Clinical Characteristics and Treatment of Malignant Granuloma

Chongjin Feng[1]
Junbing Guo[1]
Yong Chen[2]

[1] Department of Stomatology, First Affiliated Hospital, Sun Yat-sen University of Medical Sciences, Guangzhou, 510080, China.
[2] Department of Radiation Therapy, Tumor Hospital, Sun Yat-sen University of Medical Sciences, Guangzhou, 510080, China.

Correspondence to: Chongjin Feng
Tel: 86-20-8775-5766 ext. 8721 or 8414

This work was supported by the Guangzhou Science and Technology Foundation (No. 99-Z-101-01).

OBJECTIVE To analyse the clinical characteristics of malignant granuloma (MG) and evaluate its treatment.

METHODS From March 1985 to May 1998, 101 cases of malignant granuloma were treated with radiation (RT) alone or radiotherapy followed by chemotherapy or chemotherapy followed by radiotherapy. For chemotherapy, a CCNU, COMP (CTX, VCR, MTX, PDN) or CHOP (CTX, ADM, VCR, PDN) regimen was given. Radiation was directed through the anterior field of the nose mainly for nasal and paranasal sinus malignant granuloma, and through the faciocervical field for malignant granuloma of Walderyer's ring or for patients with cervical lymphadenectasis. Total dose was 45–65 Gy over 5–6 weeks.

RESULTS The overall 3-year, 5-year and 10-year survival rates were 78.2%, 56.1% and 39.7% respectively. The 5-year survival rate was: RT group 60.3%, RT + CHOP or CHOP + RT group 64.7% (P >0.05), RT + CCNU group 40%, and RT + COMP group 33.3%. The 5-year survival rates of patients with one involved focus and more than 2 involved foci were 75.6% (34/45) and 39.3% (22/56) (P<0.001). The 5-year survival rates of patients with or without body symptoms were 39.6% (18/48) and 67.9%(36/53) (P< 0.05). The 5-year survival rate of the 50–60 Gy group and the <50Gy group were 60.1% (40/66) and 20% (1/5) (P <0.05). The local and regional recurrence rate was 20.8% (21/101).

CONCLUSION Radiotherapy alone should be the treatment of choice for patients with one site involvement and without body symptoms. Radiation fields should be large enough to include the potentially involved sites. The recommended dose is 50-60 Gy over 5-6 weeks. It is suggested that patients with more than 2 foci involvement and those with body symptoms should receive the combination therapy.

KEYWORDS: malignant granuloma, radiotherapy, chemotherapy.

Malignant granuloma is a clinical entity characterized by progressive unrelenting ulcerations and necrosis of the midline facial tissues, which are usually in the nasal cavity, the hard palate and the midline of the nasopharynx. In the past decade, with the development of immunohistochemicals and molecular biology, it has been shown that malignant granuloma is a type of malignant lymphoma, with the malignant cells being derived mainly from T-cells. [1-3] Thus, some scholars call it "Midline Peripheral T-cell Lymphoma". [4,5] The clinical symptoms of this disease are very

Received January 19, 2005; accepted March 3, 2005.
Chinese Journal of Clinical Oncology
E-mail: CJCR@sina.com Tel(Fax): 86-22-2352-2919

complex; as a result, it is very difficult to make a definite diagnosis. In addition, the level of malignancy is very high and the prognosis is poor. In order to analyze the clinical characteristics of this disease and improve the clinical diagnosis and treatment, we have compiled data from 101 cases of malignant granuloma patients we have treated over the period from March 1985 to May 1998.

MATERIALS AND METHODS

Background information

There were 101 cases; 68 male and 33 female. The ratio of males to females was 2.1:1. The patients ranged in age form 1.5 to 66 years (median: 37 years). Their case histories ranged from 1 month to 2 years (median: 5.5 months). All cases were diagnosed by pathologists and 35 had also been diagnosed via immunohistochemial analysis.

The initial sites of the disease

Sixty-five patients developed malignant granuloma in the nasal cavity, 21 in the nasopharynx, 8 in the hard palate of the mouth and 7 in their tonsils. The tumor always affects several anatomic regions of the body. Fourty-five patients had only one malignant granuloma involved site (44.5%), 36 had 2 sites involved (35.6%), 17 had 3 sites involved (16.8%), and 3 had 4 sites involved (3%).

