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Case Report

Multiple Myeloma Muscle Infiltration with Atypical Presentation: Lower Extremity Treatment with Three Arc VMAT Radiotherapy Plans

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Abstract

Extramedullary myeloma can occur in a variety of organs; however, muscle involvement is rarely reported. We present a case of multiple myeloma patient who progressed with extramedullary lower extremity muscle involvement while receiving chemotherapy. Pathologic plasmacytoma was confirmed by involvement biopsy. Palliative radiotherapy was planned for the patient who complained of severe pain, weakness and edema in the leg. Due to the very large radiotherapy field, a special three-arc VMAT plan was made for the patient.

Introduction

Multiple myeloma (MM) is a type of cancer that affects plasma cells, which are found in bone marrow and produce antibodies to fight infections. One potential complication of MM is muscle infiltration, which occurs when cancerous plasma cells invade and replace healthy muscle tissue (1). Muscle infiltration can be caused by the spread of MM to nearby tissues or by the release of harmful proteins from cancerous plasma cells. This infiltration can cause muscle weakness, pain, and other symptoms that can significantly impact a patient's quality of life (2, 3).

Symptoms of MM muscle infiltration may include muscle weakness, pain, and stiffness, as well as fatigue, difficulty breathing, and numbness or tingling in the extremities (1, 4). Diagnosis is typically made through a combination of imaging tests, such as positron emission tomography (PET) scan and a magnetic resonance imaging (MRI) and blood tests that measure levels of certain proteins and antibodies (5, 6). Early detection is crucial for successful treatment of muscle infiltration, as it can cause irreversible damage if left untreated (1).

Treatment options for MM muscle infiltration may include radiotherapy (RT), chemotherapy and stem cell transplant (7). The choice of treatment depends on the extent and severity of muscle infiltration, as well as other factors such as the patient's overall health and age. In some cases, surgery may also be necessary to remove cancerous tissue (8).

Case report

A 69-year-old male patient had been receiving systemic therapy for 1.5 years with the diagnosis of MM. The patient was first referred to our clinic with complaints of eyelid closure, exophthalmos and decreased vision. There was a retroorbital mass in orbital MRI and the diagnosis of plasmacytoma was confirmed by biopsy. Successful RT was applied to the patient's left retroorbital plasmacytoma region. Subsequently, severe pain and swelling developed in the right leg. Although deep vein thrombosis was considered primarily, lower extremity doppler and MRI findings supported MM muscle involvement. Figure 1 A-C shows MRI findings of MM. Muscle biopsy performed from the right cruris muscle location revealed plasma cell neoplasia. Thus, the diagnosis of multiple myeloma muscle involvement was confirmed. According to the patient's radiological, clinical and pathological findings; there were soft tissue lesions (figure 1B) and muscle involvement covering the entire right cruris, starting from the right hemipelvic lymphatics and continuing along the femoral region and cruris, which could not be clearly separated from the adjacent muscle planes (figures 1A and 1C). In addition, there was a global increase in size in the right leg compared to the left leg (figure 1A, 1B, 1C). Orbital MRI shows a soft tissue mass of left retroorbital plasmacytoma (figure 1 D).

