CASE REPORT

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Successful Treatment of Bulky Abdominal Plasmacytomas With Radiotherapy and Pomalidomide

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ABSTRACT

Extramedullary myeloma itself is a rare entity and treatment of recurrent extraosseous myeloma can be challenging during the prolonged disease course. We report a multiple myeloma (MM) patient with extramedullary bulky abdominal masses treated with palliative radiotherapy (RT) and concomitant pomalidomide.

A 59-year-old woman diagnosed with MM presented with pancytopenia, widespread lytic bone lesions and intraperitoneal implants. The patient received multiple series of chemotherapy. Following autologous stem cell transplantation (ASCT), imaging studies displayed bulky abdominal masses. Due to the rapidly progressing symptoms, palliative RT 30 Gy in 15 fractions with concomitant pomalidomide was administered. Post-RT imagings showed near-complete regression.

Extraosseous extramedullary MM has a poor prognosis and is an area of unmet clinical needs. Our report describes the treatment of a relapsed extramedullary myeloma case with RT and concomitant pomalidomide resulting in a near-complete response of disease inside the radiated area. To conclude, it was demonstrated that RT is an effective treatment modality to obtain symptom palliation and can be safely administered with an immunomodulatory drug.

Keywords: Extramedullary myeloma, bulky abdominal masses, radiotherapy, immunomodulatory drugs, pomalidomide

Introduction

Multiple myeloma (MM) accounts for 1.5% of all cancers and 13% of all hematologic malignancies (1). It is usually seen in older ages and the median age is 65 years (2). It is characterized by clonal plasma cell proliferation in the bone marrow. Hypercalcemia, renal failure, anemia, bone lesions and recurrent infections are common features at presentation (3).

When myeloma cells form tumors in extraosseous locations such as soft tissue and viscera it is called extramedullary myeloma(EMM) which has an aggressive clinical course.EMM occurs in less than 5% of the patients at diagnosis, but in 3.4-10% at relapse (4). Pleura, liver, and lymph nodes are commonly involved regions in EMM.Improved survival rates are achieved with the emergence of novel agents including proteasome inhibitors and immunomodulatory drugs.However, clinicians are confronted with recurrent EMM during this prolonged disease course (5).

Previous studies have demonstrated that approximately two-thirds of MM patients required radiation treatment during the course of the disease, mostly for palliative intent (6). MM is a highly radiosensitive neoplasm and the main indications for RT are pain control, spinal cord compression, treatment of pathological fractures and extramedullary disease (7).

We report a MM patient with extramedullary multiple bulky abdominal masses treated with palliative RT and concomitant pomalidomide at our department.

Case Report

A 59-year-old woman has diagnosed with lambda light chain MM 2 years ago.She presented with pancytopenia, widespread lytic bone lesions and intraperitoneal implants, and international staging system III (ISS III) disease at diagnosis. Concomitant radiotherapy to D2-9 vertebras 30 Gy in 10 fractions for compression fractures was administered with high dose dexamethasone firstly. Subsequently, 2 cycles of vincristine, doxorubicin, dexamethasone (VAD) chemotherapy and zoledronic acid were applied.

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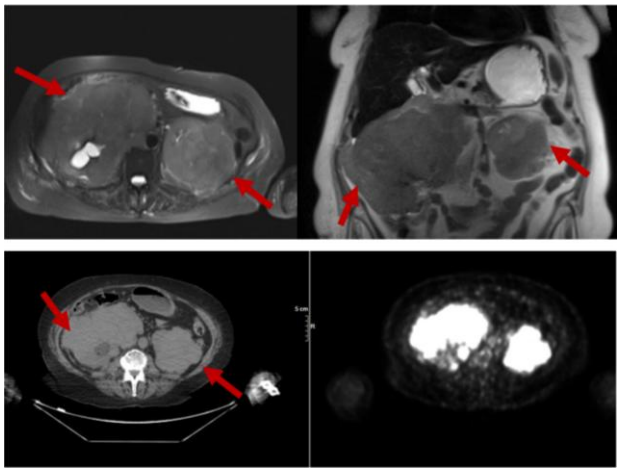

Fig. 1. Pretreatment T2-weighted MRI scan; axial (a), coronal (b) and F-18 FDG PET/CT(c) scans

Only minimal response was achieved and therapy was changed to bortezomib-cyclophosphamide-dexamethasone (VCD) regimen due to progressive disease.Total Therapy 3 (VTD-PACE: bortezomib, thalidomide, dexamethasone-cisplatin, doxorubicin, cyclophosphamide, etoposide) was given followed by stem cell collection.She received RT to the sacral region and underwent autologous stem cell transplantation (ASCT) in May 2018. Partial remission was achieved at 3 months after ASCT.

