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Mantle Field Radiation for Hodgkin's Lymphoma: An Effective Treatment, But at What Cost?

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Abstract

This retrospective case study investigates the clinical presentation of a 53-year-old female who underwent mantle field radiotherapy roughly 26 years ago. This patient presents with diffuse muscle atrophy and weakness in the cervical musculature, as well as sensory deficits in the upper extremities. We sought to compare our patient's symptoms with other patients who had been formally diagnosed with Dropped Head Syndrome (DHS) by reviewing the existing literature. We found that the clinical presentation under investigation was consistent with other patients who had received radiotherapy for Hodgkins's disease and were then diagnosed with DHS. Electromyography (EMG), nerve conduction studies, and a cervical MRI were unable to identify a separate neurological cause for the symptoms, but the MRI did confirm the presence of diffuse muscle atrophy in the cervical musculature. After reviewing the existing literature and imaging results, we compared our patient's symptoms to those that define DHS, and both the time of onset, presenting symptoms, and progressing course are consistent with a diagnosis of Dropped Head Syndrome.

Keywords

Mantle Field Radiotherapy, Radiation Injury, Dropped Head Syndrome, Cervical Spine Weakness, Cervical Extensor Muscle Weakness

1. Introduction

It has been established in the literature that Dropped Head Syndrome (DHS) is a condition that causes considerable weakness in the extensor musculature of the

cervical spine [1]. The condition often manifests as neck pain to start but gradually develops into crippling instability of the musculature supporting the head, forcing those living with it to either manually support their head with their hands or employ a cervical soft collar for generalized neck support. Our patient's condition is likely secondary to mantle field radiotherapy performed 26 years ago, which adhered to the prevailing treatment protocol for Hodgkin's Disease (HD) at that point in time.

2. Case Study

While traveling home from a wedding in August of 1997 (26 years of age), our patient began to realize pain in her left shoulder. Upon probing the area, our patient found a lump situated under her left collarbone. After repeated visits to her primary physician's office, she was formally diagnosed with Hodgkin's Lymphoma in November of 1997 via a liquid biopsy. Three months later, in February of 1998, our patient received a lymphadenectomy and began mantle field radiotherapy treatment targeting cervical, supraclavicular, mediastinal, and axillary lymph nodes. Treatment concluded in the Spring of 1998. Quarterly checkups were conducted over the course of five years to monitor cancerous growth, and the patient remains in remission.

The patient was referred to our clinic for further assessment of her right-sided neck and shoulder instability in December of 2023. She claimed these areas felt "hard and stiff" to the touch and that the pain was moving up into the jaw, causing headaches and a sore throat. In 2015, we treated a 53-year-old male with a highly comparable clinical presentation to the patient actively under study. This middle-aged male presented with significant atrophy and weakness in the extensor musculature of the cervical spine 37 years after receiving mantle field radiotherapy to treat his diagnosed Hodgkin's Disease. His initial symptoms of pain and weakness in the neck and shoulders began roughly 8 years prior to his consultation with us. At the time of his visit to us, his inability to support the weight of his head had progressed to such an extent that he found himself supporting his head with his hands for much of his daily activity [2]. He was ultimately diagnosed with late-onset Dropped Head Syndrome secondary to mantle field radiation. Considering the marked overlap in clinical presentation between the patient under study and this 53-year-old male, we suspect our patient could likewise be suffering from the earlier stages of late-onset Dropped Head Syndrome secondary to radiation therapy.

The patient states that the pain and weakness in her shoulders began in or around 2010. At that time, even "easy things" like lifting a bag of dog food would cause considerable discomfort in her shoulders for months on end. In 2019, she began to realize significant stiffness in the right thoracic section of her back, which ultimately progressed into the cervical issues she's experiencing today. The patient states the pain has been most severe for the past year, and she rates her pain level at 7/10 on VAS. She experiences allodynia in the areas of the mantle field radiation.

She also experiences numbness and tingling in the arms bilaterally and in her left thigh. The patient denies any dysphagia, odynophagia, tinnitus, diplopia, or dysphonia. She finds relief when manually supporting her head to place her cervical spine in either a neutral or slightly extended position or while lying supine.

