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Early-onset dropped head syndrome after radiotherapy for head and neck cancer: dose constraints for neck extensor muscles

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ABSTRACT

Dropped head syndrome (DHS) is a famous but unusual late complication of multimodality treatment for head and neck carcinoma. We reported this early-onset complication and analyzed the dose to the neck extensor muscles. We examined the records of three patients with DHS after radiotherapy. The doses to the neck extensor muscles were compared between three patients with DHS and nine patients without DHS. The mean dose to the neck extensor muscles of the three patients with DHS were 58.5 Gy, 42.3 Gy and 60.9 Gy, while the dose was <50 Gy in all nine patients in the control group. The onset of this syndrome was 5 months, 6 months and 15 months. The early-onset DHS may have something to do with dose to the neck extensor muscles. The proposed dose to the neck extensor muscles might be <46 Gy (or at least <50 Gy).

KEYWORDS: early-onset dropped head syndrome, radiotherapy, chemoradiotherapy, unusual complication, dose constraints to the neck extensor muscles

INTRODUCTION

Dropped head syndrome (DHS) is caused by various neuromuscular disorders [1–8]. It is also a famous but rare complication of radiotherapy [6]. This syndrome is characterized by weakness of neck extensor muscles, causing an inability to extend the neck and resulting in the patient's posture having the head flexed forward. The etiology and treatment remain unclear due to its rarity. This syndrome has been reported as a late-onset complication following radiotherapy [6]. Recently, a few case reports have been published about early-onset DHS after multimodality treatment for head and neck carcinoma [7, 8]. We have had experience of three patients with early-onset DHS. These patients were treated with intensity-modulated radiotherapy (IMRT) for head and neck carcinoma. This study was conducted to report this rare complication, to analyze the dose to the neck extensor muscles, and to propose dose constraints.

MATERIALS AND METHODS

We have had experience of three patients with DHS following radiotherapy for head and neck carcinoma. Details of patient characteristics, treatment and clinical course are described. The irradiated dose to the neck extensor muscles was analyzed. The neck extensor muscles were contoured, including the splenius muscles, semispinalis muscles, and spinalis muscles. The doses to the neck extensor muscles were compared between the three patients with DHS and the nine patients without DHS as a control. The dose to the right, left and both neck extensor muscles was analyzed. The compared parameters were mean dose, $V_{10\ Gy}$, $V_{20\ Gy}$, $V_{30\ Gy}$, $V_{40\ Gy}$, $V_{50\ Gy}$, $V_{60\ Gy}$ and $V_{70\ Gy}$ (%). The control group patients were selected because they were irradiated with IMRT in the same time period and the level V area was included in the radiation fields (located in close vicinity to the neck extensor muscles). Six patients

Table 1. Patients' characteristics

	Age	Sex	Disease	Stage	Treatment	Radiotherapy	Chemotherapy	Mean dose to neck extensor muscles/fractions	Latent period
Patient 1	62	M	Hypopharyngeal carcinoma	T3N2bM0	CRT	IMRT 70 Gy for hypopharyngeal carcinoma	CDDP + 5FU	58.5 Gy/35 fractions	5 months
			Esophageal carcinoma	T3N2M0		3DCRT 60 Gy for esophageal carcinoma			
Patient 2	73	F	Nasopharyngeal carcinoma	T2N0M0	RT	IMRT 70 Gy and additional 3DCRT 10 Gy for primary disease		42.3 Gy/40 fractions	6 months
Patient 3	55	M	Nasopharyngeal carcinoma	T1N2M0	CRT	IMRT 70 Gy	CDDP	60.9 Gy/35 fractions	15 months

CRT = chemoradiotherapy; RT = radiotherapy; IMRT = intensity-modulated radiotherapy; 3DCRT = 3D conformal radiotherapy.

had nasopharyngeal carcinoma, two patients had oropharyngeal carcinoma, and the remaining patient had hypopharyngeal carcinoma. One patient with oropharyngeal carcinoma and two patients with nasopharyngeal carcinoma were treated using radiotherapy alone, and the others were treated using chemoradiotherapy. Our institutional review board (The National Cancer Center Institutional Review Board, Japan) approved this study.

