Annals of Clinical and Medical Case Reports

Case Report ISSN 2639-8109 Volume 6

IMRT Combined with Cetuximab for Locally Recurrent Nasopharyngeal Carcinoma Case and Literature Review

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Received: 04 Feb 2021
Accepted: 27 Mar 2021
Published: 01 Apr 2021

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Citation:

Wang F, Xie XQ. IMRT Combined with Cetuximab for Locally Recurrent Nasopharyngeal Carcinoma Case and Literature Review. Ann Clin Med Case Rep. 2021; V6(10): 1-5.

Keywords:

Recurrent nasopha ryngeal carcinoma; Intensity modulated radiotherapy; Cetuximab

1. Abstract

1.1. Objective: Objective to explore the efficacy and safety of IMRT combined with cetuximab in the treatment of locally recurrent nasopharyngeal carcinoma.

1.2. Methods: Combined with IMRT combined with cetuximab for the treatment of locally recurrent nasopharyngeal carcinoma, and to observe the effect of its application

1.3. Results and conclusions: Intensity modulated radiotherapy combined with Erbitux in patients with locally recurrent nasopharyngeal carcinoma can prolong their survival and patients can afford it.

2. Basic Situation

The patient, female, 40 years old, started to have respirable snots and turned dark red in January 2006. She was diagnosed with nasopharyngeal poorly differentiated squamous cell carcinoma T2N1M0 stage II after relevant examination. Physical examination at admission: KPS 100 points. Specialist Physical examination: The upper left neck can touch a lymph node with a size of about 1x1cm², and the right upper neck can touch a lymp h node with a size of about 0.8x0.8cm². There are no obvious abnormalities in blood routine, blood biochemistry, routine urine and electrocardiogram. From 2006.6.12 ~ 2006.7.24 Radiation therapy was performed in the outer hospital, and sensitization was given to him during radiotherapy. Conformal radiotherapy was performed after 36Gy of nasopharyngeal conventional radiotherapy, 360cGy (90%) x 8 times, 3F / w, and the total amount of neck was 60Gy. The neck did not touch the enlarged lymph nodes. According to the WHO Recist curative effect evaluation, it was CR. The patient developed nosebleeds in 2008 and was admitted to our hospital on July 13, 2008. The pathological results showed: <left sphenoid sinus and top of nasopharyngeal. They are all poorly differentiated squamous cell carcinomas. After refining relevant examinations, they diagnosed with nasopharyngeal carcinoma recurrence T4N0M0 stage IVa. The intensity modulated radiotherapy was performed from July to September 2008. Strong, GTV 66Gy, CTV 54Gy, a total of 31 times. Combined with cetuximab molecular targeted therapy during radiotherapy, 600mg in the first week, 400mg per week afterwards, until the end of radiotherapy. After the end of treatment every three months to review a year later review every six months, every three years after the review year, 5 years and 6 months, no signs of nasopharyngeal local tumor recurrence.

3. Discussion

3.1. IMRT for Nasopharyngeal Carcinoma

Radiotherapy is the first choice for the treatment of nasopharyngeal cancer. For a long time, conventional two dimensional irradiation technology

mainly based on bilateral facing through the field has been used. Although the radiation therapy technology has been improved and the treatment equipment has been updated in recent years, the efficacy of nasopharyngeal cancer has been obvious. Increased, but the local uncontrolled and recurrence rate is still as high as 10% 40% [1, 2]. It is characterized by: (1) the time of local recurrence is mostly within 2 3 years after treatment; (2) the middle and advanced cases are more Early relapses; early relapses in early patients; (3) poor re treatment effects; longer recurrence intervals are better than short durations; (4) recurrent cases are prone to distant metastases. There are many reasons f or the recurrence of nasopharyngeal carcinoma after the first radiotherapy, Such as radiotherapy technology, irradiation dose, individual differences, etc. Radiotherapy is still the main method for the treatment of recurrent nasopharyngeal carcinoma. Although patients with local recurrence after the first course of radiotherapy can have the opportunity of re radiation, the overall survival rate is significantly reduced, and radiation damage is significantly increased. This leads to increased mortality and decreased quality of life for patients, and the overall effect is difficult to satisfy. The main reasons may be: (1) there is a population of radiation-insensitive cells in recurrent nasopharyngeal carcinoma, which causes relapse (figure 1) after a certain period of incubation period, Re-radiation sensitivity Poor; (2) After the first course of radiotherapy, the nasopharyngeal and neck tissue structure changed, showing fibroproliferation, poor tissue blood supply, affecting the sensitivity of re-radiation therapy, and a t the same time, it was difficult for chemotherapeutic drugs to reach effective drug concentrations in tumors. The treatment effect is often unsatisfactory; (3) Because the anatomical position of the nasopharynx is close to the important tissues and organs such as the brain stem, temporal lobe, pituitary gland, optic cross, and optic nerve, these organs have received a tolerable dose of radiation during initial radiotherapy, and then The radiation dose is limited during the course of radiotherapy.