The patient claims she feels like a "bobblehead" at times and finds herself having to support her head with either her hands or by laying it on her desk at work for relief. She claims she constantly must position her head in "a spot that is comfortable" to temporarily relieve her symptoms and takes several breaks throughout the day to sit in a recliner where she rests her head and neck. She has tried conservative measures such as acupuncture and chiropractic work but has realized only temporary relief in her discomfort from both. Her neck discomfort has progressed to such an extent that even driving a car can become intolerable.

3. Physical Examination

Physical examination revealed a well-developed female with balanced muscle tone in all muscle groups except for the posterior thorax and neck with proportionately small neck girth. Additionally, visual inspection revealed significant muscle atrophy throughout the neck girdle, sternocleidomastoids, cervical spine area, and superior aspect of the pectorals, trapezius, and supraspinatus muscles. The skin was taught to the cervical spine in a somewhat shrink-wrapped fashion.

Strength testing was 4/5 throughout the bilateral upper extremities, with the right upper extremity being weaker than the left. Deep tendon reflexes (DTR) were +2/4 throughout bilateral upper extremities, and Hoffman's reflex was negative bilaterally. The range of motion in the cervical spine was restricted in all planes, but other than this, all major joints exhibited a full range of motion. Spasms in the cervical paraspinal and trapezius muscle groups were more distal than cephalad, and the patient had a visually apparent forward head tilt.

4. Laboratory Investigations

A cervical MRI conducted in 2024 after consultation with a musculoskeletal radiologist showed evidence of generalized atrophy of the cervical musculature grossly. There is mild spondylotic change without chord encroachment at C3-4 and C4-5. There is trace anterolisthesis of C4 upon C5. Otherwise, there's no malalignment, and the cervical spinal cord demonstrates normal caliber and, within the limitations of these images normal signal intensity pattern. The region of the craniocervical junction is unremarkable.

Within the last 6 months, the patient has developed numbness and tingling in the hands, which has become a regular occurrence. We sought the opinion of a board-certified, EMG nerve conduction trained physiatrist physician with our working diagnosis of Dropped Head Syndrome to explore the patient's neck and shoulder pain. This physiatrist performed electromyography (EMG) and nerve conduction studies in December of 2023 to better establish the origin of the patient's symptoms in the hands and wrists. Further discussion with the physiatrist

identified EMG specifically for DHS but it wouldn't have changed the treatment approach, so it wasn't done.

EMG results showed significant prolongation of the right median transcarpal latency, as well as relative prolongation of the right median antidromic sensory latency and left median transcarpal latency to their respective ulnar controls. These findings are consistent with a diagnosis of Carpal Tunnel Syndrome (CTS). However, the study showed no evidence of cervical radiculopathy or contributing neurocompressive lesions that would help account for the patient's continued neck discomfort and weakness. These studies ultimately did not provide a specific diagnosis that matched the patient's symptoms. We then discussed with the physiatrist other options for further diagnosis, which included a muscle biopsy. While muscle biopsy may have been able to show changes in the musculature, it would not alter the treatment options, so the patient deferred.

5. Differential Diagnosis

Considering the patient's history, physical exam, and test results, a diagnosis of late-onset Dropped Head Syndrome was presumed. The symptoms under investigation are likely a consequence of neurological damage and muscular atrophy secondary to mantle field radiotherapy for Hodgkin's Disease 26 years ago.

6. Discussion

Dropped Head Syndrome is a rare, long-term complication of radiotherapy techniques such as mantle field radiation. The symptoms typically emerge 5 - 30 years post-radiation treatment and have a deleterious impact on the patient's quality of life. The condition involves notable weakness and atrophy in the extensor musculature of the neck: cervical, paraspinal, and shoulder girdle muscles [1].

While the exact pathophysiology resulting in Dropped Head Syndrome is unknown, several theories have been proposed based on a small number of cases. Some findings suggest the condition manifests via pure primary neuropathy, others a pure myopathy, and one study points to microvascular toxicity [2]-[7]. A previous study has also posited that radiotherapy could lead to a selective injury in the lower motor neurons of the spinal cord, which would be consistent with the muscle atrophy observed in our patient [4]. It is important to note that the pathology of DHS is not exclusively limited to cervical spinal lesions but rather a combination of decompensation and compensation throughout the entire spine [8].