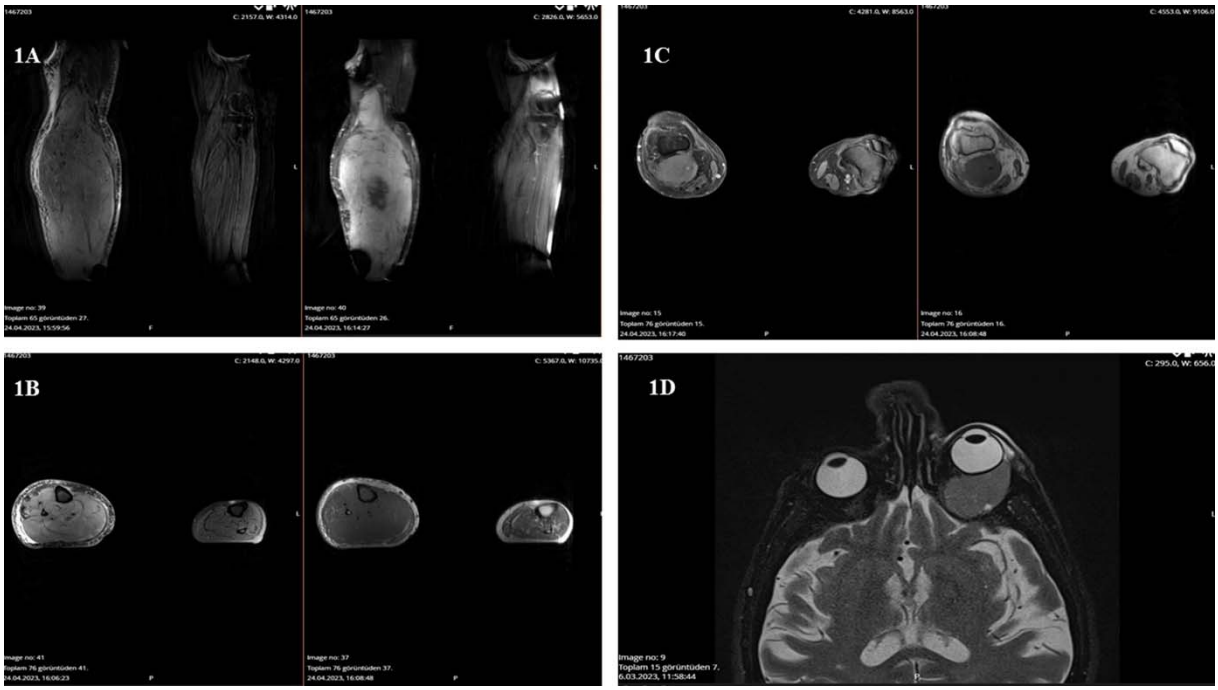

Figure 1. Magnetic resonance images of multiple myeloma involvement of the right lower extremity and left retroorbital region of the patient with atypical presentation. Soft tissue lesions that cannot be clearly separated from the adjacent muscle planes along the femoral region and cruris, and muscle involvement in the entire right cruris are seen (figure A-C). Left retroorbital 22x32x22mm mass in orbital MRI (D).

Radiotherapy Delivery

Palliative RT was planned for the patient. During the simulation of our patient, whose treatment area was approximately 100 cm, three separate centers were considered, considering that the treatment area would fit into a 3-center plan. These centers were determined as the ankle, under the kneecap and pelvis regions. CT imaging was taken in the supine position and with the foot inside, with a slice thickness of 3 mm. The right hemipelvic lymph nodes, inguinofemoral canal, and gross tumor volumes along the femur as the target volume, and the entire right cruris were contoured as the target volume due to muscle and skin involvement (Figure 2).

