosuppression, gastrointestinal toxicity.

Group B: total hysterectomy combined with chemotherapy, consisting of 29 cases, aged 43-47 years, with mean age of 45 years.This method is using under following conditions: (1) Patients should have good general condition and tolerance to operation; blood HCG before operation should be controlled at lower level , lesions should be confined to the uterus, and the blood HCG did not fall continuously; for the patients without fertility requirement, total hysterectomy can improve the chance of curing. (2) When prime uterine lesions and

metastasis lesions have perforated and lead to hemorrhages, the patients need to take an emergency operation to save their lives. (3) There were no active and metastatic lesions except from surgical site; no evidences indicated that there were drug resistant and disseminated lesions. (4) Patients are without fertilizing requirements and no condition to follow-up.

Group C: RFA combined with chemotherapy, consisting of 12 cases who were voluntary to receive , aged (19-33 years, a mean age of 27.5 years), all had fertility requirements, and strongly asked to retain uterus.

In this group, We improved related auxiliary examinations before operation and excluded surgical contraindications. Preoperative treatment chemotherapy and preoperative gynecological ultrasound helped us to know the lesions size and the degree of uterine muscular invasion. Patients were given preoperative cleaning enema, intravenous anesthesia, and proper filling of bladder. Patients took the bladder lithotomy position. The electrode plate was placed in the lumbosacral portion. We adjusted power parameter settings at 25~40W, and disinfected fully the vulva, vagina, and reset the vaginal speculum to expose the cervix. Under the guide of ultrasound, we probed the lesions attached places of choriocarcinoma or invasive hydatidiform mole, we probed the relationship between uterine palace cavity, and we selected puncturing spots and directions. Inserting the self-curing knife into the center or one side of lesions, we ensured that the self-curing knife was inserted in the lesions and the tip of self-curing knife was from the serous layer 0.8 to 1.0cm by ultrasound observation on longitudinal and vertical sections. All precedures were operated under the control of computers. When the tissue impedance was up to 100%, the therapeutic apparatus could automatically alarm and stop the treatment. We exited the knife from the solidification places, and punctured again to the lesions places without solidification. Under the ultrasound monitoring, the therapeutic process manifested as gasification, solidification shrinkage, and strong-echo round shadows regarded as completely treated under the longitudinal and transverse sections of ultrasound after treating successfully. Generally, we can achieve effective results through one treatment, while sometimes we can retreat when it is necessary. In the aim of preventing the intrauterine infection caused by blocking blood flow after RA, we

used the large oval forceps to remove the intrauterine necrosis. One patient who had a fever and the highest temperature of her was up to 39.5 degree Celsius after RA, and we gave her symptomatic treatments consisting of anti-inflammatory and drainage by uterine cavity drainage tube. All patients receiving surgery were reexamined by blood HCG and gynecological ultrasound on the third day of treatment to ensure that there was no significant blood flow signal in the uterine lesions and gave combined chemotherapy to them within one week [9].

1.3 Curative efficacy standard

At the end of every course of chemotherapy, the blood HCG should be measured once a week, combined with gynecological examination and ultrasound imaging examination. At the end of every course of chemotherapy within 18 days, the blood HCG will drop at least 1 log to become effective. Indications of drug withdrawal: Low-risk patients with the blood HCG negative 3 times in a row were given at least one course of chemotherapy, and high-risk patients were given continuously 3 courses of chemotherapy.

1.4 Follow-up

All patients were followed up for more than 2 years. At 1,3,6month and 1,2years after treatment All patients were followed up in outpatient clinic by checking the blood HCG, gynecological ultrasound chest X-ray.

1.5 Statistical analyses

Statistics analyses were performed by SPSS software. The statistical information used chi-Square test, inspection level $\alpha=0.05$.

2 Result

2.1 Comparing the curative efficacy of the two groups

The remission rate of RFA combined with chemotherapy was 100%; total hysterectomy combined with chemotherapy was 93.3%; and chemotherapy alone was 93.3%. the differences between three groups had no statistical differences ($P<0.05$). The remission rates of invasive hydatidiform mole and chorio carcinoma respectively were 93.75% and 95.5%, and

differences has no statistical significance ($p > 0.05$). the remission rate of GTT has statistical significance between different stages ($P < 0.05$), but the differences has no statistical significance among the groups of different ages, and therapeutic methods ($p > 0.05$). Shown in Table I. The percentages of short chemotherapy courses (2-5 courses) in group B and group C were 82.7%,83.3% respectively which were significantly higher than group A.which was 25.8%($P < 0.05$).Shown in Table II.