With the development of computer technology and medical imaging technology, tumor radiotherapy has entered a new era of three dimensional conformal radiotherapy by the traditional two-dimensional irradiation technology. Intensity Modulation Radiated Therapy (IMRT) The most advanced technology, which is characterized by: using the CT simulator and the reconstruction function of the 3D treatment planning system, to establish a visual 3D image of the target volume and surrounding endangered organs, the shape of the irradiation field and the shape of the target area are consistent in the 3D direction, and the target The dose in the area can be distributed according to the prescription requirements, which can more

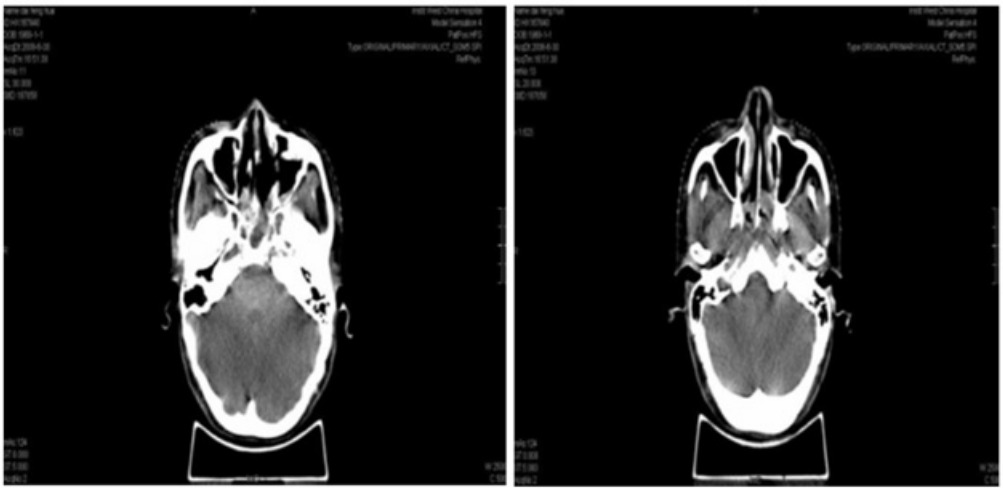

Figure 1: Picture before the first relapse June 30, 200 CT

accurately irradiate the tumor target volume and protect the endangered organs, and significantly reduce the exposure dose and volume of the surrounding endangered organs. It can also partially compensate the irradiation field by increasing the dose intensity at the edge of the field. It can increase the tumor do se to improve the local control rate and tumor free survival rate, thereby reducing the distant metastasis rate, and improving the quality of life by reducing the radiation dose of normal tissues. IMRT can make the parotid gland tolerant due to its dosimetric advantages. Protected by dose, there is more literature in this area [3-5]. The conventional irradiation field covers too many important organs, such as the brain stem, Temporal lobe, salivary glands, etc., cause