Clinical symptoms and stages

There were 52 patients who presented with stuffiness in the nose and bloody mucous; 21 presented with sore throats; 48 presented with fever and night sweats; 38 patients presented with significant weight loss and weakness; and 5 presented with swollen cervical lymph nodes. The tumor sites usually show progressive ulcers and necrosis. The ulcers were greyish-yellow and gave off an abnormal odor. Subsequently the patients developed ulcers or even perforations in their nasal septums and hard palates of the mouth. In more advanced cases, a large part of the patients' facial tissues around the nasal area underwent necrosis which eventually resulted in a cavity in this area. All these patients had undergone the following standard tests: a X-ray or a CT scan of the chest , nasopharynx , and paranasal sinus, an abdominal B ultrasound or a CT scan, tests of liver or kidney function and a hemogram; some patients were also subjected to a bone-marrow biopsy. According to the Stewart [6] criteria, 32 patients were in the first stage (prodromal), 64 in the second stage (active), 5 in the third stage (terminal).

Treatments and regimens

Among the 101 patients in this report, 68 were treated with radiotherapy alone and 33 were treated with chemotherapy plus radiotherapy. ^{60}Co-γ, 10MV-X-ray and electronic beam were used in a radiation-only regimen. The radiation fields were administered in accordance with the diseased anatomic region. For example, radiation was given through the anterior field of the nose mainly for nasal and paranasal sinus malignant granuloma; if the disease affected the nasopharynx, tonsils and the lymph nodes in the neck were swollen, the faciocervial field was to be radiated at a dosage of 45-65 Gy/5~6 weeks. Among patients in this report, 66 underwent radiation with a dosage of 50-60Gy/5~6 weeks, 5 with a dosage of <50 Gy, and 30 with >60Gy. For chemotherapy, before and after radiation treatment, the patients underwent more than 2 periods of chemical treatment. The regimens for chemiotherapy were as follows: before 1991, CCNU, COMP (CTX, VCR, MTX, PDN) were mainly used, while after 1991, CHOP (CTX, ADM, VCR, PDN) were mainly used.

RESULTS

Survival rate

Patients in this report were followed until June 2003. Among them, 6 were lost to follow-up and therefore were classified to the deceased group. The rest of the patients were followed-up for 5 years. The percentage of the patients who were followed-up was 94.1%. The 3-year, 5-year, and 10-year survival rates were 78.2% (79/101), 56.1% (46/82) and 39.7% (23/58) respectively.

For the relation between the diseased region (s) and survival rate see Table 1. For the relation between the physical symptoms and survival rate see Table 2. For the relation between the radiation dosage and survival rate see Table 3.

Treatments and the survival rate

Sixty-eight patients underwent radiation treatment only and their 5-year survival rate was 60.3% (41/68); thirty-there underwent chemotherapy plus radiotherapy and their 5-year survival rate was as follows: 40% (4/10) in the CCNU group, 33.3% (2/6) in the COMP group and 64.7% (11/17) in the CHOP group. There was no significant difference between the 5-year survival rates of the radiation-only group and the CHOP group (P>0.05).

The local and regional recurrence rate

In this research, the local and regional recurrence rate was 20.8% (21/101). Among them, 3 patients relapsed again, and the new sites involved were mainly on the border of the radiation field. Among these patients, 4 underwent a second radiation treatment and survived without a tumor up to the present time.

DISCUSSION

Malignant granuloma is a tumor bearing mutations, which develops very fast and is very lethal. Since the main symptom of the first stage of malignant granuloma is inflammation, symptoms vary without conclusive evidence as to the nature of the disease. In addition, it's always accompanied by infection and necrosis of large areas of tissue. Malignant granuloma symptoms include a mixture of typical tumor and inflammatory symptoms. Thus, malignant granuloma is very easy to be misdiagnosed as simple inflammation. As a result, in those suspicious cases,

Table 1. Diseased region(s) and survival rate

		5-Year survival rate		
Diseased region(site)	Total number of the cases	Survival cases	%	*P*
1	45	34	75.0	<0.001
≥ 2	56	22	39.3	-