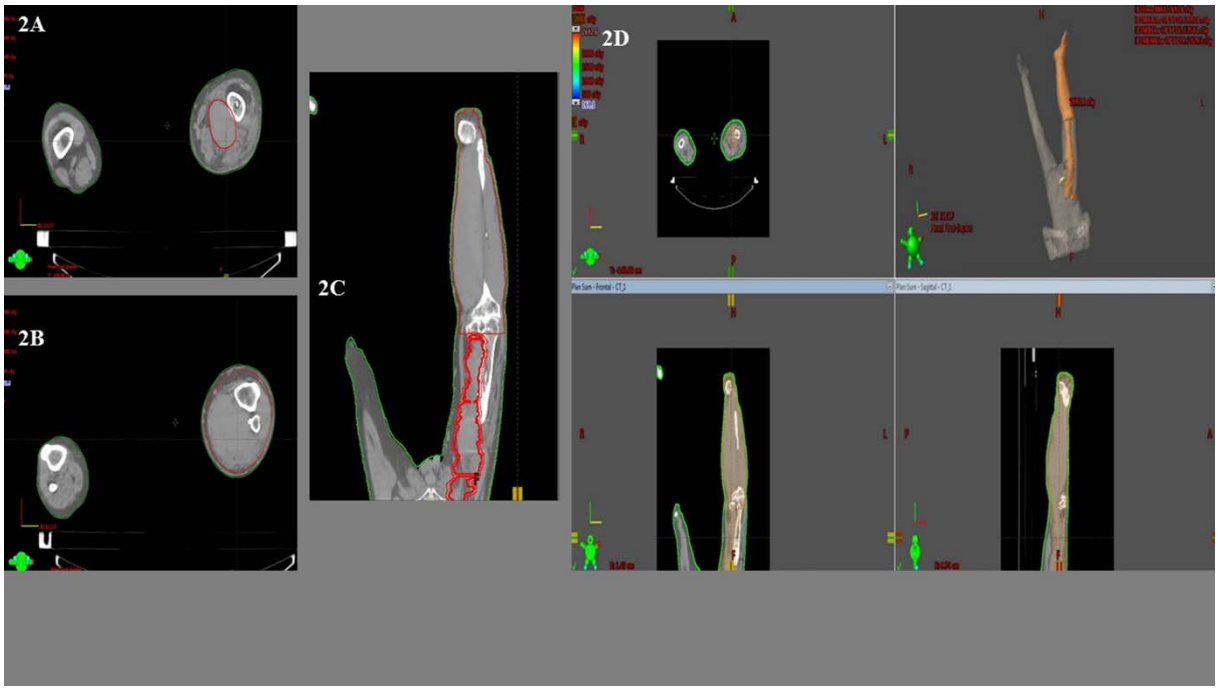

Figure 2. Radiotherapy contouring. Right hemipelvic lymphatics, gross tumor volume contouring from right inguinofemoral to popliteal region (A, C). Radiotherapy target volumes (B, C) involving all right-rule muscles. Axial, coronal, sagittal and 3D reconstructed 3D images of all target volumes (D).

Treatment planning volumetric modulated arc therapy (VMAT) planning was carried out by selecting 3 isocentric and 3 full arc in the Eclips brand 13.6 version planning system (figure 3A-D). In order to prevent the opposite foot from entering the treatment area, this foot was protected by throwing between 210 and 300 sectors. A total of 30 Gy of external RT was given from 300 cGy/fraction daily. Since the cruris area is included in the entire leg RT area, including the skin, a dose of 24 Gy is limited to this area to minimize the risk of future lymphedema. Figure 3 shows images of RT planning.

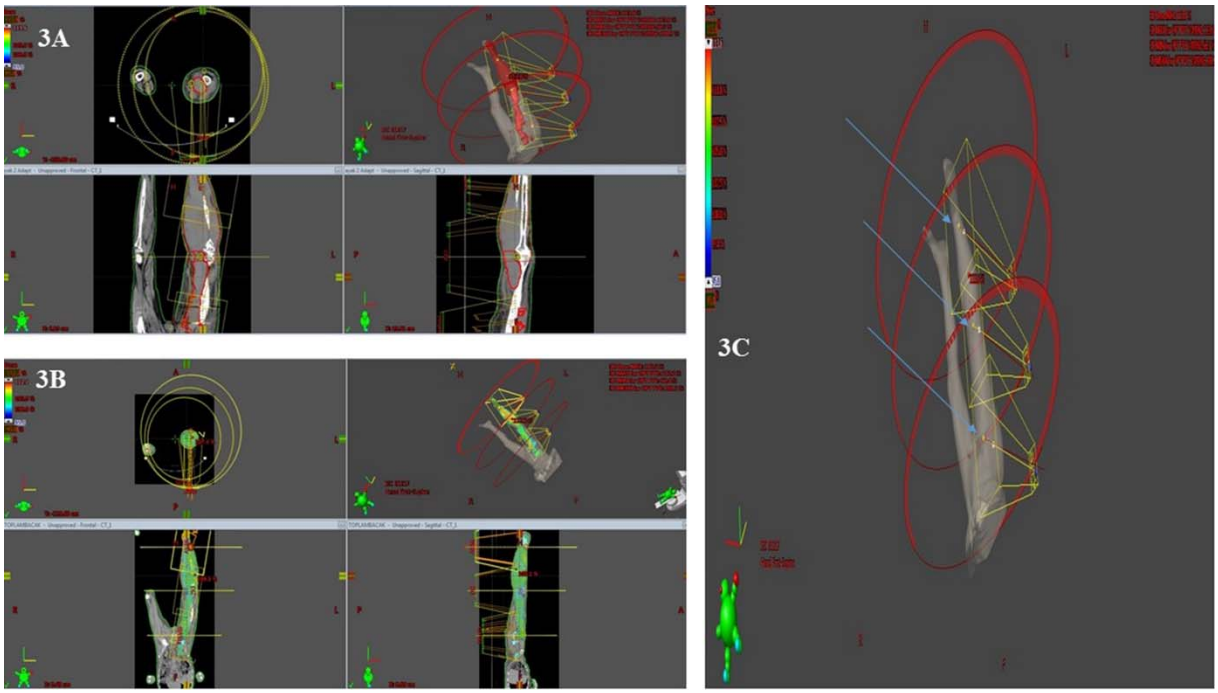

Figure 3. Images of the three-arc VMAT plan of external beam radiotherapy planning. 3D dose distributions of various planes (A-B). Simulation of the treatment area and 3D reconstruction with 3 markers (C) (blue arrows show markers).

During the simulation, a 1mm skin marker radiopaque marker was placed on the patient's skin at these three centers. Radiopaque markers were also contoured; so that the markers were visible in the DRR during set-up as a reference. As a result, these references facilitated field match with the KV field port that was pulled during treatment, providing set up accuracy and ease (figure 3-C and figure 4A-C; arrows).

