Journal of Clinical and Nursing Research

Research Article

Photodynamic Therapy for Advanced Gastric Cancer: A Case Report

Hongyan Zhang[1], Lule Wu[2], Xiaoxiong Hu[2], Jianwen Sheng[2], Yuwen Wu[2], Huizhen Fan[1*]

[1]Campus of Chemistry and Bioengineering, Yichun University, China

[2]Department of Gastroenterology, Yichun People's Hospital, China

Abstract: ***Background and Study Aims:*** To observe the efficacy of photodynamic therapy in patients with advanced gastric cancer and analyze the reasons affecting the efficacy. Methods: In this paper, a patient with advanced gastric cancer in our hospital was selected.HoPorfin is used as a photosensitizer and photodynamic therapy was performed 48 hours and 72 hours later. Results: One month after the photodynamic treatment, the patient came to our hospital to reexamine the gastroscope. Through the comparison of gastroscopy before and after the photodynamic treatment, the gastric cancer lesion of the patient after the photodynamic treatment was not significantly smaller than before, and the effect of photodynamic treatment was not ideal. Conclusion: The four reasons for the unsatisfactory effect: individual differences of patients, photosensitizer, light source and oxygen.

Keywords: Gastric cancer; Photodynamic therapy; Photosensitizer

Publication date: March, 2021
Publication online: 31 March, 2021
[*]***Corresponding author:*** Huizhen Fan, fhz9205@163.com

1 Introduction

Gastric cancer (Gastric Cancer,GC) is a malignant tumor originating from gastric mucosal epithelium. Due to the atypical early symptoms, it is difficult to make early diagnosis. Most cases are in the middle and late stage at the time of diagnosis, while the 5-year survival rate of patients with advanced gastric cancer who undergo radical resection is only 20% to 30%. In addition, as an adjuvant therapy, radiotherapy and chemotherapy are often used, but the effect is not ideal, and the side effect is large.In recent years, photodynamic therapy (PDT) technology has been continuously developed, coupled with its unique advantages such as small trauma, low toxicity, good selectivity, good applicability, repetitive treatment, palliative treatment, and synergistic surgical treatment to improve curative effect and elimination of occult cancer lesions, protective appearance and vital organ functions, provides a new model for clinical tumor treatment[1]. In this paper, a case of advanced gastric cancer with poor curative effect after photodynamic therapy was reported, and the process of diagnosis and treatment and the reasons affecting the curative effect were discussed.

2 Case summary

The patient is a 64-year-old male. He was admitted to hospital mainly because of "black stool for more than two months" on July 8, 2019. There was no obvious abnormality in liver and kidney function and blood coagulation function, hemoglobin 50.0g / L, gastroscopy revealed that the gastric body was large mucosal eminence, the nature of which was to be determined (MT?). Ultrasonographic gastroscopy showed that the nature of giant ulcers in the gastric body remains to be examined (MT, T4N1) (Figure 1). Pathological diagnosis: (gastric body) poorly differentiated adenocarcinoma, immunohistochemical results: CAM5.2 (+), CKpan (+), CD34 (-), Ki67 (80% +). (Figure 2). The family members of the patients refused operation, radiotherapy and chemotherapy and agreed to photodynamic therapy.

On July 18, 2019, intradermal injection of 0.01mg/ml hematoporphyrin injection (HiPorfin) was given 0.1 ml, and HiPorfin was given after negative skin test. According to 3mg/kg, it was dissolved in 0.9% sodium chloride injection 250mL and continuously injected intravenously for 1 hour. Photodynamic therapy was performed 48 hours and 72 hours later to keep the patient away from light. During this period, there was no itching, erythema and other discomfort. The first photodynamic therapy was performed 48 hours after administration (Figure 3): the treatment apparatus was PDT630-A therapeutic apparatus (Shenzhen Leiman Technology Co., Ltd.) with a laser wavelength of 630nm. 3cm columnar optical fiber was introduced under the guidance of electronic fiber endoscope with a transmission efficiency of 1.44. The output power was set for 2w, and the irradiation range was the whole focus and the mucosal tissue adjacent to 2cm. The irradiation time was 1000s*3 times and the interval time was 5minutes. After treatment, the focus was observed, the color of the focus turned purple in varying degrees, no active bleeding and perforation were found, and safely returned to the ward.After 72 hours of administration, the second photodynamic therapy (Figure 4) showed that the surface of the lesion was obviously blackened and necrotic yesterday. The necrotic matter on the lesion surface was cleaned first, and the adjacent lesions were irradiated. The irradiation time was 1000s*2 times, 300s*1 times, the interval time was 5 minutes, and the rest were the same as before. After photodynamic therapy and related symptomatic treatment, the patient was in stable condition and was discharged on July 29, 2019.One month after photodynamic therapy, the patient came to our hospital for another photodynamic therapy on August 21, 2019. Gastroscopy revealed gastric body cancer and chronic superficial gastritis (Figure 5). Through the comparison of gastroscopy before and after photodynamic therapy, the focus of gastric cancer was not significantly reduced after photodynamic therapy, and the effect of photodynamic therapy was not ideal, so photodynamic therapy was not continued. Follow-up, the patient is currently taking traditional Chinese medicine to recuperate, the condition is OK.