Table 2. Physical symptoms and survival rate

		5-Year survival rate		
Symptom	Total number of the cases	Survival cases	%	*P*
With fever	48	18	39.6	<0.05
Without fever	53	36	67.9	-

Table 3. Radiation dosage and survival rate

		5-Year survival rate		
Dosage(Gy)	Total number of the cases	Survival cases	%	*P*
>60	30	17	56.7	<0.05
50~60	66	40	60.1	<0.05
<50	5	1	20.0	-

P refers to the comparison with that of the group with <50 Gy.

which are doubtfully classified as "chronic inflammations and inflammatory necrosis", it's necessary to conduct biopsies and other diagnostic tests more than once. If it is difficult to identify the type of the malignant cell based on microscopy alone, then immunohistochemial tests should be conducted to determine from where the malignant granuloma cells originate. Diagnosis and treatment in the early stages of the malignant granuloma disease is the most effective method to improve the results.

The radiation treatment for malignant granuloma

Malignant granuloma is very sensitive to radiation treatment, so the main method of treatment is still radiotherapy. In this report, the result of research showed that the 5-year survival rate, which was 60.3% for patients who underwent radiotherapy, is very close to the survival rates published in previous medical reports.[7,8] The results are satisfactory if the dosage is 50-60 Gy/5~6 weeks. In addition, the patients do not suffer from any side-effects. The 5-year survival rate of patients with first stage malignant granuloma but who presented with no body symptoms reached to 80% (24/30). Thus, we suggest that these kinds of patients be treated with radiotherapy first. Since malignant granuloma affects more than one anatomic region, the region adjacent to the diseased region is likely be affected after radiation. As a result, the radiation field should be expanded to include those adjacent regions, which could be affected by the disease after initial radiation. If the disease affects the Walderyer's ring, or the lymph nodes in the neck are swollen, patients should receive radiation on the faciocervial field. At the same time, data from our report also indicate that those patients who suffer from a malignant granuloma relapse in a local region or regions adjacent to the area treated by radiation, should also receive active treatment, since some of these patients have survived without further tumors after receiving a second round of radiation.

Combination therapy for malignant granuloma

Since malignant granuloma is a type of malignant lymphoma, at present, the combination of radiotherapy and chemotherapy is widely used. According to the results in our report, the survival rate of those patients who have been affected by malignant granuloma in more than two anatomic regions drops significantly ($P<0.001$). And the survival rate of those who have physical symptoms is significantly lower than that of those who have no fever or night sweats. In order to improve the effectiveness of treatment, a regimen of chemotherapy and radiotherapy should be administered. This report showed that of the patients who received a regimen of CCNU and COMP, their survival rate was low, while the 5-year survival rate of those who received CHOP was greater (64.7%). However, there was no significant difference between the CHOP group and the radiotherapy group. The reason for this result may be because the chemotherapy is usually given to those patients whose disease is in a late stage. Moreover, there is also a need for further research on the effects of chemical treatments for malignant granuloma, too.

REFERENCES

1 Liu WP, Li GD, Xu SL. Pathomorphological and immunohistochemical study of midline malignant reticulosis. Chin J pathol. 1991; 20: 103–105.

2 Feng CJ, Ding XQ, Chen XH. A clinicopathologic and immunohistochemical study of malignant granuloma. Acad J SUMS. 1999; 20:76–77.

3 Wang GB, Liu C, Zhao B, et al. CT, MRI and pathology study of malignant granuloma. Chin J MIT. 2001; 17: 632–634.

4 Armitage JO, Greer JP, Levine AM, et al. Peripheral T cell lymphoma. Cancer. 1989; 63: 158–163.

5 Li JX, Liu YH, Xue XH. Midline peripheral T –cell lymphoma –A disease entity recognized anew. Chin J Oncol. 1990; 12:206–208.

6 Stewart JP. Progressive lethal granulomatous ulceration of the nose. J laryng.1933; 48:657–701.

7 Gu ZP, Song ZE, Wang DC. The long term treatment result of malignant granuloma treated with radiotherapy. Chin J Radia Oncol. 1996; 5:171–173.

8 Zhou CH, Wang XY, Wang XY. Radiotherapy of malignant granuloma. Chin Oncol .1999; 9:61.