certain complications and sequelae, such as dry mouth, radioactive dental caries, difficulty opening mouth, skin and soft tissue fibrosis, etc., which affect the quality of life of patients. IMRT has become an ideal method for NPC treatment. This is mainly because: (1) NPC is mainly radiotherapy, and the survival time after radiotherapy is long, and the quality of life is relatively high; (2) the shape of the target area is extremely irregular, and the complete target area needs to include the entire nasopharyngeal wall, Pharynx space, pharyngeal space (including anterior and posterior styloid space), skull base, sphenoid sinus, pterygopalatine fossa, nasal cavity and maxillary sinus, and deep lymph nodes of the upper neck, etc .; (3) NPC is adjacent to important surrounding structures such as the brain stem , Pituitary, optic nerve, salivary glands and other tissues and organs that need to be protected; (4) Different radical doses are required for different parts of the target area, so the dose in the target area can be distributed according to re quirements; (5) The nasopharynx has a midline structure No relative movement of the organs; (6) The position fixation during the irradiation process is simple, reliable, repeatable and accurate. Therefore, IMRT technology is attractive in NPC treatment, which can maximize the advantages of radiation technology and can be multi field Multi directional target area for nasopharyngeal carcinoma Given uniform and effective high dose irradiation, at the same time, important structures around the target area such as the brain stem, pituitary, and salivary glands can be effectively protected, and it is inevitable that it will become the mainstream

radiotherapy technology for nasopharyngeal cancer. 20 patients in Kristensen et al. 'S study 11 patients were treated with IMRT, (figure 2) and 3 patients were treated with 3D CRT. Comparing the two, IMRT significantly increased the target volume dose and the protective effect of normal organs. [6] According to the clinical research results of European and American countries in this area in recent years, IMRT is more effective than three dimensional conformal radiotherapy. More advantageous. [7]

Intensity-modulated conformal radiotherapy has the unique advantage of adjusting the irradiation intensity of the tumor target area and adjacent sensitive organs separately: the dose distribution in the target area is uniform, and the side effects of normal tissues are small. Through the adjustment of the dose intensity, the tumor target area is accurately irradiated, so that the tumor can obtain Higher irradiation doses and fractional doses than conventional radiotherapy, while significantly reducing the dose of surrounding normal tissues, protecting normal organ function and improving quality of life.

The efficacy of radiotherapy for nasopharyngeal cancer is related to the volume of the target area covered, the target area dose, and the uniformity of the target area. IMRT treatment for recurrent nasopharyngeal cancer is no exception. The effective coverage of the target area and the dose of the target area do not reach the curative dose, which can easily cause relapsed tumors to be uncontrollable; if the uniformity of the dose in the target area is not good, it is likely that part of the GTV area does not reach the curative dose, and part of the G TV area reaches High doses are likely to cause local necrosis, reducing the efficacy of treatment and increasing local radiation damage.

Studies by Xianming Li et al. [9] showed that age, gender, KPS scores, t and n stages, and clinical stages are the most important independent prognostic factors affecting the survival of patients with nasopharyngeal carcinoma. IMRT can achieve a satisfactory local control rate in the treatment of nasopharyngeal carcinoma. The main cause of treatment failure is distant meta stasis, and t and n staging are important influencing factors for distant metastasis of tumors. In general, good intensity disease control can be achieved by IMRT in the treatment of recurrent T1-T2 nasopharyngeal carcinoma. However, Attention should still be paid to the occurrence of serious complications and the protection of important organs.

3.2. Cetuximab Molecular Targeted Therapy

EGFR is closely related to nasopharyngeal carcinoma. The EGFR expression rate of nasopharyngeal carcinoma is 83% 100% [10], Ma et al [11] reported that EGFR overexpression is an independent prognostic factor for overall survival of nasopharyngeal carcinoma, suggesting a target for EGFR Drugs may benefit EGFR overexpressors of nasopharyngeal cancer. Moreover, high expression of EGFR is associated with decreased disease free survival, decreased overall survival, and increased risk of metastasis / invasiveness, and is a predictor of poor prognosis for

advanced nasopharyngeal cancer [12] West Toximab is a monoclonal antibody against EGFR. It plays an antitumor role by inhibiting tumor cell proliferation, promoting tumor cell apoptosis, blocking tumor blood vessel formation, and enhancing radiosensitivity [13-15] (figure 3).

