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HIGH DOSE FRACTION RADIOTHERAPY FOR MUCOSAL MALIGNANT MELANOMA OF THE HEAD AND NECK

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Objective: To evatuate the results of high dose fraction radiotherapy for mucosal malignant melanoma of the head and neck (HNMM). Methods: From 1984–1994, 35 patients with HNMM were enrolled in this study. Among them, 27 cases localized to the nasal cavity or para-nasal sinus, 8 to the oral cavity. All patients received high dose fraction radiotherapy (6–8 Gy/fraction) with the total dose ranged from 40 to 60 Gy. Results: The minimum follow-up was 2 years (ranged 2–7 years). The overall 3- and 5-year survival rate was 45.7% and 24%, respectively. Conclusion: High dose fraction radiotherapy is effective for local control of HNMM.

Key words: Mucosal melanoma, Head and neck, Radiotherapy.

Mucosal malignant melanoma of the head and neck (HNMM) represent a few percent of all melanoma. The reference vary from 0.4 to 4%.[1] Distant metastasis can occurred in early stage. The prognosis was poor. The 5-yrar survival rate ranged from 16 to 26%. High dose fraction radiotherapy (HDFR) had been proven to be effective for malignant melanoma. But only a few papers have mentioned the therapeutic possibilities of irradiation to HNMM. From 1984 to 1994, HDFR had been done in 35 patients with HNMM (excepted conjunctiva) in our hospital. The results are reported as follow.

MATERIALS AND METHODS

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Clinical Details

Between April 1984 to April 1994, 38 patients with histological verified HNMM were referred to our hospital and, 35 patients were entered the study. In 35 cases, 27 were males and 8 were females. The age at presentation ranged from 24 to 78 years old (mean age 59.2 years). Distant metastases were not present in any patient at the time of diagnosis. Tumors localized to the nasal cavity in 25, to the para-nasal sinus in 2, to the oral cavity in 8 (hard palate 4 cases, maxillary gingiva 2 cases, buccal mucosa 1 case, tonsil 1 case). The clinical details and survival rates are given in Table 1.

Table 1. Clinical details and survival rates of 35 patients

	Nasal cavity or paranasal sinus (n=27)	Oral cavity (n=8)
Stage		
I	19	5
II	8	3
Neck lymph node positive	8	3
Survival		
3-year	13/27 (48.1%)	3/8 (37.5%)
5-year	5/20 (25%)	1/5 (20%)

The case histories were relatively short, ranged from 2 months to 18 months. The main symptom from malignant melanomas in the nasal cavity was nasal

obstruction, follow by epistaxis, visual symptoms and headache. The main symptoms of oral melanoma were sensation of swelling or pain, black nodule or melanosis of the mucosa. Staging was based on clinical presentation, physical findings and roentgenographic findings or computed tomography (CT) scanning. According to Ballanlyne's staging: 24 patients in stage I, 11 patients in stage II.

Treatment

External-beam irradiation was administered with ^{60}Co, 6MVX-ray, 8MVX-ray or electron beam. Irradiation of tumors in the nasal cavity. Three-field technique was used. A single anterior port was used when tumor was confined to the nasal cavity. For the oral melanoma two lateral fields were used. The neck was treated in only 11 patients, those that had positive neck nodes. The dose fraction was 800cGy (32 cases) or 600cGy (3 cases). Fractions were given at daily to weekly interval, total tumor doses were 40 to 48Gy for primary tumor and 48–60Gy for neck metastatic lymph node.

18 patients were treated with HDFR alone, of these, 6 patients refused to receive operation. 5 patients were clinically treated by surgery, resulting in remnant tumors, followed by postoperative radiation therapy. Patients who had no remnant tumor after surgery received postoperative radiation therapy. 4 patients received pre- or postradiation chemotherapy. Drugs were DTIC、VCR、DDP、PYM.

3 patients developed recurrences after HDFR within 2 years, 1 as late as 3 years and another 5 years later. 4 patients received additional radiation with dose fractions were 500cGy and total doses from 30 to 40Gy.

RESULTS

Minimum follow-up was 2 years (ranged 2 to 7 years). The survival period was calculated respectively from the first day of the treatment to the last day of follow-up or death. The overall 3- and 5-year survival rates were 45.7% 24% respectively. 25 patients were died, of these, 16 patients died of distant metastases. 5 patients died of persistent local diseases. 2 patients died from local recurrence and distant metastases. 2 patients died of other disease. The sites of distant metastases were skin (5 cases), lung (5 cases), bone (4 cases), abdomen (2 cases), and liver (2 case).

The effects of HDFR and multimodel therapy are given in Table 2.

