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Nasopharyngeal granulomatous mass after radiotherapy for nasopharyngeal carcinoma

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ABSTRACT

Objective: To evaluate the diagnosis, management and nasal endoscopic surgical outcome of nasopharyngeal granulomatous mass in post-radiation nasopharyngeal carcinoma (NPC) patients.
Materials and methods: A total of 23 cases of granulomatous mass after radiotherapy for NPC from 2008 to 2013 treated with nasal endoscopic surgery were retrospectively reviewed.
Results: Radiotherapy dose ($p = 0.036$) and chemotherapy ($p < 0.001$) correlated with the latency period after the treatment against NPC. The symptoms of the 23 patients before the treatment were nonspecific including nasal obstruction, purulent discharge, headache, epistaxis, foreign body sensation and/or hearing impairment. 12 patients (52.2%) were misdiagnosed to be recurrence of NPC by imaging examination (CT/MRI). After the endoscopic surgery treatment, 18 patients were disease free while the other 5 patients had developed a recurrence. Four of those five recurrent patients were cured with the repeated treatment. Histologic findings of granulation tissue with fibrin and inflammatory cells were found in all of the patients.
Conclusions: In situ granulomatous masses in post-radiation NPC patients are very prone to be misdiagnosed as recurrence of nasopharyngeal carcinoma. Chemotherapy is a significant independent factor affecting latency period ($p = 0.029$). The nasal endoscopic surgery is an effective therapy for post-radiation nasopharyngeal granuloma; surgery can not only alleviate symptoms, what is more important, but it also helps to confirm the diagnosis.

1. Introduction

Nasopharyngeal carcinoma (NPC) is a common head and neck cancer in Southeast Asia. Considering its anatomic restrictions and sensitivity to radiation, radiotherapy has been used as a first-line treatment in NPC for decades. However, during the therapy, normal tissue is inadvertently involved in the radiation field, especially within the nasopharynx, as it receives the full radiation dose. Vascular hyalinization, hypoxia, microcirculation disorder, and immunodepression caused by radiotherapy may lead to granulomatous masses with variable amounts of fibrin [1]. The severity of radiation damage after treatment is reported to be relative to radiation dose, as well as the use of chemotherapy [2]. Unlike xerostomia, cranial nerve neuropathy and otitis media, which are common complications of radiotherapy [3], the granulomatous mass in nasopharynx attracts limited attention since it was first

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described in 1989 [4]. Although the symptomatology and imaging characteristics of nasopharyngeal granulomatous mass may mimic those of recurrent nasopharyngeal carcinoma, the treatment approaches are fundamentally different [5].

The objective of this study is to review nasopharyngeal granulomatous mass after radiotherapy against NPC and to assess the role of chemotherapy and its action during disease progression.

2. Materials and methods

We performed a retrospective review of 23 patients treated with radiotherapy against NPC and who were diagnosed with nasopharyngeal granulomatous mass between 2008 and 2013. All patients were followed up more than 1 year. Those who had a recurrent tumor or a secondary primary tumor were excluded.

Strategies of treatment against NPC were collected from department of radiotherapy in Affiliated Eye Ear Nose and Throat Hospital, Fudan University. Chemotherapy consisted of cisplatin or carboplatin combined with 5-fluorouracil.

All data were analyzed with SPSS version 22.0. Statistically significant p-values were defined as <0.05. Spearman rank correlation was used to determine the relationship between radiotherapy dose and the latency period. Kaplan–Meier curves were used to perform the survival analysis. Radiotherapy dose and treatment against NPC were analyzed for their association with latency period using Cox proportional hazards regression models.

No preoperative treatment was taken before the surgery. Surgery was performed under hypotensive general anesthesia in all cases and second-generation cephalosporin was used for antimicrobial prophylaxis. The nasal cavities were packed prior to surgery with cotton pledges soaked with 1% tetracaine and 0.1‰ adrenaline for 10 min to achieve decongestion. The granuloma was visualized under the nasal endoscopy and the pedicle of granuloma was exposed to visualize an arterial pulse. After the achievement of hemostasis with diathermy, the granulation lesion was removed with a microdebrider. Necrotic tissue and sequestra were also excised and nasal packing was placed after the surgery. Transoral approach with microdebrider was used in 3 cases for the granuloma expanding into the oropharynx. Postoperative treatment included administration of antibiotics and nasal irrigation.

3. Result

Among the 23 patients, 17 were male (73.9%) and 6 were female (26.1%). The mean age was 53.5 ± 9.3 years (range 40–72 years). The tumor histopathologies of patients were undifferentiated (52.6%) or poorly differentiated (47.4%) squamous cell carcinoma. The latency period between the completion of radiotherapy and the diagnosis of nasopharyngeal granulomatous mass ranged from 1 month to 27 years, with a mean latency period of 6.3 years. The total radiotherapy dosage data were only available for 19 patients and ranged from 64 to 132 Gy (mean 81.1 Gy). Among those 19 patients, 11 patients were treated with added chemotherapy (Table 1).

Table 1
Case summary.

Case	Age (Y)	Gender	RT dose (Gy)	Treatment	Latency period (Y)	Osteonecrosis	Recurrence (after surgery)
1	*49*	*M*	*64*	RT	14	+	3 years
2	72	M	NA	RT	16	+	–
3#	56	M	64 + 66	RT + CT	0.1	–	–
4*	55	M	66	RT	27	+	11/10/6 months
5#	47	F	62 + 66	RT + CT	1.7	–	8 months
6#	47	M	64 + 68	RT	0.1	–	1.5 years
7	*61*	*F*	*74*	RT + CT	0.7	–	–
8	49	M	72	RT	3	+	–
9	69	F	NA	RT	27	+	–
10	66	F	66	RT + CT	0.75	–	–
11#	52	M	62 + 66	RT + CT	0.5	+	–
12	50	M	70	RT + CT	0.5	+	–
13	61	F	68	RT + CT	0.5	–	–
14	71	M	69	RT	4.5	+	–
15	45	M	69	RT + CT	0.33	–	–
16	43	M	68	RT + CT	1.4	+	–
17	41	M	NA	RT	10	+	3 years
18	50	M	64	RT + CT	1.5	–	–
19	49	M	70	RT + CT	0.5	–	–
20	52	M	NA	RT	17	+	–
21	49	M	64	RT	9	–	–
22	40	M	70	RT	1	–	–
23	57	F	68	RT	7	–	–
Mean	53.5		81.1		6.3	11	

NA, unavailable; RT, radiotherapy; CT, chemotherapy.
Patient 4* had granuloma that recurred repeatedly with nasal obstruction and epistaxis, and osteonecrosis was found at the third reexamination.
Patients 3#, 5#, 6# and 11# had been given a second radiotherapy for a recurrent NPC.
Patients 11, 12, 13 and 15 had received induction chemotherapy with cisplatin and 5-fluorouracil and concurrent chemotherapy with cisplatin.
Patients 3, 7, 10, 16, 18, and 19 had undergone concurrent chemotherapy with cisplatin.