Table I Chi-square test of Trophoblastic Disease factors[n(%)]

Index	Whether remission after treatment		n	P
	YES	NO		
Diagnosis				0.592
Invasive hydatidiform mole	45 (93.75)	3 (16.6)	48	
choriocarcinoma	23 (95.8)	1 (9.1)	24	
Staging				0.022
Phase I	45 (100)	0 (0.0)	45	
Phase II	10(83.3)	2 (16.6)	12	
Phase III	11(84.6)	2(15.3)	13	
Ages				0.764
<21years old	1 (100)	0 (0.0)	1	
21~30 years old	14 (100)	0 (0.0)	14	
31~40 years old	24 (92.3)	2 (7.6)	26	
>40 years old	29 (93.5)	2 (6.45)	31	
Therapy Methods				0.655
Group A	28 (93.3)	2 (8.3)	12	

Group B	28 (93.3)	2 (8.3)	30
Group C	12 (100.0)	0 (0.0)	30

Table II Chi-square test of Chemotherapy courses [n(%)]

	2-5courses	5-8courses	n	p
Therapy methods	N(%)	N(%)		0.000
Group A	8 (25.8)	23 (74.2)	31	
Group B	24 (82.7)	5 (17.2)	29	
Group C	10(83.3)	2(16.6)	12	

2.2 Comparing complications of the two groups

The main side effects were myelosuppression, gastrointestinal toxicity, and alopecia,. The myelosuppression was accured in 14 cases, and got remission after ascending white blood cells. and oral ulcer were occurred in 24 cases , Alopecia was happened in 5 cases, and all of them were mild. There were no obvious hepatic and renal function damage cases. There were no deaths caused by chemotherapy-related severe complications. one patient whose blood HCG dropped slowly after the fifth courses of chemotherapy refused to get treatment was recommended to surgical treatment after seventh courses of chemotherapy. After twice chemotherapy, a patient who took total hysterectomy refused to get further treating duo to her economical condition, and died after 14 months later (The patient was not carried out any treatment after she had refused treatment and left from hospital, and the cause of her death was unknown).

3 Discussion

Gestational trophoblastic tumors are very sensitive to chemotherapy, There is abundant blood supply in the lesions of gestational trophoblastic tumors, so it is easy to be killed by drugs, that is why chemotherapy can be a good way to treat GTT. 80-90% of patients could be cured

if they are diagnosed on time and received standardized chemotherapy. In the study, the curative rate of single chemotherapy was 93.3%, and it was higher than that of reported documents. The earlier the staging is, the higher the curative rate will be [10,11]. Although chemotherapy is the main method to treating GNT, in some special conditions such as drug resistance, resistant lesions on uterus, the hysterectomy still plays an important role in treating GNT [8]. Scholars found that patients with GNT who received operation had the significantly lower hospitalization time and total chemotherapeutic courses [7,8]. The curing method of combining surgery not only can shorten the course of chemotherapy, but also reduces the drug resistance and recurrence, which can improve the quality of life. In this report the curative rate of group B was 93.3%, and the average courses of chemotherapy were 3.42 courses, which were lower than those of reported. There is no effective guidance for the treatment of patients with extremely high risks, such as with drug resistance and recurrence. Therefore, it is necessary to study about Effective combination therapy according to the different characteristics of patient in different regions [12-13].

In the recent 30 years, RFA techniques have serving as a new kind of method to treating tumors and drawing the attentions. Scholars had done numerous researches on RFA, and the tumor curative efficacy was certified by lots of experimental treatments; scholars also made primary discussion about its mechanisms and obtained primary achievements [14-16]. Now days RFA is Extensively used in gynecology with the advantages of retain the uterus and keep the birth abilities. RFA can be used for the GTT patients whose lesions confined to the uterus, and blood HCG does not fall continuously, AFR not only shorten the courses of chemotherapy by coagulating the cancer cells, but also retain uterus, so that it improves the quality of life. In our study, 12 patents received AFR combination with efficacy rate of 100%, and the average course of chemotherapy was only 3.25 courses. So RFA can reduce the courses and side effects of chemotherapy. RFA may be a safe, effective and new kind of method for the GTT patients with the advantages of retaining the uterus.

Chemotherapy is considered main treating method for GTT. This study showed that the efficacy rate in three kinds of methods did not show significant differences ($P > 0.05$)

between different disease classifications、 stagings、 patient ages. the choice for treating methods should be based on getting the maximum efficiency and the minimum side effect . In this paper the chemotherapy courses in the patients who is in combining chemotherapy with hysterectomy or AFR group obviously shorter than the one in the single chemotherapy group . Total hysterectomy combined with chemotherapy is also suitable for elderly patients with metastasis and without fertility requirements. RFA combined with chemotherapy can be best choice for younger patients with fertility requirements. To sum up, GNT patients can get satisfactory treatment effects through chemotherapy, hysterectomy ,as well as AFR .

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