

Clinical Manifestations of Late-onset Dropped Head Syndrome Secondary to Mantle Field Radiotherapy for Hodgkin's Disease

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Introduction

It has been previously described in the literature that dropped Head Syndrome (DHS) is a condition causing significant weakness and instability in the extensor musculature of the cervical spine. This condition often manifests as neck pain associated with a loss in the ability to maintain sufficient paraspinal muscle tone in the neck. This course eventually leaves the patient with a flexed head, and an inability to raise the chin from the neck in the Sagittarius plane. Our patient's condition is likely secondary to mantle field radiotherapy performed 37 years prior using the prevailing treatment protocol for Hodgkin's disease (HD).

Case Study

During a routine sports physical in 1977 (16 years of age) our patient was found to have three enlarged lymph nodes in the neck and axilla. He stated that after lymphoid tissue biopsy the patient was diagnosed pathologically with likely Hodgkin's disease (HD). After exploratory laparotomy and lymph angiogram and concomitant splenectomy, the patient was clinically staged as IIA HD. As the patient's lymphoma remained supradiaphragmatic in its presentation, the treatment plan would include mantle field radiotherapy targeting cervical, supraclavicular, mediastinal and axillary lymph nodes. Radiotherapy consisting of 6 weeks of external beam radiation at fractions of 180 rads began in April of 1978. Treatment concluded in May 1978. Follow up consisted of quarterly checkups for five years and the patient still remains in remission. It is also noted that over the recent years he was diagnosed with testosterone deficiency and was started in a testosterone supplement. He also stated that some years ago he was diagnosed with bilateral gynecomastia after taking Cimetidine therapy and had a subsequent surgical removal and bilateral inferior pectoralis adipose supplementation bilaterally.

The patient was referred to our clinic in 2015 for consultation on the potential benefits of interventional pain management procedures

to the cervical facet joints and/or trigger-points of upper posterior torso, trapezius and cervical para spinal musculature for refractory chronic neck pain. The patient arrived to our clinic with a working diagnosis of cervical degenerative disc disease and foraminal stenosis.

The patient states initially have some initial symptoms of pain and weakness in or around 2007. At that time he began experiencing significant neck pain in absence of trauma as a spectator at a sporting event. The patient is right-handed dominant and described his symptoms as pain and weakness in the neck and shoulders, on the left more so than the right. The pain would often localize to the medial left neck and manifests as an aching pain without a radicular pattern and was not associated with either parenthesis or burning with the exception of numbness and tingling in the hands bilaterally starting at the wrists. The patient rated his pain level at 6/10 on VAS and ranging from 2/10-10/10 on any given day and worse toward the end of the day. He denied any loss of sensation to the neck, shoulders or upper extremities bilaterally. The patient denies any dysphagia, dysphonia, odynophagia, tinnitus or diplopia. He complained of pain with physical activity and onlanfoung relief when manually supporting his head to place his cervical spine in either a neutral or slightly extended position or while lying supine.

In the eight years since this onset of the initial subtle symptoms, our patient has sought relief through numerous modalities including physical therapy, topical analgesics, home-based traction, epidural steroid injections, muscle relaxants, opioids, soft-tissue massage, osteopathic manipulation and neurosurgical consultation. To date the patient has only found mild relief of symptoms with a combination of rest, acupuncture, duloxetine and hydrocodone-acetaminophen.

Physical examination revealed a well-developed and well-nourished male with balanced muscle tone in all muscle groups with the exception of the posterior thorax and neck which is proportionately small neck girth. It was noted that throughout the interview the patient appeared very engaged and inquisitive. He

would frequently place his thumb or fist under his chin as though pondering an idea or thought. He also frequently complained how his shoulder and upper back were stiff as he would raise his right arm, adduct it so his elbow was under his chin and then flex his elbow so his hand could grasp is contra lateral trapezius and hold that position. He would also place his hands in a classical praying position and then place the tips of his fingers under his chin made continuous efforts to support his head. At first the patient simply appeared to be quite animated while speaking, but it became apparent that the patient was compensating for his inability to maintain appropriate neutral cervical posture. Throughout the interview the patient continuously yet fluidly carried out a well orchestrated adjustment in posture with natural but deliberate motions to accommodate his head.

The patient would effortlessly adjust from resting his chin upon his palm or distal 5th digit, to resting his mandible in the antecubital fossa of an upper limb while holding the contralateral shoulder with his hand. He would then often slide or slouch down into his chair so that his head would enter a slightly extended position, allowing for the appearance of natural head carriage. Further visual inspection of the neck and upper torso revealed thickened taught skin and significant muscle wasting throughout the neck girdle, sternocleidomastoids and decreased muscle bulk in the cervical spinal area, superior aspect of the pectorals, trapezius and supraspinatus muscles.