RESULTS

Table 1 shows the details of the patients with DHS. Patient 1 was a 62-year-old man with synchronous hypopharyngeal and esophageal carcinomas treated with chemoradiotherapy; he presented with head drop 5 months after completion of radiotherapy. The patient suffered from pain and bending deformity of the neck, and disturbed daily activity. The physical examination, CT and MRI showed no atrophy of the neck extensor muscles. The disease relapsed at the left hilar and mediastinal lymph node 13 months after radiotherapy. Salvage chemotherapy was administered without response. The patient was observed for 22 months after the occurrence of DHS, and the symptoms were slightly improved despite the salvage chemotherapy. IMRT was applied to the treatment of the hypopharyngeal carcinoma. The mean dose to the neck extensor muscles was 58.5 Gy/35 fractions. A total of two cycles of concurrent chemotherapy of 5FU (700 mg/m^2 Days 1–4) and cisplatin (70 mg/m^2 Day 1) were administered.

Patient 2 was a 73-year-old woman with nasopharyngeal carcinoma treated with radiotherapy alone, and she presented with head drop 6 months after completion of radiotherapy. The patient suffered from pain with neck bending. The physical examination and MRI showed no atrophy of the neck extensor muscles. She had no recurrence and was observed for 8 months after the onset of DHS. The symptoms did not change. The radiotherapy dose was 70 Gy/35 fractions for nasopharyngeal carcinoma and, additionally, 10 Gy/5 fractions were prescribed as a boost for the primary disease because the tumor response was not good. Mean dose to the neck extensor muscles was 42.3 Gy/40 fractions.

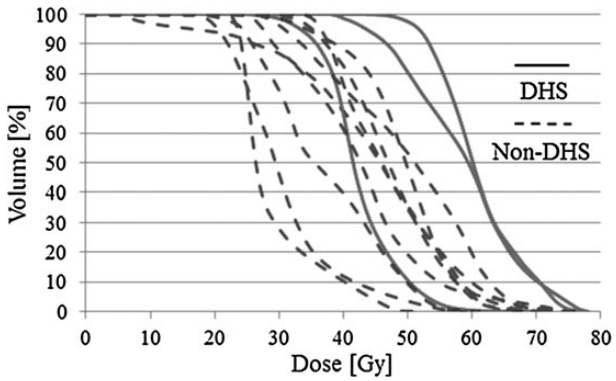

Fig. 1. Dose–volume histogram of the neck extensor muscles of three patients with dropped head syndrome and nine patients without dropped head syndrome.

Patient 3 was a 55-year-old man with nasopharyngeal carcinoma treated with chemoradiotherapy, and he presented with head drop 15 months after completion of radiotherapy. The patient suffered from pain with neck bending. The physical examination, CT and MRI showed no atrophy of the neck extensor muscles. His symptom of DHS was slightly improved till 19 months after the onset of DHS. The mean dose to the neck extensor muscles was 60.9 Gy/35 fractions. A total of three cycles of concurrent chemotherapy of cisplatin (80 mg/m^2 Day 1) were administered. Additionally, two cycles of adjuvant chemotherapy of 5FU (700 mg/m^2 Days 1–5) and cisplatin (70 mg/m^2 Day 1) were administered.

