Case Report:

Samarium-153-ethylene diamine tetramethylene phosphonate (EDTMP) therapy in the management of refractory bone pain in a patient with carcinoma prostate and diffuse bone metastasis

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ABSTRACT

Samarium-153-ethylene diamine tetramethylene phosphonate (samarium-153 EDTMP) is a novel systemic radiopharmaceutical, used for treatment of bone pain due to metastatic disease. We report a patient with carcinoma prostate, diffuse metastatic bone disease with severe back pain that was refractory to analgesics and morphine. He was also found to be anaemic (haemoglobin 8.1 g/dL). Inspite of anaemia and diffuse metastatic bone disease being relative contraindications for the use samarium-153-EDTMP, because of its potential for causing radiation induced myelotoxicity, the patient was treated with this modality and showed a remarkable response in pain control within a few days. He developed mild radiation induced myelotoxicity, which was subsequently managed with blood transfusion and supportive care. The present case highlights the utility of samarium-153 EDTMP therapy in patients with intractable pain due to diffuse metastatic bone disease.

Key words: *Samarium-153-EDTMP therapy, Bone pain, Diffuse bone metastasis*

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INTRODUCTION

Pain palliation is an integral part in management of patients with advanced stages of cancer. It can be achieved by using various modalities like administration of non-steroidal anti-inflammatory drugs (NSAIDs), morphine, nerve blocks etc. Samarium-153-ethylene diamine tetramethylene phosphonate (EDTMP) radionuclide therapy is an alternative pain palliation therapy available to cancer patients suffering from severe bone pain due to metastatic bone disease. It is a safe and simple, out-patient department based procedure. After intravenous administration, it reaches the target metastatic sites in affected bones through circulation within a few minutes. Its concentration in metastatic sites depends on the local osteoblastic activity. Following therapy, patients get relief in bone pain by three to five days due to the effects of local tissue irradiation with the soft beta emissions released during radioactive decay. The physical half-life of this medicine is 46.3 hours, and treated patients remain pain free for 5 to 6 months. Samarium-153 EDTMP is indigenously produced and supplied by Board of Radiation Technology (BRIT), Government of India, Mumbai and is easily available.

Samarium-153-EDTMP therapy is effective in control of bone pain in 70% patients. In less than 10% patients, it may cause a mild self remitting transient myelotoxicity. When the disease is diffuse and wide spread, the grade of myelotoxicity may be more and the patient may need supportive treatment during the recovery phase.

We report the hitherto seldom documented therapeutic application of samarium-153-EDTMP therapy in relief from untractable bone pain in a patient with carcinoma prostate and diffuse bone metastases.

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CASE REPORT

An 80-year-old male, who was diagnosed to have carcinoma of prostate in June 2012, presented with severe body pain predominantly in the lumbar and sacral regions, since the preceding two months. There was no history of trauma. He was started on treatment with daily oral non-steroidal anti-androgens with depot injections of luteinizing hormone-releasing hormone (LHRH) agonist for hormonal suppression. For bone pain palliation, he was administered a combination oral morphine sulphate 10 mg, and paracetamol 500 mg thrice-a-day. His bone pain relief with these medications was intermittent and partial. With this background he was referred to us for consideration for administration of systemic radionuclide palliative bone pain therapy with samarium-153-EDTMP as an alternative treatment.

His performance status, as assessed by using Karnofsky performance scale[1] was 50, pain severity score on visual analogue scale (VAS)[2] was 9 and analgesic score[3] was 6. His laboratory investigations showed, haemgolobin 8.1 g/dL, total white cell count 3,200/mm^3, platelet count 119,000/mm^3, serum creatinine 1.3 mg/dL, estimated glomerular filtration rate (GFR) using Cockcroft-Gault formula[4] 53.6 mL/min, serum calcium 7.5 mg/dL, serum phosphate was 4.0 mg/dL and serum alkaline phosphatase 2043 IU/L. Technetium-99m-methylene diphosphonate (Tc-99m-MDP) bone scintigraphy revealed diffuse increased radiotracer concentration in axial and appendicular part of the skeleton, suggestive of diffuse metastatic bone disease (Figure 1). These findings correlated well with computed tomography (CT) (Figure 2), which showed diffuse sclerotic changes in vertebral bodies in spine.

In the light of anaemia and diffuse metastatic bone disease as evident on bone scintigraphy, therapy with samarium-153-EDTMP was relatively contraindicated as it had the potential to cause high grade myelotoxicity. Considering the terminal illness and severity of bone pain, 1 mCi/Kg body weight (85 mCi) samarium-153-EDTMP was administered intravenously. Post-therapy whole body images of samarium scintigraphy (Figure 3) revealed identical tracer uptake pattern with pre-therapy Tc-99m-MDP bone scintigraphy. The procedure was uneventful and patient was discharged and was advised to undergo weekly blood tests for close monitoring of myelotoxicity.