After one month of history of nausea, vomiting, abdominal pain, loss of appetite and icterus, the patient applied to our hematology department in December 2018, at the 9th month of ASCT. Physical examination revealed icterus and diffuse abdominal distension and palpable multiple masses of 10 cm in size starting from bilateral upper quadrants and extending to the lower quadrants of the abdomen. Her performance score was ECOG 4. Routine laboratory tests revealed hemoglobin: 6.7 (13.6-17.2) g/dL, platelets 72 (156-373) 103/µL, white blood cell 2.6 (4.3-10.3)103/µL, creatinine 1.46 (0.7-1.2) mg/dl, total protein 4.7 (6.4-8.3) g/dL albumin 3.2 (3.5-5.2) g/dL, total bilirubin 6.01 (0.2-1.2) mg/dl direct bilirubin 4.96 mg/dl (<0.3), AST 51 IU/L (<32), ALT 24.1 IU/L (<33), GGT 205 IU/L (<40), ALP 182 U/L (35-105), LDH 297 IU/L (<250), Ca++ 0,48 mmol/L (1.15 - 1.29) and beta-2 microglobulin 6430 ng/ml (800-2200). Abdominal magnetic resonance imaging (MRI) displayed a 165x154x157mm mass adjacent to the right kidney and a 103x100x78mm mass adjacent to the left kidney (Figure 1). Tru-cut biopsy from the right perirenal mass was performed and histology revealed lambda light chain extramedullary multiple myeloma.

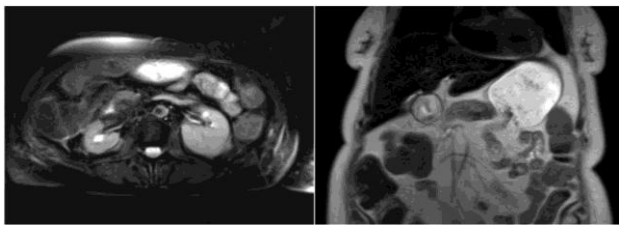

Fig. 2. Posttreatment T2-weighted MRI scan; axial (a) and coronal (b) scans

Carfilzomib/dexamethasone regimen was started but the patient remained refractory. She developed Wernicke's encephalopathy during the course of the disease caused by decreased oral intake and persistent vomiting. Due to the rapidly progressing symptoms caused by compression from the abdominal masses, palliative RT with concomitant pomalidomide plus dexamethasone was planned. However, due to the large volume of the masses radiotherapy was applied only to the most symptomatic right-sided lesion which caused compression to the bowels and biliary tract. Short fractionation schemes were not preferred due to the large target volume and severe symptoms. We irradiated the patient with 30 Gy in 15 fractions over 2 weeks with the VMAT technique and completed the treatment in March 2019.After eight fractions of RT, symptoms began to relieve: loss of appetite and ileus regressed. Serum lambda light chain levels decreased from 326mg/L to 22(5.71-26.3)mg/L at the end of radiotherapy. After RT pomalidomide plus dexamethasone were continued for two more cycles. Post-RT MRI and CT scans showed near-complete regression (Figure 2).

Clinical and instrumental subsequent controls reveal no progression in the treatment field after 3 months of follow-up. However, many new medullary and extramedullary tumoral lesions developed outside the RT area under pomalidomide treatment. Unfortunately, the patient died in August 2019 due to progressive disease, bone marrow failure and sepsis.

Discussion

MM is an incurable disease despite advances in therapy. Relapse is inevitable and remission duration decreases with each regimen. Clinical manifestations of abdominal EMM vary depending upon the site and duration of involvement. Patients can have nonspecific gastrointestinal symptoms like abdominal pain, nausea and vomiting or present with life-threatening symptoms, such as gastrointestinal bleeding, ileus and perforation.

The introduction of novel agents such as proteasome inhibitors (PI), immunomodulatory drugs (IMiDs) and ASCT improved the overall survival of MM patients.MM is a clonally diverse disease and multiple relapses develop from the expansion of different plasma cell subclones during the course of the disease. The extramedullary disease occurs usually during the end stages of the disease. There is no standard treatment algorithm defined yet for the treatment for EMM because of the comparatively low incidence and, remains still a hardly controlled neoplasm. Surgery, RT, or surgery plus RT might be the treatment of choice for symptomatic relief. It is generally believed that these tumors are highly radiosensitive and can be treated with local RT. Concerning the radiation dose, most clinicians believe that good local control rates without severe radiation injury can be obtained by using 40 to 50 Gy doses (8). A local control rate of 94% can be achieved at doses higher than 40 Gy but 69% at those under 40 Gy (9). A common conception is that doses higher than 40Gy is an effective treatment approach to EMM. However, in the case of bulky disease, it is reasonable to reduce doses to protect the surrounding tissue. Operation and postoperative RT are feasible treatment choices in such situations (10).

In conclusion, recurrent EMM during this prolonged disease course is still a problem despite the new drugs and immunotherapy. Our report describes the treatment of a relapsed extramedullary myeloma case with RT and concomitant pomalidomide resulting in a near-complete response of disease inside the radiated area. In our case, it was demonstrated that RT is an effective treatment modality to obtain rapid symptom palliation and can be safely administered with an IMiD. Although radiotherapy is not the first choice nowadays, it should be noted that it is a very successful, treatment modality for local control and palliation. Further comprehensive studies are necessary to determine appropriate treatment concerning radiation dose and fractionation scheme and their concomitant use with novel agents.

Conflict of Interest: On behalf of all authors, the corresponding author states that there is no conflict of interest.

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