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case report

Neck extensor muscle weakness (Dropped head syndrome) following radiotherapy

Sumita Bhatia, Robert C. Miller, Daniel L. Lachance

Department of Radiation Oncology (S.B., R.C.M) and Department of Neurology (D.L.L.), Mayo Clinic, Rochester, Minnesota, 55905, USA

Background. *Dropped head syndrome is an unusual condition in which the head cannot be held upright in its normal anatomic position secondary to pronounced, isolated, neck extensor muscle weakness.*
Case report. *A case of dropped head syndrome in a female with a history of radiotherapy for Hodgkin's lymphoma and a clinical history consistent with multiple sclerosis is presented, and potential etiologies are discussed.*
Conclusions. *Muscular atrophy and lower motor neuron injury secondary to isolated anterior horn cell injury from radiotherapy emerge as the most likely etiology.*

Key words: Hodgkin disease - radiotherapy; muscular athrophy; muscle weakness; head

Introduction

Dropped head syndrome, a result of neck extensor weakness, is a rare but striking clinical entity. Patients with this condition experience significant neck muscle weakness that leads to an inability to elevate the head from the chest. Our report presents a case of a woman with a clinical history of probable multiple sclerosis (MS) who developed dropped head syndrome after sequential courses of thoracic and cervical spine irradiation ten years apart.

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Correspondence to: Assist. Prof. Robert C. Miller, MD, Division of Radiation Oncology, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, USA; Phone: +1 507 284-2949; Fax: +1 (507) 284-0079.

Case report

In 1972 a 46 year old female presented with mild, intermittent symptoms of diploplia, dysarthria, fatigue, ataxia, and incoordination and was subsequently diagnosed with probable multiple sclerosis on clinical grounds by an experienced neurologist at our institution. She had mild neurological deficits from approximately 1972 to 1995, corresponding to an Eastern Cooperative Oncology Group/Zubrod performance status of 1, with minimal relapses and no history to suggest transformation to secondary progressive MS. Her past medical history was otherwise unremarkable, although she had received four fractions of radiation therapy to the left wrist for a possible fracture of the pisiform bone in the 1940's.

In 1975, the patient presented with in-

guinal adenopathy and a biopsy revealed mixed cellularity Hodgkin's lymphoma (MCHL). Her clinical stage was IIA, with involvement of inguinal and external iliac adenopathy. She received treatment to the pelvis and para-aortic lymph nodes with radiotherapy using an "inverted Y-technique." Approximately one year later, a chest x-ray revealed right hilar adenopathy. Salvage radiotherapy was instituted. She was treated with radiotherapy alone to a modified mantle radiotherapy field that also included the entire volume of both lungs to a dose of approximately 18 Gy followed by treatment to a traditional mantle field to a total central axis dose of 33 Gy. The dose delivered to the cervical spinal cord from the C3 to C7 vertebral bodies was approximately 31.1 Gy in 16 fractions.

The patient developed a pathologically confirmed recurrence of MCHL ten years later, in 1986, in the right parotid gland. Treatment was once more in the form of radiotherapy alone, to dose of 36 to 44 Gy. Opposed lateral 6 MV photon beams were used to treat a field encompassing the neck and Waldeyer's Ring, with 9 MeV electron beams being employed over the spinal cord to limit the maximum spinal cord dose in the cervical region to 9 Gy in 20 fractions. Assuming no unintended overlap of the matched radiotherapy fields, the total cervical spinal cord dose for all radiotherapy was approximately 41 Gy. She received no other therapy.

There was no evidence of MS exacerbation or any other change in neurological function during or immediately after either course of radiotherapy. In 1995, the patient developed progressive neck extensor weakness resulting in an inability to hold her head upright. A detailed exam by her neurologist demonstrated new symmetrical, isolated neck extensor weakness with accompanying muscle atrophy. The neurological exam otherwise showed no changes in her chronic deficits consisting of a mild mixed spastic ataxic gait and mild dysarthria, which were presumed secondary to MS. A provisional diagnosis of "dropped head" or "floppy neck" syndrome was made. At presentation, the neck weakness was mild, but became progressively more severe, resulting in an inability to hold her head upright without assistance over the next year. A Tensilon test was negative for myasthenia gravis. She never developed evidence of myelopathy over ten years of observation. However, over the last few years she has developed progressive dysphagia seemingly related to a combination of her baseline deficits, the severely flexed position of her head, and progressive bulbar weakness, eventually requiring initiation of gastrostomy tube feedings. We wondered if perhaps this weakness was in part related to the same process affecting her cervical segments given the likely exposure of her brainstem to radiotherapy when the localized parotid recurrence was treated. Unfortunately, the patient never had an EMG (electromyography) or magnetic resonance imaging (MRI) of her spinal axis to better define her condition. However, clinically, she has not developed signs of more widespread motor neuron disease, paraneoplastic syndrome, or more widespread central nervous system demyelination.

The patient currently remains alive, free of recurrence of Hodgkin's lymphoma (HL), but debilitated by age, multiple medical comorbidities, and dropped head syndrome. Aggressive interventions are being avoided and testing declined. Her neck extensor weakness has been managed with a soft cervical collar.