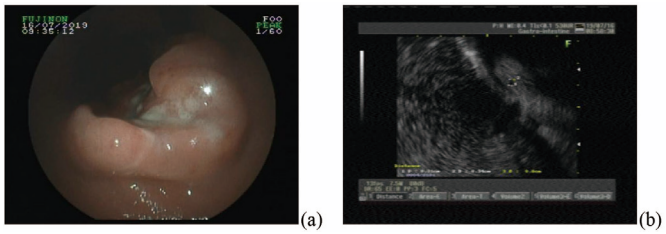

Figure 1. Preoperative gastroscopy (a) showed a huge irregular ulcer in the middle part of the gastric body, with white moss at the bottom; ultrasound, (b) showed that the focus is hypoechoic, the mucosa of all levels of the lesion is confused, and part of the serous layer is incomplete.

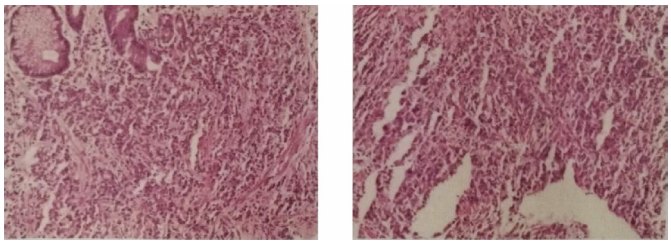

Figure 2. Preoperative pathological diagnosis: (gastric body) poorly differentiated adenocarcinoma, immunohistochemical results: CAM5.2 (+), CKpan (+), CD34 (-), Ki67 (80% +).

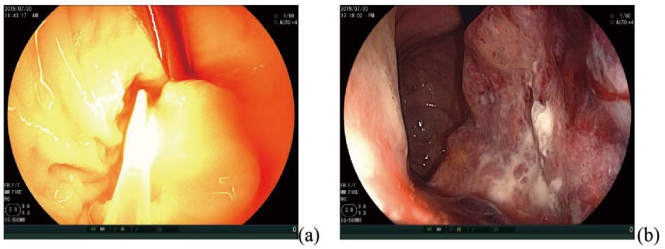

Figure 3. (a) during the first photodynamic therapy 48 hours after administration; (b) the lesions became purple in varying degrees after treatment.

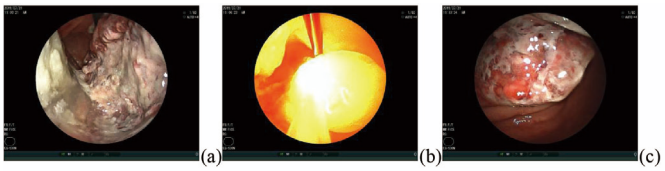

Figure 4. (a) On the second day after treatment, the surface of the lesion was obviously blackened and necrotic, covered with white and dirty fur. (b) During the second photodynamic therapy 72 hours after administration; (c) After treatment, the color of the focus changed to purple in different degrees.

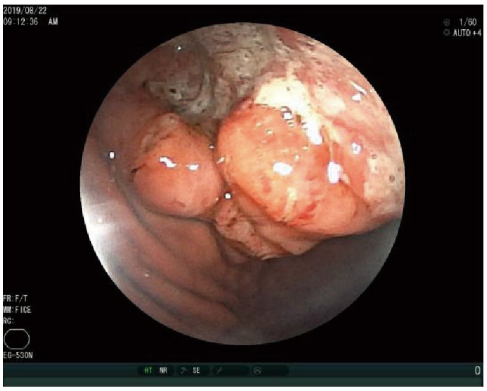

Figure 5. One month after treatment, the focus was not significantly smaller than before.