Mantle field radiotherapy falls under the extended-field radiotherapy (EFRT) classification and was considered the standard treatment for Hodgkin's Disease from the middle of the 20th century up until the 1990s. The mantle field was considered to encapsulate the mastoid process down to the diaphragmatic insertion while extending laterally to both humoral heads [2]. Historically, this treatment regimen called for radiation doses in the 40 - 45 Gy range, but recent findings surrounding post-treatment complications have brought the standard dose down to around 20 Gy [9]. We are unable to verify the dose our patient received at this

time.

Van Leeuwen-Segarceanu, *et al.* report severe atrophy in the sternocleidomastoid muscle in 67% (13/20) of patients who had received 20 fractions of 2 Gy for a total mantle field radiotherapy dose of 40 Gy [10]. Additionally, small motor units consistent with the amount of atrophy observed were present in 71% of the muscles entirely situated within the radiation field, and 20% of the neck muscles showed neuropathic changes, which they presume can be explained by vascular injury leading to nerve damage [9]. Mostly, neuropathic damage was identified via EMG for those muscles situated outside of the radiation field, like the deltoids, suggesting primary affection of the nerve roots and brachial plexus, both of which are situated in the radiation field for a long distance [9].

Over the past three decades, the prevalence of radiation treatment for Hodgkin's Lymphoma, which achieved a 10-year relapse-free survival rate of around 70%, has decreased considerably. The advent of effective chemotherapy regimens in the mid-1980s yielded higher overall survival rates (96.4% among ages birth to 19 years and 89.8% among ages 20 and 64 years) for those diagnosed with the disease and was rid of the long-term toxicities found to be associated with extended field radiotherapy [3] [11]. Gradually, the use of combined modality treatment has become standard in the treatment of HL and has demonstrated a significant decrease in secondary complications via dose reductions in concert with more accurately placed radiation [2].

Our patient does not present any other adverse effects of the radiation therapy beyond the DHS under investigation, but it is worth noting that she did undergo concurrent chemotherapy (ABVD) with the radiation treatment. ABVD is the standard chemotherapy treatment for HL patients and is comprised of four medications: doxorubicin, bleomycin, vinblastine, and dacarbazine. Many of these medications have not been shown to cause secondary neuropathic complications that could help to explain the symptomatology of our patient, aside from vinblastine, which may cause a predominately length-dependent small fiber sensory peripheral neuropathy [12]. Despite this complication resulting from vinblastine, it's unlikely that it plays a major role in the manifestation of DHS because of the homogeneity in EMG findings in case reports both with and without chemotherapy utilization [2].

Currently, therapy options for DHS are limited and lack a standardized protocol. Most therapeutic efforts are focused on supportive care measurements like soft neck collars or posterior spinal arthrodesis surgery in cases that are more severe [9]. Alternative options include physical therapy to strengthen the extensor musculature in the neck [2]. A recent study highlighted a novel rehabilitation program, referred to as the "Short and Intensive Rehabilitation Program" (SHAiR), that shows promise in outcomes for DHS patients. SHAiR incorporates cervical paraspinal muscles exercise, range of motion exercise, cervical and thoracic mobilization, deep cervical flexor muscle exercise, hip lift exercise, anterior pelvic tilt exercise, and walking exercise [13]. It is believed that this could promote the

formation of collateral vessels which contribute to both maintaining muscle strength and integrity and increasing vascularization of the musculature [9]. If further studies support these preliminary findings, this conservative regimen could become the first standardized approach for the treatment of DHS.

7. Conclusion

Dropped Head Syndrome is a rare complication of high-dose mantle field radiation therapy for Hodgkin's Disease that has significant effects on a patient's quality of life. To date, there has been little advancement in the understanding of the pathophysiological mechanisms responsible for the manifestation of the disease, which limits treatment options and their associated efficacy. Our patient offers insight into the clinical manifestations of the condition before it progressed to a completely debilitating state. It is our hope that the symptomatology elaborated on in this study will encourage clinicians to investigate the diagnosis of and treatment for Dropped Head Syndrome secondary to extended field radiotherapy. Specifically, future studies should investigate the specific pathophysiological mechanisms induced by radiotherapy which lead to the condition. From here, more specific treatment regimens can be made that address the etiology, ideally leading to more robust responses among patients.

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Patient Consent for Publication

Obtained.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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