Figure 1 shows the DVHs of the neck extensor muscles of all 12 patients, and Table 2 shows doses analyses for both, right and left neck extensor muscles. Two of the three patients with DHS were exposed to >50 Gy mean dose to the neck extensor muscles. Patients

Table 2. The comparison of dose to the neck extensor muscles between patients with and without dropped head syndrome

Both neck extensor muscles	Patient 1 (DHS +)	Patient 2 (DHS +)	Patient 3 (DHS +)	DHS –	DHS –	DHS –	DHS –	DHS –	DHS –	DHS –	DHS –	DHS –	DHS + mean	DHS – mean	*P* value
Mean dose (Gy)	58.5	42.3	60.9	47.3	29.2	45.7	30.6	49.7	35.5	47.2	42.7	49.6	53.9	41.9	0.061
$V_{10\ Gy}$ (%)	100	100	100	100	100	100	100	100	100	100	97	100	100	99.7	0.58
$V_{20\ Gy}$	100	100	100	100	100	100	96	100	99	100	94	100	100	98.8	0.37
$V_{30\ Gy}$	100	99	100	100	28	88	46	99	74	100	87	96	99.7	79.8	0.22
$V_{40\ Gy}$	99	66	100	83	10	68	12	88	40	77	61	76	88.3	57.2	0.12
$V_{50\ Gy}$	80	11	98	35	0	35	4	48	9	36	19	53	63.0	26.6	0.068
$V_{60\ Gy}$	47	0	51	5	0	10	0	4	0	6	6	20	32.7	5.7	0.015*
$V_{70\ Gy}$	10	0	11	0	0	1	0	0	0	0	2	1	7.0	0.4	0.0056*
Rt neck extensor muscles															
Mean dose (Gy)	60.2	42.2	60.3	48.0	27.9	44.7	25.6	52.7	37.1	46.1	41.3	46.8	54.2	41.1	0.065
$V_{10\ Gy}$ (%)	100	100	100	100	100	100	100	100	100	100	98	100	100	99.8	0.58
$V_{20\ Gy}$	100	100	100	100	100	100	93	100	99	100	95	100	100	98.6	0.38
$V_{30\ Gy}$	100	98	100	100	18	86	16	100	80	100	83	96	99.3	75.4	0.26
$V_{40\ Gy}$	100	65	100	83	6	64	0	99	43	75	56	70	88.3	55.1	0.14
$V_{50\ Gy}$	87	11	96	40	0	33	0	67	13	31	12	43	64.7	26.6	0.075
$V_{60\ Gy}$	53	1	47	6	0	9	0	9	0	2	0	8	33.7	3.8	0.0070*
$V_{70\ Gy}$	13	0	12	0	0	1	0	0	0	0	0	0	8.3	0.1	0.0035*
Lt neck extensor muscles															
Mean dose (Gy)	57.3	42.4	61.4	46.5	30.6	46.6	35.1	47.3	33.9	48.2	44.1	52.4	53.7	42.7	0.070
$V_{10\ Gy}$ (%)	100	100	100	100	100	100	100	100	100	100	97	100	100	99.7	0.58
$V_{20\ Gy}$	100	100	100	100	100	100	100	100	99	100	94	100	100	99.2	0.52
$V_{30\ Gy}$	100	99	100	100	39	90	73	98	69	100	91	97	99.7	84.1	0.23
$V_{40\ Gy}$	97	68	100	83	15	72	23	77	36	79	68	81	88.3	59.3	0.11
$V_{50\ Gy}$	77	10	99	30	0	37	7	28	6	40	27	64	62.0	26.6	0.081
$V_{60\ Gy}$	46	0	55	4	0	11	0	0	0	11	12	31	33.7	7.7	0.035*
$V_{70\ Gy}$	6	0	11	0	0	0	0	0	0	0	4	2	5.7	0.7	0.022*

*$P < 0.05$; DHS = dropped head syndrome.