Post-therapy, after one week, the patient reported marked relief in bone pain and at one month he completely stopped pain medications. On clinical examination, his performance status as assessed using Karnofsky performance scale[1] was 60. Pain severity on VAS[2] was 2 and analgesic score[3] was 0. His post-therapy haematological investigations at one month revealed decrease in haemoglobin

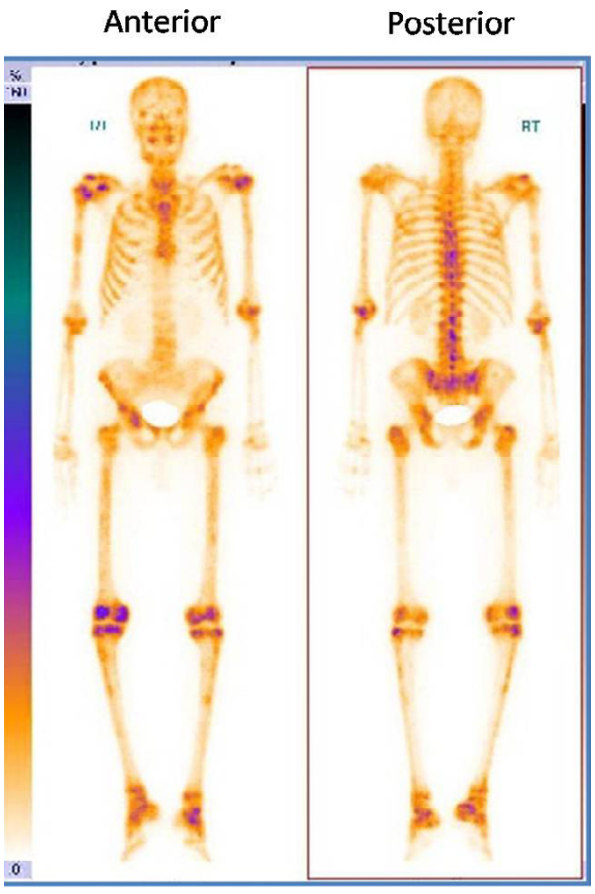

Figure 1: Technetium-99m MDP bone scintigraphy, anterior and posterior whole body images obtained after 03 hours, showing diffuse increased radiotracer uptake in axial and appendicular parts of skeleton
MDP=methylene diphosphonate

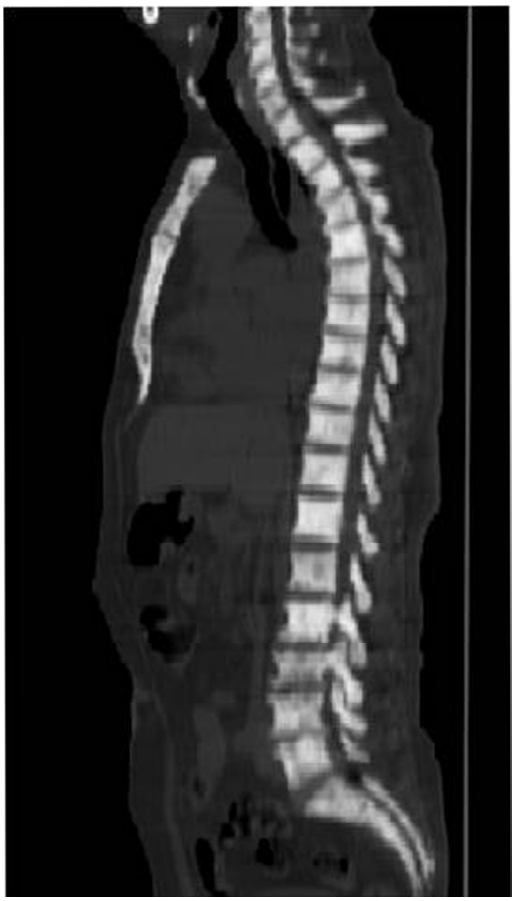

Figure 2: Computed tomography (sagittal image) showing diffuse sclerotic changes in spine and other bones