Strength testing of the upper extremities was 4/5 at the trapezius, 5/5 grip, 5/5 flexion and extension of extremities. Deep tendon reflexes (DTR) were +2/4 throughout bilateral upper extremities, pulses were 2+ and sensation to light touch and vibration remained intact. Hoffman's reflex was negative bilaterally. The patient's bilateral hand numbness and tingling were reproducible in a median nerve distribution via a positive Tinel's sign bilaterally.

Prior workups include MRI studies in 2014 and 2006. Both reports showed evidence of bilateral chronic facet joint arthritis and moderate chronic spondylosis at C4-5, C5-6 and C6-7 without progression since the prior study. There was no evidence for fracture or lytic lesions nor was there evidence supporting cord damage or impingement. Disc spaces appear maintained with no indication for disc bulge, and evidence for only borderline foraminal canal compromise, on the right more so than left.

Electromyography (EMG) of the neck and upper extremities was performed in December 2014, after we sought the evaluation of a neurologist with our working diagnosis of dropped head syndrome, to explore the patient's neck and shoulder pain, as well as to further evaluate the patients worsening bilateral paresthesias of the hands. The study was intended to better establish the origin of the patient's symptoms, confirm our working diagnosis of dropped head syndrome and to further determine if the nature of the pain might be a cervical radiculopathy, bilateral carpal tunnel syndrome or peripheral neuropathy.

EMG results showed significant prolongation of median nerve

motor and sensory signals with a trans-carpal latency resulting in a diagnosis of Carpal Tunnel Syndrome (CTS). However the study showed no evidence for cervical radiculopathy or contributing neurocompressive lesions that would account for the patient's continued pain and weakness in the neck and shoulders. Given the patient's history, physical exam, EMG and MRI results, a diagnosis of late-onset Dropped Head Syndrome was made. These symptoms are likely due to neurological damage and resulting muscular atrophy secondary to prior mantle field radiotherapy for Hodgkin's disease.

Discussion

Dropped Head Syndrome is a rare but notable complication of radiotherapy with significant implications for the patient's quality of life. Dropped head syndrome manifests as an isolated neck extensor and shoulder girdle weakness with a late-onset of typically 2-30 years post high-dosage mantle radiation therapy for Hodgkin's disease [1-3]. Mantle radiotherapy is considered to be an extended-field radiotherapy (EFRT) and this was the standard of care from the middle of the 20th century until the mid 1990's [4,3]. "WHEN"??? The mantle field was considered to extend anatomically from the mastoid process to the diaphragmatic insertion, extending laterally to the humeral heads. Historical radiation doses would often range from 40-45 Gy and may have included adjuvant chemotherapy depending on the severity of clinical. One thought regarding the development of Dropped Head Syndrome is related to possible burnout of collateral nerves that grow as a result of damage during Msntle Radiotherapy. The idea is that, similar to post polio syndrome, the newer collateral nerve fibers begin to fatigue leading to progressive weakness staging [3,5,6].

While there is some controversy surrounding the pathophysiology resulting in DHS, much of the discussion suggests radiation toxicity to anterior horn cells of the cervical spine. This process ultimately leads to a late onset of isolated muscle atrophy of the extensor muscles of the neck presenting as slowly progressive pain, weakness and chin-on-chest head drop. Weakness can also be seen in the sternocleidomastoid, supraspinatus infraspinatus, splenius capitis, trapezius and deltoid musculature [7]. Some case reports suggest a pure primary myopathy, others a pure neuropathy, and some suggest a combined myelo-neuro-radiculopathy, and one study suggests possible microvascular toxicity, all within the radiation field [3,5,7,8].

Advances in HD radiotherapy has led to a reduction in radiation doses over the past quarter century. Technology and better clinical staging has allowed for a more concentrated Involved Field Radiotherapy (IFRT) with dose reductions to 20 Gy [4,6]. This dosage reduction in concert with more accurately placed radiation has led to a significant decrease in secondary cancers, cardiac anomalies and adverse effects widely experienced with high dose radiation.

Our patient demonstrated no adverse effects of the radiation beyond the DHS discussed, and did not receive chemotherapy

as part of his therapy. When questioned about his continuous chin resting the patient claimed to only be able to maintain head carriage independently for 3-5 minutes at a time before fatiguing. The patient claimed that this particular symptom had slowly progressed in severity over the course of the past 8 years to the point where he must hold his head up for a majority of his daily activity.

