EDİTÖRYAL / *EDITORIAL*

Simultaneous Use of Targeted Radiotherapy with External Beam Radiotherapy in the Treatment of Bone Metastasis

Kemik Metastazı Tedavisinde Hedefleyici Radyoterapinin Eksternal Işın Radyoterapisi ile Eşzamanlı Kullanımı

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In cancer patients, skeletal system metastases are the third most localized organ after lung and liver. 70% of bone metastases (BM) involve the axial skeleton and are mostly multiple. The most common area is the vertebrae. Metastases to the bone are mostly caused by breast, prostate, lung, kidney and thyroid cancers.[1] Prolonged survival in patients with BM due to developments in cancer treatment and waiting for complications in one of every three cases with bone involvement reveal the importance of an appropriate treatment approach[1–3]. In our previous study on 181 cases, the rate of bone metastasis was seen most frequently in lung, breast and prostate cancer. In terms of anatomical distribution, the vertebra, lower extremity and upper extremity were found to be the metastatic location, respectively[1]. With early diagnosis and treatment, the patient's quality of life will be improved by reducing possible complications such as pain, fracture, hypercalcemia and spinal cord compression that may occur due to BM. Pain is a common symptom in CM and decreases the quality of life. Studies show that cancer patients experience severe pain at a rate of 30% at the time of diagnosis and 60–90% at the advanced stage[2–4].

Treatment of BM is done by palliative methods. Local treatments (surgery and radiotherapy), systemic treatments (cytotoxic chemotherapy, hormonotherapy, bisphosphonates, gallium nitrate, etc.) and supportive treatments (analgesics, psychological support and social support) are the main methods used[2–6]. Depending on the prevalence of the disease, the severity of the symptoms, previous treatments, and concomitant diseases, one of these treatment methods or its combined use is preferred. A limited number of BM can be treated with surgery and/or radiotherapy (RT). In more diffuse bone involvement, radiopharmaceuticals, hormones and chemotherapeutics are more preferred. Each treatment has its own advantages and disadvantages. The use of analgesics for these long periods is limited due to their side effects. It has been reported that the palliation provided by chemotherapeutics or hormonotherapy does not occur in a short time and is not effective and long-lasting[4–7].

The purpose of RT in the treatment of BM is to prevent or relieve the symptoms and dysfunctions of the patient for the rest of his life. RT is used for palliative and prophylactic purposes. Palliative application in bone pain, pathological fracture formation, peripheral nerve compression and spinal cord compression. Prophylactic application is applied in cases with risk of cord compression and pathological fracture. RT is usually used to reduce pain due to BM. After treatment, pain response usually begins in the first 48 hours. It becomes apparent within four weeks. This is a permanent response in 70% of the patients[2,3,4–7]. With RT, 80–90% of the patients respond to pain, while 40–60% of them provide full control. In lesions, it provides symptomatic improvement in 96% and recalcification in 78%[7].

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Nowadays, radionuclide therapy is successfully applied in refractory metastatic pain. Multiple metastatic foci can be treated simultaneously with radionuclide therapy. The radioisotope administered intravenously to the body shows its therapeutic effect by reaching all targets in the body that show osteoblastic or mixed bone activity. Therefore, this treatment method is also called "targeted radiotherapy". With this treatment, it improves the quality of life by reducing pain in the patient. It reduces the need for analgesics, RT and chemotherapy. It also improves the course of the disease and survival[3,5,6,8]. Although the idea of using bone targeted radioisotopes for the treatment of common BM in the advanced stage of the disease is dominant. These agents are also used in the early stages of diseases in order to increase the response to treatment in the early metastatic period[9]. With the targeted radiotherapy method, the complete or partial success rate varies between 60% and 90%, respectively. Pain control can usually start in the first days of treatment, or it may take up to the second or third week. Retreatment can be safely performed on days when there is no adequate response to treatment or when pain begins to recur after successful treatment[6,8].

P-32 and Sr-89 radioactive isotopes are the first radiopharmaceuticals used in radionuclide treatments. Clinical use of P-32 has been restricted due to its high energy, the prominence of its side effect of myelotoxicity and long-term beta scattering in the tissue. Sm-153, Re-186, Re-188, which are newly developed radioisotopes that spread beta over time, have taken their places in routine practice[5,10]. The most common complication is myelotoxicity. It is recommended to reduce the dose by 50% in patients with moderate renal impairment (GFR >30 and <50 mL/min)[4,6,11]. Although all beta emitting isotopes show different physical properties, the superiority of radionuclides used in the treatment of BM has not been demonstrated in clinical studies. Patient-dependent characteristics appear to be the determining factor in the choice of radionuclide in routine practice[5].

There is contradiction in the literature regarding which of the external RT or radionuclide treatments are more effective and reliable. The effect of radionuclide therapy on survival is controversial. Studies have shown that the effect of radioisotopes used in palliation of pain is not much different from external RT[3,12]. In the study of Buchali et al. [13] comparing the Sr-89 treatment group with placebo in patients with prostate cancer, it was reported that Sr-89 treatment prolonged the survival[13]. In addition, in randomized and multi-center studies conducted in Europe, it has been reported that Sr-89 treatment decreases the life span in painful metastatic bone cancers compared to local RT applications[12]. In another study, it was reported that Sr-89 increases the quality of life in the patient, but does not affect the life span[2].

Nowadays, combined therapies have come into question in cases where pain due to BM cannot be adequately controlled with the treatments applied. There are a limited number of studies in the literature on this subject. One of them is the use of radionuclide treatments (Re 186 HEDP or Sm 153) together with external RT. Hiçsönmez et al.[3] examined the efficacy of combined therapy in 33 cancer patients with painful BM and in patients who were given systemic radionuclide therapy after localized external radiotherapy. They stated that between Re 186 HEDP and Sm 153 hematological toxicity was not high and there was no difference in response to treatment. They also reported that combined therapy reduced pain and analgesic intake. In the study conducted by Heianna et al.[4], they reported that Sr-89 was effective and safe in cases requiring simultaneous emergency treatment with external radiotherapy for more than one CM. In a randomized controlled study involving 126 prostate cancer patients by Porter & McEwan, in the study where RT and Sr-89 were used in combination, they reported no contribution to survival, but the number of new pain zones was significantly lower for the group receiving Sr-89[14]. In another study, it was reported that when adjuvant is used, Sr-89 does not contribute additionally in areas receiving external RT, but prevents pain in areas with CM.

As a result, bone pain caused by skeletal system metastases is the most common type of chronic pain seen among cancer patients. Treatment of bone pain secondary to metastasis is difficult and requires a multidisciplinary approach. This multidisciplinary approach includes treatments such as pain relievers, hormone treatments, chemotherapy, bisphosphonates, RT and systemic radionuclide. Simultaneous use of radionuclide external beam RT in pain palliation in multiple BM seems to be an effective and safe treatment option in cases requiring emergency treatment. However, clinical studies are needed to better evaluate the follow-up and treatment of cancer patients in these combined treatment applications.

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