The treatment was tolerated. The acute treatment toxicities were mucosal reactions: mucosal crusting and dryness, mucosal ulceration. Only 2 patients required a rest for one week before resumption of radiotherapy due to mucosal ulceration. No patients developed tissue necrosis.

. The effect of HDFR and multimodel therapy for 35 patients

	CR		PR	
	Prim	Neck lymph node	Prim	Neck lymph node
Nasal/para-nasal	20/25	5/8	4/25	3/8
Oral cavity	4/6	2/3	1/6	1/3
Total	24/31	7/11	5/31	4/11
HDFR alone	15/18	3/6	2/18	3/6
HDFR for recurrence after surgery	2/4	1/1	1/4	0/1
HDFR for remnant tumor after surgery	4/5	1/1	1/5	0/1
Chemotherapy+HDFR	3/4	2/3	1/4	1/3
HDFR for recurrence after HDFR	2/4	0/1	2/4	1/1

DISCUSSION

Nasal melanomas originated in the anterior part of the nasal septum, in the middle and inferior turbinates. This entity often involved adjacent structures (i.e., para-nasal sinus, orbit or anterior cranial). Oral melanoma was much more common on the upper jaw than the lower jaw, the second most

common site was gingiva.[1,3] HNMM are often large and ulcerative at the presentation. CT and MRI are useful in staging the tumor and determining the target volume location.

It is generally agreed that treatment for HNMM should be a wide resection of the lesion with or without lymph node dissection.[1,4] As HNMM are often asymptomatic, many lesions are not detected until they are very large. Anatomic restraint often make radical surgery difficult.[3,6] Ruan Hy[5] reported 2 of 4 patients who underwent operation alone developed local recurrences with 1 year. Bethlsen[1] reported 9 of 20 patients who underwent surgery developed remnant or recurrent tumors locally. Our experience supports the findings reports by them that local recurrence after surgery alone is relative high. In our series, 4 patients who considered being free of tumor postoperatively recurred at the primary site after surgery alone. Postoperative irradiation can be effective for HNMM.[1,5] Ruan Hy[5] reported 3 patients were initially treated by surgery followed by postoperative radiation therapy, resulted in no recurrence with 1 year. In our series, 5 patients had residual tumor after surgery received postoperative radiation. 2 patients were tumor free for 2, 4 years. 4 patients who had no remnant tumor underwent postoperative radiation. No patients developed local recurrence with 3 years. 2 patients survival for 4, 7 years. We believe that postoperative radiation can destroy the remnant tumor and prevent local recurrence.

Malignant melanomas are generally considered to be radio-resistant tumors. Because of the broad shoulder on the cell survival curve as demonstrated in radiation biology experiment.[7,9] These authors concluded that the radio-resistance may be due to an increased level of cell hypoxia or a large capacity for repair of radiation damage in the melanoma cells. Habermalz[7] and Hornsey[8] have indicated that a greater percentage of tumors respond to large single-dose fraction. The successful cases of HNMM achieving local control by HDFR were reported by Harwood et al.[9] They reported 6 of 7 HNMM patients treated with dose fraction more than 400cGy and received chemotherapy concomitantly had complete response. Nishimura[6] reported 3 HNMM patients with dose fraction of 600–800cGy had complete response. In our series, the complete response rate was 77.8% (21/27). The overall response rate was 92.6% (25/27). Our study suggests that HDFR is effective for local control.

In regard to melanomas in the nasal cavity and in the oral cavity, the metastatic frequency of the former is relatively low, lymph node metastases and distant metastases of the latter occur more frequently.[1,10] This corresponds to our observations. Hornsey[8] treated lymph node metastases of malignant melanoma with dose fraction between 400 and 800cGy. The overall response rate was 80%, and reduced to 35% when dose fraction less than 300cGy. In our study, neck lymph node metastases were treated with HDFR (600–800cGy per fraction, total dose 48–60Gy). The overall response rate was 81.8% (9/11). We believe that HDFR is also effective for neck lymph node metastasis of HNMM.

Several reported trials of HDFR for malignant melanoma have resulted in severe late normal tissue damage.[6] In our series, two of five patients who survival more than 5 years and developed radiation retinopathy after 3 and 4 years for HDFR. In both cases the partial orbit was included in the treatment portal. Apart from above, no other late reaction was observed. 4 patients received additional HDFR after HDFR. The acute reaction was severe (mucosal and skin reaction), but all patients were completed the treatment.

Most patients died from systemic metastasis and it is quite possible that microscopical metastasis are present in most patients either at initial diagnosis or on some occasion during their disease. We found metastasis can occur many years after control of the primary. Multinodality therapy include surgery, radiation, chemotherapy and immunotherapy must be considered.

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