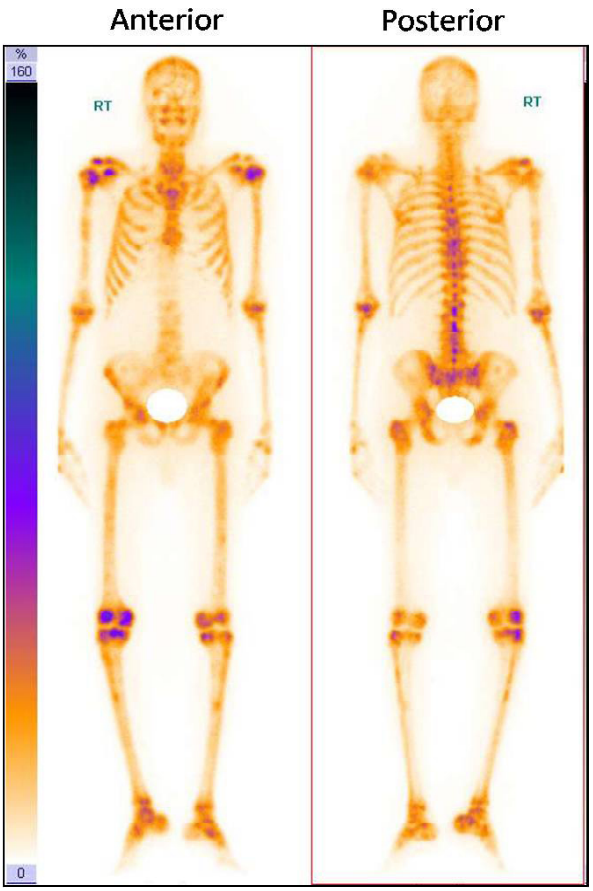

Figure 3: Samarium-153 EDTMP scintigraphy (anterior and posterior whole body images) showing radiopharmaceutical localization in bones, identical to MDP bone scintigraphy

EDTMP=ethylene diamine tetramethylene phosphonate; MDP=methylene diphosphonate; RT=right side

from 8.1 g/dL to 6.2 g/dL (grade 03 myelotoxicity).[5] Total leucocyte count decreased from 3,700/mm^3 to 2,200/mm^3 (grade 02 toxicity).[5] Platelet count decreased from 119000/mm^3 to 87000/mm^3 (grade 01 myelotoxicity).[5] Patient was managed with two units of whole blood transfusion and he is on further follow-up.

DISCUSSION

In cancer patients, metastasis is a common consequence and localized in skeleton, lung, liver, brain, lymph nodes, etc. The prevalence of metastatic bone disease varies from 65%-75% in breast and prostate cancer, 60% in thyroid cancer, 40% in bladder cancer, 30%-40% in lung cancer and 20%-25% in renal cancer.[6] In most of the patients initially bone metastasis are silent and do not produce symptoms, but as the disease progresses, complications arise from bone lesions in metastatic bone disease. Bone pain is the most common complication and accounts for 50%-90% of all the complications arising from bone lesions in metastatic bone disease, other common complications being pathological fracture (10%-40%) and hypercalcaemia (10%-20%).[7] Bone pain is a somatic pain, initiated and maintained through local tissue injury, via different mediators like substance-P, tumour necrosis factor (α and β) transforming growth factor (α and β), gamma amino butyric acid (GABA), interleukins, etc.[8] Treatment of painful skeletal metastasis requires multidisciplinary approach and comprises the use of systemic analgesics, hormones, chemotherapeutic agents, steroids, external beam radiation therapy (RT), radiofrequency ablation, surgery, and systemic radiopharmaceuticals.[9]

Samarium-153 EDTMP is a radiopharmaceutical that is used for bone pain palliation in a dose of 1 mCi/kg body weight. Samarium-153 targets hydroxyapatite at sites of increased osteoblastic activity, where it decays with physical half life of 46.3 hours. It emits β-particles with maximum energy of 0.81 mega electron volts (MeV) and γ-rays of 103.2 kilo electron volts (keV). The former have therapeutic effects while the latter allow imaging of the skeleton.[10,11] Patient selection criteria include the presence of foci of increased uptake on Tc-99m-MDP bone scan corresponding to the pain sites.[12] Presence of diffuse increased uptake on bone scan is considered to be a relative contraindication for Samarium-153 EDTMP therapy, as it may pose a potential risk of bone marrow toxicity. These patients can be treated at lower dose levels or with smaller fractionated doses, but low doses have a disadvantage of having lower response rates.[10]

The reported incidence of myelotoxicity in patients treated with samarium therapy is less than 10%,[5] and grade 1-3 myelotoxicity has been decribed.[5] It is usually transient and has spontaneous remission, but in some patients who are terminally ill with compromised haematological parameters, blood transfusion and other supportive care may be required during the recovery phase.

An online MEDLINE search using keywords Samarium-153 EDTMP therapy, prostate cancer and diffuse uptake on bone scintigraphy, did not result in retrieval of any published case reports in the medical literature in English language. The present case highlights the utility of samarium-153 EDTMP in the treatment of intractable bone pain due to metastatic bone disease who had relative contraindication for its use, such as anaemia.

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