3 Discussion

Photodynamic therapy (PDT) is a new technique for the treatment of diseases by photodynamic response. The main principle is that tumor cells and normal tissues have different affinity for photosensitizers, that is, more photosensitizers are absorbed and retained by tumor tissues than normal tissues, and then the photosensitizers absorbed by tissues are excited by laser irradiation of specific wavelength. the energy is transferred to the oxygen in the biological tissue, and after receiving energy supply, oxygen molecules become reactive oxygen species such as free radicals and / or singlet oxygen, resulting in cytotoxicity, resulting in tumor cell damage and even death, and finally achieve the purpose of treatment[2.3]. It can be seen that photosensitizer, light source and oxygen are the three key elements of photodynamic therapy, any of which can affect the efficiency of PDT. In addition to the technical deficiencies of photodynamic therapy itself, the individual differences of patients may also be another important factor affecting the curative effect. The following is an analysis of these factors.

3.1 Individual differences of patients

Liu Huilong et al. in the analysis of 5 cases of upper digestive tract cancer with early stage cured by photodynamic therapy, it was found that the depth of lesion invasion was the main limiting factor of whether the clinical effect was satisfactory or not[4]. Among the 5 patients, the invasion depth of the lesions was relatively superficial and there was no regional lymph node or distant metastasis. Among them, the depth of lesion invasion was limited to the submucosa in 4 patients, which was a standard early cancer. Due to the superficial lesion, the lesion disappeared completely after 1 course of PDT. A patient with invasion to the superficial musculus needed 2 courses of PDT before the lesion disappeared completely. In the same period, some patients with deep tumor invasion were not satisfied with the curative effect, and the recurrence and metastasis were common.Song Dongxing et al. concluded from the analysis of the efficacy of photodynamic therapy combined with chemotherapy in the treatment of advanced cardiac cancer that PDT was ineffective in advanced patients with giant cardiac cancer, and has no effect on tumor invasion to deep tissue, abdominal metastasis, hematogenous metastasis and extraluminal lymph node metastasis[5].

This patient is a patient with advanced gastric cancer, the focus is located in the gastric body, and the pathological type is poorly differentiated adenocarcinoma. The focus has infiltrated into the serosa layer with regional lymph node metastasis. therefore, it is considered that the poor curative effect of the patient is related to the insufficient course of treatment and the deep invasion of the tumor with distant metastasis.

3.2 Photosensitizer

Photosensitizer is one of the three elements of PDT. Ideal photosensitizer is characterized by high targeting, low phototoxicity and high quantum yield of singlet oxygen[6]. The distribution and concentration changes of photosensitizer in tumor tissues have an important influence on the efficacy of PDT.

The photosensitizer used in this case was HiPorfin, a hematoporphyrin porphyrin derivative exclusively produced and operated by Chongqing Huating Modern Biopharmaceutical Co., LTD., which was dissolved in 0.9% sodium chloride injection 250mL at 3mg/kg. HiPorfin is divided into the first generation of photosensitizer. Although the first generation photosensitizer has achieved remarkable curative effect in clinic, its composition is complex, and the role of various components in the curative effect is not very clear. Moreover, the stability of tissue selectivity and photodynamic injury intensity is poor, the metabolism is slow, and it is easy to cause phototoxicity reaction, and a long time to avoid light after treatment, bring great inconvenience to patients. In addition, because the absorption band of this kind of photosensitizer in the red part is weak,

the treatment depth is not enough, which affects the effect of treatment[1, 3]. At present, the required dose of photosensitizer is usually calculated according to the patient's body weight or body surface area, but the results show that when the drug dose and metabolic time are exactly the same, the photosensitizer retained in the target tissue will be significantly different because of the individual differences of the patients and the target tissues of different parts[7].

3.3 Light source

The main characteristic parameters of PDT light source include the type of light source (laser or non-laser light source, pulse or continuous output), wavelength, output power or power density of the light source, and transmission mode of the light source (ball head, columnar or flat-cut fiber) [13].The treatment instrument used in this patient is PDT630-A therapeutic instrument (Shenzhen Leiman Technology Co., Ltd.). The laser wavelength is 630nm and 3cm columnar optical fiber. The penetration depth of laser into human tissues is proportional to the wavelength of light, that is, as the wavelength of light increases, the depth of laser irradiation in tissues also deepens. The laser within 630 ~ 800 nm can penetrate the depth of the tissue about 3~8 mm [14]. However, due to the strong absorption and scattering of visible light in the wavelength range of some biological tissues, the laser attenuation is caused, and its penetration ability to the gastric wall is limited, and the endoscope and imaging technology are also inadequate. it is difficult to irradiate a large gastric wall with ordinary flat-cut optical fiber or cylindrical dispersion optical fiber, so it is difficult to achieve effective treatment of deep tissue [2].

