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. 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).
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 SFU (700 mg/m² Days 1–4) and cisplatin (70 mg/m² 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.

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/m² Day 1) were administered. Additionally, two cycles of adjuvant chemotherapy of SFU (700 mg/m² Days 1–5) and cisplatin (70 mg/m² Day 1) were administered.

Figure 1 shows the DVHs of the neck extensor muscles of three patients with dropped head syndrome and nine patients 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 + 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   |
| V10 Gy (%)               | 100               | 100               | 100               | 100   | 100   | 100   | 100   | 100   | 99    | 99    | 99    | 99    | 99.7       | 99.7       | 0.58    |
| V20 Gy                   | 100               | 100               | 100               | 100   | 100   | 96    | 100   | 99    | 99    | 100   | 94    | 100   | 98.8       | 99.8       | 0.37    |
| V30 Gy                   | 100               | 99                | 100               | 100   | 28    | 88    | 46    | 99    | 74    | 100   | 87    | 96    | 99.7       | 79.8       | 0.22    |
| V40 Gy                   | 99                | 66                | 100               | 83    | 10    | 68    | 12    | 88    | 77    | 61    | 76    | 88.3  | 57.2       | 0.12       |         |
| V50 Gy                   | 80                | 11                | 98                | 35    | 0     | 35    | 4     | 48    | 9     | 36    | 19    | 53    | 63.0       | 26.6       | 0.068   |
| V60 Gy                   | 47                | 0                 | 51                | 5     | 0     | 10    | 0     | 4     | 6     | 6     | 20    | 32.7  | 5.7        | 0.015*     |         |
| V70 Gy                   | 10                | 0                 | 11                | 0     | 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   |
| V10 Gy (%)               | 100               | 100               | 100               | 100   | 100   | 100   | 100   | 100   | 100   | 98    | 100   | 100   | 99.8       | 98.6       | 0.38    |
| V20 Gy                   | 100               | 100               | 100               | 100   | 100   | 93    | 100   | 99    | 100   | 95    | 100   | 100   | 98.6       | 75.4       | 0.26    |
| V30 Gy                   | 100               | 98                | 100               | 100   | 18    | 86    | 16    | 100   | 80    | 100   | 83    | 96    | 99.3       | 75.4       | 0.14    |
| V40 Gy                   | 100               | 67                | 100               | 83    | 6     | 64    | 0     | 99    | 43    | 75    | 56    | 70    | 88.3       | 55.1       | 0.075   |
| V50 Gy                   | 87                | 11                | 96                | 40    | 0     | 33    | 0     | 67    | 13    | 31    | 12    | 43    | 64.7       | 26.6       | 0.075   |
| V60 Gy                   | 53                | 1                 | 47                | 6     | 0     | 9     | 0     | 9     | 0     | 2     | 0     | 8     | 33.7       | 3.8        | 0.0070* |
| V70 Gy                   | 13                | 0                 | 12                | 0     | 0     | 1     | 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   |
| V10 Gy (%)               | 100               | 100               | 100               | 100   | 100   | 100   | 100   | 100   | 100   | 100   | 97    | 100   | 99.7       | 99.7       | 0.58    |
| V20 Gy                   | 100               | 100               | 100               | 100   | 100   | 100   | 100   | 100   | 100   | 100   | 94    | 100   | 99.2       | 99.2       | 0.52    |
| V30 Gy                   | 100               | 99                | 100               | 100   | 39    | 90    | 73    | 98    | 69    | 100   | 91    | 97    | 99.7       | 84.1       | 0.23    |
| V40 Gy                   | 97                | 68                | 100               | 83    | 15    | 72    | 23    | 77    | 36    | 79    | 68    | 81    | 88.3       | 59.3       | 0.11    |
| V50 Gy                   | 77                | 10                | 99                | 30    | 0     | 37    | 7     | 28    | 6     | 40    | 27    | 64    | 62.0       | 26.6       | 0.081   |
| V60 Gy                   | 46                | 0                 | 55                | 4     | 0     | 11    | 0     | 0     | 1     | 11    | 12    | 31    | 33.7       | 7.7        | 0.035*  |
| V70 Gy                   | 6                 | 0                 | 11                | 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   | 61  | M   | Hodgkin’s Lymphoma   |                  | Mantle field irradiation                                                  |                |                             | 2 years       | +               | +                    |
| 2   | 56  | M   | Hodgkin’s Lymphoma   |                  | Whole body radiation for initial treatment/Radiation therapy to the low back for recurrent disease |                |                             | 15 years      | +               | +                    |
| 3   | 53  | F   | Hodgkin’s Lymphoma   |                  | Mantle field irradiation and groin radiation therapy                      |                | MOPP                        | 26 years      | +               | +                    |
| 4   | 55  | M   | Hypopharyngeal carcinoma | T3N3M0           | Total laryngectomy, right modified radical neck dissection and radiotherapy | 66 Gy/33 fractions |                             | 2 months      | +               | No                   |
| 5   | 62  | M   | Oropharyngeal carcinoma | T1N2cM0          | Laser resection, NAC and CRT/salvage neck dissection                      | 68 Gy/34 fractions | Taxotere, CDDP, SFU/CDDP  | 6 months      | +               | No                   |
| 6   | 52  | M   | Oral cavity carcinoma | T4aN2cM0         | Partial glossectomy, bilateral neck dissection and CRT                     | 66 Gy/33 fractions | CDDP                        | 3 months      | +               | No                   |
| 7   | 63  | M   | Oropharyngeal carcinoma | T4N2cM0          | NAC (TPF) and CRT                                                         | 68 Gy/34 fractions | TPF/CDDP                    | 4 months      | +               | +                    |
| 8   | 51  | F   | Oropharyngeal carcinoma | T4N2bM0          | NAC (TPF) and CRT                                                         | 68 Gy/34 fractions | TPF/CDDP                    | 5 months      | +               | +                    |
| 9   | 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 $V_{60\text{ Gy}}$ and $V_{70\text{ Gy}}$ were significantly greater in the patients with DHS compared with those without DHS. The mean value of $V_{60\text{ Gy}}$ and $V_{70\text{ Gy}}$ 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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