Cetuximab has a synergistic effect with radiotherapy, which is mainly manifested in: (1) the effect on the cell cycle dynamics, which can prevent cells from entering the S phase, reduce the proportion of cells in the S phase, and make the cells gather in the G1 and G2 phases; 2) Increased radiation induced apoptosis; (3) Inhibited radiation induced EGFR phosphorylation; (4) Inhibited radiation damage repair. Bonner et al. [16] performed a cetuximab combined with radiotherapy in 2006 A multicenter randomized controlled study of locally advanced SCCHN (squamous cell carcinom a of head neck). This study included 424 patients with locally advanced SCCHN, and randomized groups were given radiotherapy or radiotherapy combined with cetuximab and cetuximab. Use weekly, with an initial dose of 400 mg / m 2 and subsequent weekly doses of 250 mg / m 2 until the end of radiotherapy. The results showed that the addition of cetuximab group significantly increased the patient's median local control time, Median non progressive PFS, and median OS, with the exception of rash and infusion reactions, the adverse reactions of cetuximab combined with radiotherapy did not increase. Burtness et al. [17] implemented a phase III clinical trial to evaluate cetuximab The efficacy of monoclonal antibodies for patients with relapsed or metastatic SCCHN, 117 patients were randomly assigned Received cisplatin chemotherapy (100mg / m 2, once / 4 weeks), the experimental group was added with cetuximab every week, and the control group was added with placebo. The experiment ended with Progression Free Survival (PFS) The median PFS of the experimental group and the control group were 4.2 months and 2.7 months, respectively, P = 0.09. The median OS of the experimental group and the control group were 9.2 months and 8.0 months, respectively, P = 0.21. There was no statistically significant difference between PFS and OS, however, the response rate of the experimental group was significant-

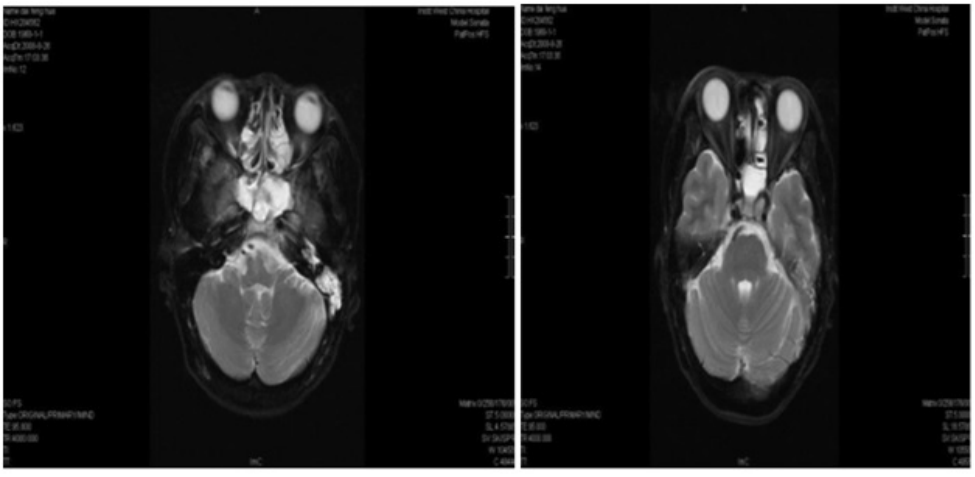

Figure 2: Picture after first relapse treatment August 25, 2008 MR

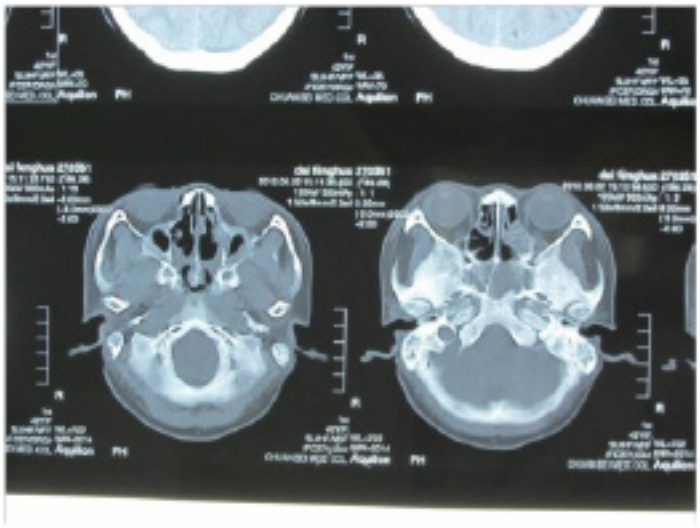

Figure 3: 2 years after treatment picture April 25, 2010 MR

ly better than that of the control group.