The treatment of our patient was completed without any problems, and at the end of the treatment, mild regression of the lesions was observed in the physical examination as an early response.

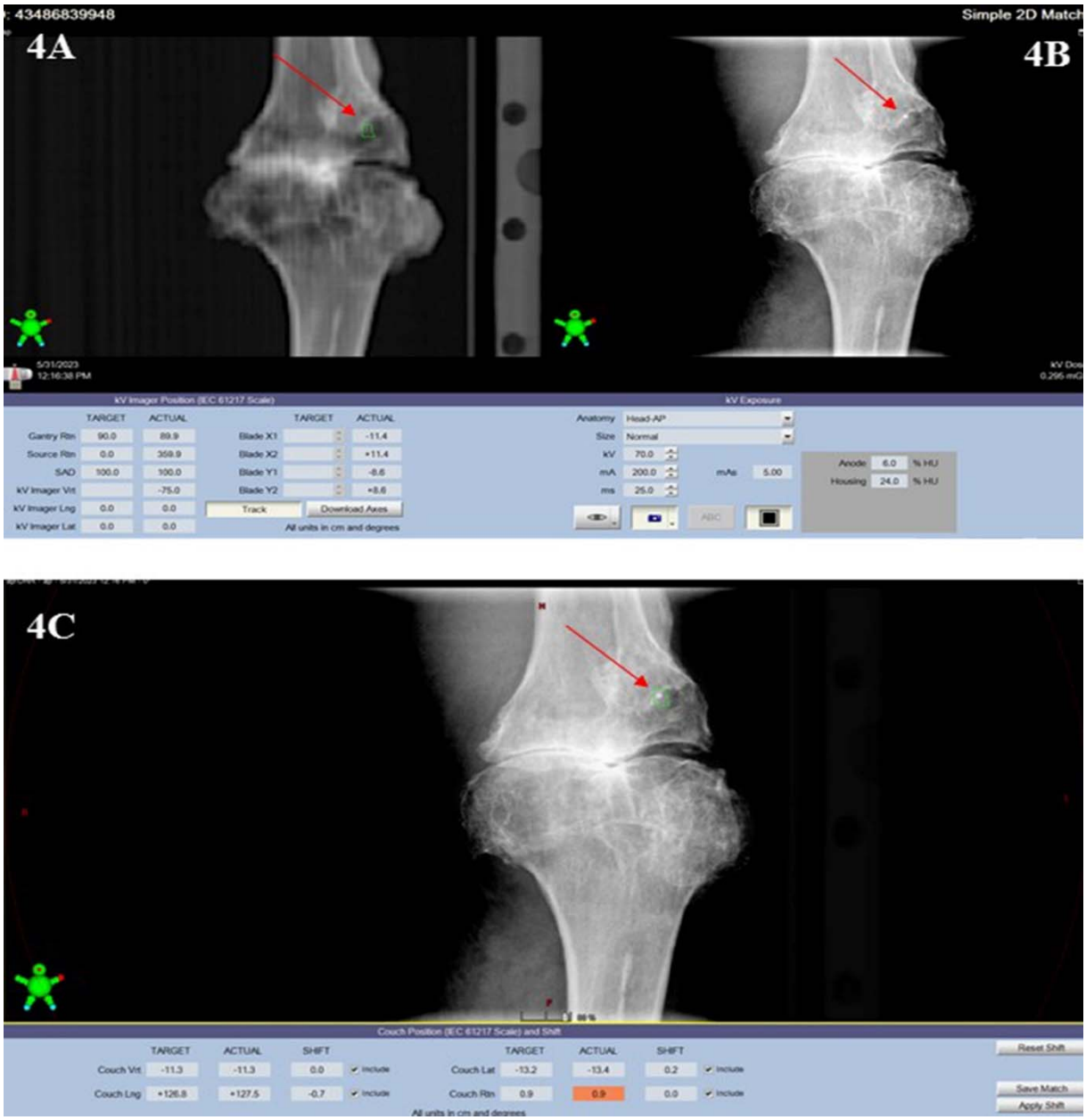

Figure 4. Treatment application, radio-opaque marker appearance providing ease of radiotherapy set up. The radiopaque marker appears as marked (red arrow) on the Digitally Reconstructed Radiograph (DRR) from the treatment planning system (A). The marker (red arrow) on the patient's skin is visible on the KV port taken during set-up before the treatment starts (B). Image (C) where both markers overlap (red arrow) by matching both images.