It became apparent that the patient had been compensating for this deficit for so long that he had become desensitized to the ever-varying postures he employed to maintain head carriage. The subtlety he demonstrated in keeping his chin elevated was such that detection in a social setting or short medical consult would prove to be difficult, and this likely led to the delayed detection of his emerging DHS.

It should also be noted that this particular case appears to be more of an emerging or developing DHS in nature, as the patient is still able to maintain independent head carriage, even if only for a short period of time. The fact that this presentation falls well outside the typical timeline for onset of symptoms and has yet to manifest itself as a full-onset DHS helps to explain the delay in diagnosis.

A literature review demonstrated a singular case-report with a slightly longer onset of radiation induced DHS of 39 years post-irradiation therapy, as reported by Appels and Goekoop in The Netherlands in "WHEN"?? 2009 [9]. This patient had full onset DHS unlike our patient who is still able to partially compensate. Rowin et al report a case of DHS diagnosis 36 years post-mantle field radiotherapy for HD, however this patient also received MOPP (Mustargen, Oncovin, procarbazine and prednisone) chemotherapy as well as groin radiotherapy [1]. Our literature search did not reveal any case reports or instances of a diagnosis of late-onset DHS secondary to mantle field irradiation in the United States with a later onset than in our patient.

While DHS via high-dose irradiation was first introduced by Johansson et al. in 1998, there continues to be much discussion as to why it appears to affect patients with a history of Hodgkin's a Disease (HD) in greater numbers [7]. HD mantle therapy often utilized lower radiation doses than would be seen in head and neck cancer prompting some to question if the breadth of the radiation field has a higher correlation with DHS than dosage.

Hashimoto, et al. report a rare case of DHS associated with nasopharyngeal carcinoma chemo radiotherapy, noting that their radiotherapy field encompassed the entire neck, somewhat unique as neck cancer therapy often spares the posterior neck [7]. This group also calls into question, as many have, the potential confounding factor of chemotherapy, whether adjuvant or in combination, has on the potential for DHS development. While it is noted that chemotherapy drugs can induce peripheral neuropathies and eventual muscle weakness, but these symptoms more often occur in a stocking glove pattern bilaterally in the hands and feet [10]. The lack of confirmatory EMG findings in many DHS case reports, regardless of chemotherapy utilization; suggest that this

may be a minor factor in the manifestation of DHS.

Potential contributory factors in our case include the aforementioned bilateral CTS which were confirmed independently by a neurologist but do not appear to be a confounding factor in the development of his DHS. It should also be noted that the patient has had bilateral partial mastectomies related to gynecomastia, possibly secondary to cimetidine usage.

Therapy options for DHS are limited at this point in time, and include continuous use of a cervical soft collar. Our patient has had promising relief of pain and fatigue using a soft collar. In fact, the majority of pain symptoms appear to be myofascial in nature. When he uses his neck collar or supports his head his pain symptoms resolve completely. Compliance is limited however due to a reduced quality of life, and emotional distress in social settings. Additional options include physical therapy to strengthen effected paraspinal musculature. Our patient continues physical therapy and has found it efficacious, reporting reduced fatigue as well as increased strength and head support. Our patient consulted neurosurgery for potential cervical fusion but at this time has elected to treat only with physical therapy in combination and a cervical soft collar. Our patient has also declined treatment options for his bilateral CTS [11-13].

Conclusion

Dropped Head Syndrome is a rare but significant complication of high-dose mantle field radiation therapy for Hodgkin's disease leading to neck extensor weakness. DHS diagnosis is often delayed as symptom onset occurs, in many cases, 10-20 years post-radiotherapy. Our patient presents 37 years post radiotherapy representing a potential new extreme in diagnosis delay. Additionally our patient provides us with a unique perspective into the clinical manifestations of the final stages of paraspinal neck extensor weakness, ultimately leading to dropped head syndrome.

Several maneuvers like flushing with saline, body positioning and repeat advancement has been described to reposition a malpositioned PICC [2,3]. As every malpositioned PICC should be repositioned, we tried to reposition the PICC intraoperatively but could not succeed after several attempts using different techniques [2]. The failure to correct the malposition in our case can probably be due to the higher degree of looping of the PICC. With this report we want to emphasize upon the fact that looping of PICC in AV can occur even after applying the traditionally described methods. Failure to correct the malposition of PICC should alert the clinician to a probability of higher degree of loop formation and whenever situation permits one should remove the malpositioned PICC in those cases.

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