Table 3. Previous reported cases of dropped head syndrome

No.	Age	Sex	Disease	Stage	Treatment	Radiotherapy	Chemotherapy	Latent period	Muscle atrophy	Symptom improvement
1 [6]	51	M	Hodgkin's Lymphoma		Mantle field irradiation			2 years	+	
2 [6]	56	M	Hodgkin's Lymphoma		Whole body radiation for initial treatment/Radiation therapy to the low back for recurrent disease			15 years	+	
3 [6]	53	F	Hodgkin's Lymphoma		Mantle field irradiation and groin radiation therapy		MOPP	26 years	+	
4 [7]	55		Hypopharyngeal carcinoma	T3N3M0	Total laryngectomy, right modified radical neck dissection and radiotherapy	66 Gy/33 fractions		2 months	+	No
5 [7]	62		Oropharyngeal carcinoma	T1N2cM0	Laser resection, NAC and CRT/ salvage neck dissection	68 Gy/34 fractions	Taxotere, CDDP, 5FU/CDDP	6 months	+	No
6 [7]	52	M	Oral cavity carcinoma	T4aN2cM0	Partial glossectomy, bilateral neck dissection and CRT	66 Gy/33 fractions	CDDP	3 months	+	No
7 [7]	63		Oropharyngeal carcinoma	T4N2cM0	NAC (TPF) and CRT	68 Gy/34 fractions	TPF/CDDP	4 months	+	
8 [7]	51	F	Oropharyngeal carcinoma	T4N2bM0	NAC (TPF) and CRT	68 Gy/34 fractions	TPF/CDDP	5 months	+	
9 [8]	53	F	Laryngeal carcinoma	T3N2M0	CRT and bilateral neck dissection	75.8 Gy	CDDP	Immediately after surgery	+	No

NAC = neoadjuvant chemotherapy; CRT = chemoradiotherapy; TPF = docetaxel, cisplatin and 5-FU.

without DHS were exposed to <50 Gy mean dose to the neck extensor muscles. One patient with DHS was irradiated by only 42.3 Gy mean dose to the neck extensor muscles. The dose to the right and left neck extensor muscles was not different in the patients with DHS. The comparison of the dose–volume histogram analysis revealed $V_{60\ Gy}$ and $V_{70\ Gy}$ were significantly greater in the patients with DHS compared with in those without DHS. The mean value of $V_{60\ Gy}$ and $V_{70\ Gy}$ was 32.7 and 7.0% in the patients with DHS, and 5.7 and 0.4% in the patients without DHS. The onset time was 5 months, 6 months and 15 months after radiotherapy, and the latency period did not seem to be related to dose to the neck extensor muscles.

DISCUSSION

Three patients with early-onset DHS are described in this report. The mechanism of this syndrome remains unclear. Previous reported cases of DHS are summarized in Table 3. Cases 1–3 in Table 3 (reported by Rowin *et al.*) presented with DHS many years after radiotherapy, and all three cases showed muscle atrophy [6]. Patients with DHS in our study differed from those of Rowin *et al.*'s report in that the onset was considerably earlier, the neck extensor muscles did not show atrophy, and the symptoms improved slightly. We consider that the early-onset DHS differs from late-onset DHS. Recently, early-onset DHS has been reported (Case 4–9 in Table 3) [7, 8]. In contrast to the findings of our study, neck extensor muscle atrophy was observed in the reported cases of early-onset DHS. The causes of this difference remain unknown. Two of the three patients with DHS were exposed to >50 Gy to the neck extensor muscles, whereas the neck extensor muscles in all nine patients without DHS were exposed to <50 Gy. Our hospital used 3D conformal radiotherapy (3DCRT) for head and neck carcinomas until February 2006. From March 2006, IMRT has been employed. IMRT has various advantages in head and neck radiotherapy for protecting the salivary gland, spinal cord, brain stem, brain, bone, thyroid, constrictor muscles, optic nerve and chiasma, and internal ear. However, in protecting these organs from higher doses than the tolerances, hot spot areas can appear in other regions. Hot spot appeared to the neck extensor muscles in patients with DHS. Because of spinal cord sparing and posterior neck boost irradiation using electron beams in 3DCRT, the neck extensor muscles were exposed to between 40–46 Gy, and there were no early-onset DHS patients seen in our hospital. From these results, we consider that the radiotherapy dose is associated with this early-onset DHS; therefore, we propose a dose constraint to the neck extensor muscles of <46–50 Gy. Long-term follow-up and additional cases are needed in order to elucidate the cause and treatment of this early-onset DHS.

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