Discussion

MM muscle infiltration can be treated using a variety of treatment options. One of the treatment options is RT. RT is often used to relieve pain, treat pathologic fractures, or neurological symptoms related to osteolytic lesions (9). External beam radiation therapy is the most common type of radiation therapy used to treat MM or solitary plasmacytoma (10). RT

can also be used in combination with chemotherapy to induce superior apoptosis of myeloma cells while protecting bone marrow (10, 11).

Thus, RT can be an effective treatment option for MM muscle infiltration. RT has been shown to induce complete or partial pain relief in 75-95% of patients with painful myeloma bone lesions (10). Successful treatment of cauda equina myeloma nodules with RT, lenalidomide, dexamethasone, and intrathecal chemotherapy has also been reported (12). RT is a treatment option for MM muscle infiltration that has been shown to be effective in reducing pain and improving overall quality of life for patients. RT can slow down or stop the growth of cancer cells and potentially shrink tumors (13). In terms of its effectiveness in treating MM muscle infiltration, radiation therapy may be used to treat areas of bone damaged by myeloma that have not responded to chemotherapy and/or other drugs and are causing pain. While new types of treatments are being developed, RT remains a viable option for treating MM muscle infiltration (14).

Another treatment option for MM muscle infiltration is chemotherapy. Chemotherapy is a major treatment option for MM and is often used in combination with radiation therapy. However, more aggressive chemotherapy regimens should be used in patients with recurrent MM with extramedullary involvement because the prognosis is poor (15). Chemotherapy is often used in combination with other treatments, such as radiation therapy or stem cell transplant, to improve outcomes.

There are several types of chemotherapy drugs that can be used to treat MM muscle infiltration. These drugs include melphalan, doxorubicin, and cyclophosphamide (16, 17). Induction therapy usually comprises a combination of three drugs from different classes, such as bortezomib, thalidomide, and dexamethasone (1, 2, 16). The choice of chemotherapy drugs and their dosages depend on various factors, including the patient's age, overall health, and the stage of the cancer.

Chemotherapy can cause neurotoxicity, peripheral neuropathy, muscle pain, and cranial neuropathy, which can affect the nervous system (18). Patients undergoing chemotherapy should be closely monitored to manage any side effects, complications and differential diagnosis of muscle involvement due to MM.

Stem cell transplant is another treatment option for MM muscle infiltration. High-dose chemotherapy with stem cell transplant is commonly used to treat MM. Stem cell transplant

can be divided into different phases, including induction therapy, stem cell transplantation, and consolidation therapy (1, 2). Stem cell transplant may be an option for patients with MM muscle infiltration, particularly those who have relapsed after previous treatment (7, 19).

Combination therapies are often used to achieve better treatment outcomes for MM muscle infiltration. New treatment options such as immunotherapy, chimeric antigen receptor-modified T cells (CART) cell therapy, and BCL-2 (a selective inhibitor of apoptosis) are being explored (15, 20). The combination of RT and immunotherapy has also shown promise in improving therapeutic efficacy and reducing recurrence by enhancing the immune response (9). The recent datas evaluated treating painful metastatic lesions in muscle with combination chemotherapy and RT with avelumab, a type of immunotherapy, and found promising results (21-23). As research continues, combination therapy may become an increasingly important component of treatment for MM muscle infiltration.

The recommended total RT tumor dose in the literature for extramedullary MM ranges from 3.0 to 60 Gy, with an average of 25 Gy (24). Definitive external RT alone is preferred with doses ranging from 30 to 60 Gy (25). Treatments combined with RT differ between hypofractionated regimens with a single fraction of 8 Gy and normofaction up to 50 Gy (26). Previous studies comparing these fractions have demonstrated the superiority of hypofractionated RT therapy with 30 Gy in 10 fractions compared to 8 Gy in a single fraction in terms of quality of life (27). Guidelines from the International Lymphoma Radiation Oncology Group (ILROG) recommends the use of hypofractionated regimens at a dose of 8 to 30 Gy for bone lesions, in addition a single 8 Gy fraction may be considered in patients with a poor prognosis (28). We preferred 10x300cGy=30Gy as the most appropriate dose for our patient. However, a dose of 24 Gy was applied to the below-knee region with all compartments within the RT field. The aim was to minimize the risk of future lymphedema.

Conclusion

RT is a common treatment option for MM muscle infiltration. Radiation therapy is often used to relieve symptoms such as osseous pain, pathologic fractures, or neurological symptoms related to osteolytic lesions. Although chemotherapy is the primary treatment for MM, radiation therapy often plays a supportive role in symptom relief and can also have a radical role in the treatment of the disease. Treatment for myeloma usually consists of a multi-modality approach

encompassing chemotherapy, targeted small molecule therapy, radiation, high-dose therapy with stem cell transplant, and surgery, among others.

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