Discussion

Floppy head syndrome, also commonly referred to as "dropped head syndrome", is the result of isolated weakness of the neck extensor muscles, without evidence for a more widespread neuromuscular disorder. This syndrome is characterized by an inability of

patients to elevate the chin from the chest, resulting in difficulty swallowing, speaking and breathing. Differential diagnosis for neck extensor muscle weakness includes myasthenia gravis, a variety of primary myopathies, amyotrophic lateral sclerosis, hypothyroidism, and disorders of the spine.[1-3] It has been rarely been described as a late effect of external beam radiotherapy treatment, primarily following treatment of Hodgkin's lymphoma.[4]

In the current case, the etiological considerations are influenced by the occurence of multiple courses of radiotherapy, and a preexisting neurological disorder which on the basis of history and examination in the pre MRI era was thought to be consistent with MS. Diagnostic considerations include 1) chronic progressive radiation myelopathy, 2) progression of the underlying chronic neurological illness, 3) muscle atrophy secondary to radiotherapy, 4) selective cervical segment anterior horn cell injury specifically related to radiotherapy, or 5) neuromuscular disease unrelated to MS or radiotherapy but with predominant involvement of neck extensor muscles.

This patient did not evolve the typical clinical findings of chronic, progressive, transverse radiation myelopathy. Reagen *et al.* described four manifestations of radiation induced myelopathy in 1969.[5] The first syndrome is that of a transient myelopathy, mostly manifesting Lhermitte's symptom and other sensory disturbances. The second syndrome manifests with rapidly evolving paraplegia or quadraplegia as a result of spinal cord infarction. The third syndrome of radiation myelopathy involves selective damage to anterior horn cells, resulting in limited distribution lower motor neuron disease. The fourth form manifests as a chronic progressive myelopathy. Typical symptoms of chronic progressive radiation myelopathy include pronounced sensory loss as well as weakness at all levels below the area of injured spinal cord. Patients experience sensory changes, particularly in the lower extremities, hyperreflexia and other symptoms of spasticity, and bowel and bladder dysfunction. In our case, the patient exhibited only isolated neck extensor muscle weakness in the absence of sensory or reflex changes, making it unlikely that cord infarction or chronic progressive myelopathy were the etiology of her neurological dysfunction.

A second explanation for the patient's dropped head syndrome would be progression of her previously noted neurological illness, provisionally MS, as offered by an experienced Mayo Clinic neurologist before the era of MRI. An additional consideration in this regard would be the effect of irradiation on the spinal cord in a patient with MS. Although an increased risk of neurotoxicity in MS patients receiving spinal cord radiotherapy has not been reported in the medical literature, anecdotal cases of dramatic toxicity after brain irradiation have been published.[6] Though demyelination in the spinal cord can be associated with significant lower motor neuron dysfunction in the segments affected, additional signs of myelopathy are almost always apparent. It is noteworthy that this patient never developed any additional clinical evidence for more widespread central nervous system demyelination, including other signs of progressive spinal cord dysfunction. Whether or not the presence of an underlying demyelinating disorder played any role in the appearance of dropped head syndrome in this patient could not be determined.

Gradual atrophy and lack of development of bone and muscle in children and adolescents following radiotherapy has been well documented.[7] Adult survivors of HL also report neck and shoulder symptoms, although the effects of irradiation of adult muscles and bones shows markedly less effect than is typically seen in children whose musculoskeletal systems are still not fully matured.[8] Portlock

et al. have reported a case of dropped head syndrome following Mantle irradiation for HL in which muscle biopsies confirmed the presence of non-inflammatory, nemaline myopathy within the radiation treated area and its absence outside the treated region. Nemaline myopathy unrelated to radiotherapy has also been associated with dropped head syndrome.[9]

Though an isolated neck extensor myopathy due to radiotherapy cannot be excluded, we feel that the most likely explanation for this patient's neck extensor weakness is lower motor neuron dysfunction secondary to radiation toxicity in anterior horn cells of the cervical spinal cord. Sporadic case reports, beginning in 1948, have appeared in the medical literature describing a clinical picture of "isolated motor symptoms, amyotrophy, paresis, and fasciculations" resulting from radiation injury to anterior horn cells of the spinal and/or the most proximal segment of peripheral nerves.[10] The majority of cases have followed treatment of testicular neoplasms, resulting in lumbar lower motor neuron (LMN) disease, but some reports have described cervical LMN injury after irradiation of the cervical spine.[11] Esik has provided a tabular review of 47 published cases of this syndrome and drawn parallels between this form of radiation injury and LMN injury following viral infections. Although agreement does not exist in the medical literature regarding the underlying mechanism of injury, LMN disease typically follows radiotherapy at doses lower than the typical threshold for chronic progressive radiation myelopathy, 45 Gy, and has been reported occurring in a number of cases below a dose of 30 Gy.[12]

Dropped head syndrome can be a potentially debilitating disease, resulting in dysphagia, dyspnea, and traction injury of the spinal cord in severe cases, especially in an older individual with advanced cervical spondylosis. In evaluating patients with newly diagnosed, isolated neck extensor weakness, potentially treatable neuromuscular disorders should be first considered and excluded. In the current case, differentiation between the two most probable etiologies, a direct myopathic radiation injury versus muscle weakness secondary to LMN from anterior horn cell injury, was problematic as the patient declined an aggressive investigative approach. Cervical MRI, EMG, muscle biopsy and laboratory investigation might have provided a more definitive diagnosis.

In patients with neck extensor weakness, after elimination of potentially treatable disorders, care is primarily supportive. A collar or brace should be considered to provide support for the head in a more anatomically normal position to facilitate activities of daily living and to help prevent contractures of the neck in a fixed flexed posture. Investigational therapies for dropped head syndrome with immunoglobulin and surgery have been reported in case form.[13,14]

Isolated neck extensor weakness appears to be a rare complication of radiotherapy. This case highlights the selective vulnerability of muscle, motor neurons, or both to radiation, and the need to consider the potential relevance of concurrent neurological or neuromuscular disease in the manifestation of this disabling condition.

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