3.4 Oxygen

The oxygen content in the tissues is one of the key factors for PDT to exert its efficacy, and it is an essential reaction substrate for PDT. The ground state photosensitizer absorbs the energy of the photon and transitions to the first excited state, and these excited state photosensitizer molecules transition to the triplet state through inter-system transitions. The photosensitizer molecules in the excited triplet state transfer energy to the ground state oxygen to produce biotoxic active oxygen or free radicals and other active substances [15-17].

Under normal circumstances, the oxygen in the tissue is carried and supplied by hemoglobin, and the content of oxygen is related to the content of hemoglobin in the blood vessels of the tissue.This patient has severe anemia and low hemoglobin level, with a lowest value of 43.00 g / L, and has been given several blood transfusions to improve the symptoms of anemia. Although the hemoglobin of the patient is significantly increased, it is still lower than the normal value.

It can be seen that the oxygen content in the tissue of this patient is very low, and it may even be hypoxic, and because PDT itself is also an oxygen consumption process, the tissue oxygen content in the irradiated tumor area is significantly decreased, and the sensitivity of hypoxic tumor cells to photodynamic response is reduced.Secondly, the vascular permeability of the solid tumor site is poor, and the rate of oxygen supply from the surrounding blood vessels through diffusion can not meet the rate of oxygen consumption in the target tissue, which will lead to a continuous decrease in tissue oxygen content and the production of singlet oxygen, thus affecting the efficacy of PDT [3,13,18].

4 Conclusion

At present, the factors that limit the efficacy of PDT are the lack of targeting and lethality of photosensitizers, the allergic reaction of skin to light after the end of PDT, inappropriate light source and existing light source treatment, and the hypoxic environment in the tumor.However, with the continuous development of photodynamic technology and the exploration of new models of photodynamic therapy combined with other therapies to treat gastric cancer, the clinical effect of photodynamic technology for gastric cancer will be more optimistic.

References

[1] Wan B, Deng WT. Research progress of photodynamic therapy [J]. Guangdong Chemical Industry, 2019, 46 (393): 124-127.

[2] Zhang ZQ,Yao HL,Wen Y, *et al*. Progress and prospect of photodynamic technology in the treatment of gastric cancer [J]. Journal of Laser Biology, 2012, Jing 21(4): 289-293.

[3] Lang YH, Li LB. Exploration of the three elements of photodynamic therapy and tumor recurrence after photodynamic therapy [J]. Chinese Journal of Laser Medicine, 2019, 28 (2): 100-106.

[4] Liu HL, Li HL, Jia XY, *et al*. Clinical analysis of 5 cases of upper digestive tract cancer cured by photodynamic therapy [J].

Chinese Journal of Laser Medicine, 2013, Jol 22 (2): 93-96.

[5] Song DX. Analysis of the efficacy of photodynamic therapy combined with chemotherapy in the treatment of advanced cardiac carcinoma [J]. Chinese Journal of Laser Medicine, 2007, June 16 (6): 357-361.

[6] Yoon I, Li JZ, Shim YK. Advance in photosensitizers and light delivery for photodynamic therapy[J]. Clin Endosc, 2013, 46: 7e23.

[7] Sheng C, Pogue B W, Wang E,*et al*. Assessment of photosensitizer dosimetry and tissue damage assay for photodynamic therapy in advanced-stage tumors [J]. Photochem Photobiol, 2004, 79(6): 520-525.

[8] Li BH, Xie SS,Wilson BC, *et al*. Advances in dosimetry of photodynamic therapy [J]. Progress in Biochemistry and Biophysics, 2009, 36 (6): 676-683.

[9] Ethirajan M, Chen Y, Joshi P, *et al*. The role of porphyrin chemistry in tumor imaging and photodynamic therap [J]. Chemical Society Reviews, 2010, 40: 340-362.

[10] Weishaupt K R, Gomer C J, Dougherty T J.Identification of singlet oxygen as the cytotoxic agent in photoinactivation of a murine tumor [J]. Cancer Res,1976, 36(7): 2326-2329.

[11] Yamamoto J, Yamamoto S, Hirano T, *et al*. Monitoring of singlet oxygen is useful for predicting the photodynamic effects in the treatment for experimental glioma [J]. Clin Cancer Res,2006, 12(23): 7132-7139.

[12] Krasnovsky A A. Luminescence and photochemical studies of singlet oxygen photonics [J]. J Photochem Photobiol A, 2008, 196 (2-3): 210-218.

[13] Zheng H, Chen Q, Shakil A, *et al*. Hyperoxygenation enhances the tumor cell killing of photofrin-mediated photodynamic therapy [J]. Photochemistry Photobiology, 2010, 78: 496-502.