Optimal treatment of painful bone metastases with Samarium EDTMP in a haemodialysis patient: effectiveness and safety of internal radiotherapy

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Abstract
One of the current therapeutic approaches in the treatment of osteoblastic bone metastases uses the affinity of Samarium (153Sm) ethylene-diamine-tetramethylene phosphonic acid (EDTMP) for bone areas of bone turnover. As Samarium EDTMP is a β-emitter, the radiotherapy contributes to osteoblastic bone lesion control over time. To date, the safety and effectiveness of Samarium therapy have not been established in patients with renal impairment. In this first report, we describe our experience of use of Samarium EDTMP in conjunction with biphosphonates in a haemodialysis patient for treatment of painful bone metastasis. Encouraging results were obtained in achieving pain control. The use of this radioisotope could be more widely applied to treat haemodialysis patients.

Keywords: bone metastases; haemodialysis patient; multiple myeloma; Samarium EDTMP

Case report
A 71-year-old woman treated with maintenance haemodialysis suffered from widespread metastases of breast cancer, requiring opioid analgesics (fentanyl and dextropropoxyphene) that were insufficient to alleviate pain and disability. Her medical history consisted of untreated asthma and hypertension. To relieve her bone pain, the patient underwent 99mTc-HDP (hydroxy-methylene-diphosphonate) bone scintigraphy using 540 MBq of 99mTc-HDP. Scan imaging revealed bone metastatic lesions in the spine, pelvic bone, ribs, left shoulder blade, femur and possibly left tibia and skull compatible with metastatic breast cancer (Figure 1). Pain evaluation by visual analogic scale (VAS) was expressed as 7/10, and the recorded motor score was 5/20. This patient received a course of 15 mg of pamidronic acid and the internal radiotherapy with Samarium EDTMP for improved pain relief.

Two days before Samarium EDTMP therapy, the number of leucocytes was 9.7×10⁹/L (reference range 4–11×10⁹/L), haemoglobin 98 g/L (reference range 115–145 g/L) and platelets 240×10⁹/L (reference range 150–400×10⁹/L). Considering her renal failure and impaired urinary excretion of Samarium after intravenous administration (35.3% ± 13.6%, the first 12 h), subsequent doses were decreased to only 80% of the conventional dose, i.e. 29.6 MBq/kg (0.8 mCi/kg) instead of 37 MBq/kg (1 mCi/kg), 16 h before haemodialysis. Whole body scans were done using a standard gamma camera, 6 h after receiving Samarium EDTMP therapy (Figure 2). Due to the short physical half-life of samarium (46 h), the excreted activity via the residual urine flow and the faeces was collected over 16 h.

Received for publication: 2.4.08. Accepted in revised form: 16.4.09
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The clinical follow-up included monitoring of bone response, haematological data and supportive medication. Treatment efficacy was assessed according to VAS, motor score, analgesic consumption and performance status. Painful osteoblastic lesions were significantly alleviated after internal irradiation. Onset of pain improvement took place 2 weeks after radiotherapy associated with the VAS score of 0/10 and the motor score of 19/20. There was an obvious decrease in opioid analgesic use in the active phase of the treatment. Only dextropropoxyphene was occasionally taken. In addition, complete blood and platelet counts were obtained at weekly intervals for a period of 1 month. No relevant haematological toxicity occurred. Normalization of haematological data was observed at 4 weeks following administration (leucocytes $5.1 \times 10^9/L$, platelets $186 \times 10^9/L$). However, a temporarily recoverable mild anaemia was observed (haemoglobin 96 g/L, erythrocytes 2.98 T/L). This anaemia was secondary to inflammation focused in arterio-venous fistula.

Radioprotection measures were respected. Precautions consisted in collecting organics waste (urine and faeces) and whole materials used for the preparation and administration of the radioisotope (syringe, needle, compress, gloves) that were stored at a radioactive decay site. The dialysis equipment (catheter, arterial and venous tubular, dialysis filter) was differed to the nuclear medicine department to radioactive decay. The radioisotope-containing dialysate was eliminated using the general waste disposal route.

Discussion

Samarium EDTMP (trade name: Quadramet®) is a metabolic radiotherapy used to manage bone pain secondary to metastatic bone cancer such as myeloma extension [1–4].

Metabolic radiotherapy is based on the use of $^{153}$Sm conjugated to a tetraphosphonate to form $^{153}$Sm-EDTMP chelate ($^{153}$Sm-ethylene-diamine-tetramethylene phosphonic acid). Metal phosphonate chelates such as $^{153}$Sm-EDTMP or $^{99m}$Tc-HDP have bone-seeking proprieties. Therefore, osteoblastic metastasis lesions that have high bone turnover show increased uptake of $^{99m}$Tc-HDP on bone scan and enhanced skeletal deposition of $^{153}$Sm-EDTMP. Thus, binding propriety of $^{153}$Sm-EDTMP to hydroxyapatite can be associated with a decreased, an increased or a stable osteoblastic activity, resulting in pain relief or sometimes in bone-painful side effects (flow phenomenon) during 72 h after administration [1–7].
Clinical studies have established the effectiveness and safety of a single injection of an activity of 37 MBq/kg (1 mCi/kg) of Samarium 153 [3,5,8]. Pain relief was observed in 73% of patients with a parallel 82% reduction of analgesic intake [9]. Furthermore, the management of bone pain by metabolic radiotherapy appears not related to the injected activity while there is a positive correlation with toxicity [9]. The reported myelosuppression was mild and reversible [5,10,11]. In general, the risk-to-benefit ratio of 153Sm-EDTMP in patients with painful bone metastases is considered to be favourable [6]. A comparative study of therapeutic efficacy and toxicity of 153Sm-EDTMP and pamidronate disodium showed superiority of 153Sm-EDTMP on pain relief but higher toxicity than pamidronate disodium [12].

Data published by Abruzzese et al. provide Samarium EDTMP as a novel palliative approach to the treatment of symptomatic elderly patients with multiple myeloma and not eligible for further chemotherapy. Clinical benefit observed includes improvement in bone pain, reductions in skeletal events and delay in time-to-first-skeletal-events [13].

At present, no useful data are available concerning the efficiency and the safety of the administered Samarium EDTMP in patients with renal function impairment especially in chronic renal failure with dialysis, and the benefit of the combination of pamidronate/Sm-153 EDTMP remains unknown as well. For this patient, the internal radiation was adjusted considering renal function. Therefore, the optimal activity was estimated at 80% of the conventional dose proposal. Then, palliation of metastatic bone pain was successfully reached at 2 weeks following treatment. There was no life-threatening myelotoxicity noted after this single administration. Nevertheless, bisphosphonate therapy was administered 28 days before Samarium EDTMP. It is clear that, in this therapeutic context, the therapeutic response of pamidronate can interfere with potential benefit of Samarium EDTMP therapy.

Conclusion

Management of painful bone metastases with Samarium EDTMP in a dialysis patient was successfully performed in order to improve the quality of pain relief. Our observation demonstrates that such therapy is feasible in patients treated by maintenance haemodialysis without haematological toxicity. Larger case series are required to draw conclusions.

Conflict of interest statement. None declared.

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Received for publication: 4.12.08; Accepted in revised form: 12.3.09