Acne-like rash is a common adverse reaction of EGFR inhibitors, which usually appears within 2 weeks after administration. The rash is mostly distributed on the face, scalp, chest and back. Studies by Bonner [51] and Burtness [53] suggest that the appearance of rash and the grade is positively related to the objective effect. The incidence of oral mucositis in the cetuximab combined radiotherapy group and the radiotherapy alone group was 55% and 52%, respectively, and it would not aggravate its occurrence. Shin et al. [18] confirmed that cetuximab The first dose of monoclonal antibody is 400mg / m2, and the maintenance amount of 250mg / m2 per week can make the EGFR saturation rate in tumors higher. But cetuximab belongs to biological targeted therapy, which has clear targets, biological effects and clinical effects. There is not necessarily a li near relationship. Existing data show that cetuximab is well tolerated clinically, and the main adverse reactions are mostly mild to moderate. Oral mucositis and pain are more severe after combined chemoradiotherapy, which may be inhibited. EGF is related to the repair of normal tissue radiation damage. As a new targeted therapeutic drug, it has a relatively clear effect in the treatment of tumors such as nasopharyngeal cancer. Its long term treatment benefits and toxicity have yet to be observed. For recurrent nose Is it possible to obtain and treat nasopharyngeal carcinoma in the treatment of throat cancer? The effect is unknown (figure 4).

4. Conclusion

In this patient, intensity-modulated radiation therapy combined with cetuximab was used to treat recurrent nasopharyngeal carcinoma. The patient completed the treatment as planned. During the treatment, he experienced ii-degree oral, oropharyngeal mucosal reactions, moderate dry mouth, and facial, scalp, chest, and back. A second degree acne like rash appeared, and the symptoms improved after symptomatic treatment, and the patient could tolerate it. The patient's lesions were significantly smaller after retreatment than before the treatment, and no obvious side effects of radiotherapy were observed, and the short term quality of life was not significantly reduced. Intensive radiotherapy combined with cetuximab molecular targeted therapy for patients with locally recurrent nasopharyngeal carcinoma has satisfactory short term efficacy, good local control rate, tolerable toxic and side effects, and high safety. This case is representative of the case. It is necessary to follow up more cases in the future and make long term follow up.

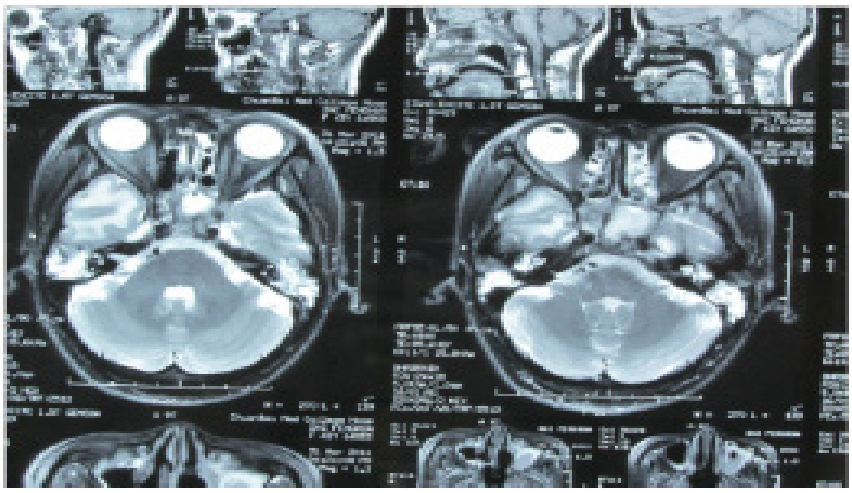

Figure 4: 3 years after treatment picture March 31, 2011 MR

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