



# Tumor regression of multiple bone metastases from breast cancer after administration of strontium-89 chloride (Metastron)

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## Abstract

We report a case of tumor regression of multiple bone metastases from breast carcinoma after administration of strontium-89 chloride. This case suggests that strontium-89 chloride can not only relieve bone metastases pain not responsive to analgesics, but may also have a tumoricidal effect on bone metastases.

## Keywords

Strontium-89 chloride, regression, bone metastasis, tumoricidal effect

Date received: 3 February 2013; accepted: 20 May 2013

## Introduction

Bone metastasis occurs in approximately 80% of patients with advanced breast cancer. Twenty to 85% of all cancer patients develop bone metastases during the clinical course, regardless of cancer type; 65–75% of these suffer from intolerable pain (1,2). To relieve bone pain, opioid analgesics and external radiotherapy have been used. However, controlling pain from multiple bone metastases is often difficult. Recently, strontium-89 chloride (<sup>89</sup>SrCl<sub>2</sub>) has been used as a palliative therapeutic option to relieve pain from bone metastases, even with multiple bone lesions (3,4). Its usefulness in relieving pain in patients with multiple bone metastases has been established, but few reports have described its tumoricidal effect on bone metastases (5). We herein report a case of tumor regression of multiple bone metastases from breast cancer after administration of <sup>89</sup>SrCl<sub>2</sub>.

## Case report

In September 2008, a 37-year-old woman underwent surgery for breast cancer in our institution. The postoperative clinical stage was T2N0M0. She underwent

postoperative chemotherapy and endocrine therapy. In January 2009, multiple osteoblastic bone tumors, which had been causing severe back pain, were found on contrast-enhanced computed tomography (CT) and magnetic resonance imaging (MRI). Bone lesions were found in the whole spine, but as she complained of severe back pain, 40 Gy external radiotherapy was given from the 5th to the 9th thoracic vertebrae. After external radiotherapy, systemic chemotherapy was continued. In August 2010, multiple liver metastases were found on contrast-enhanced CT and the patient suffered from severe left hip pain. A bone scan showed increased uptake of Tc-99m

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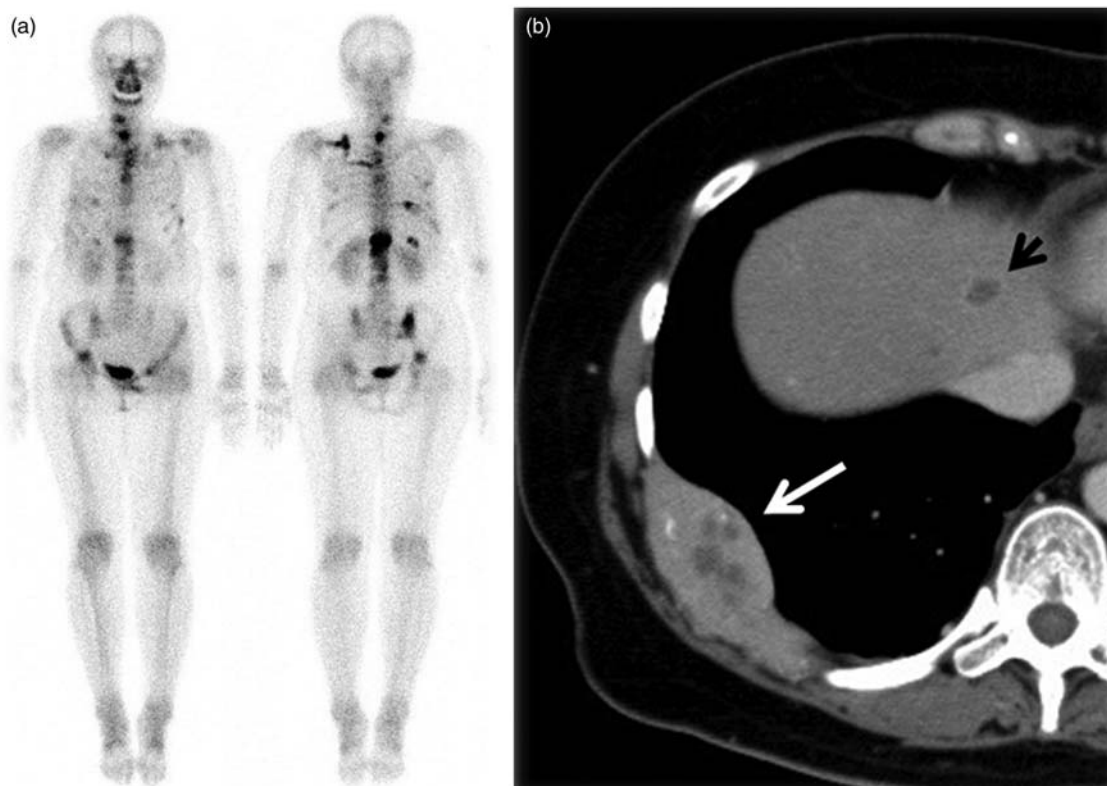
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hydroxymethylene diphosphonate (HMDP) in an area consistent with the left iliac bone. After 40Gy external radiotherapy of the left iliac bone, systemic chemotherapy was resumed. Despite continuing treatment, the multiple bone metastases and liver metastases increased in size. Serum carcinoembryonic antigen (CEA) and cancer antigen 15-3 (CA 15-3) were increased. Bone scan showed multiple uptake of Tc-99m HMDP consistent with multiple bone metastases (Fig. 1a), and on contrast-enhanced CT, the right 9th rib was destroyed by a huge bone tumor (Fig. 1b). The multiple bone metastases were more progressive in size than the liver metastases and the severe pain could not be controlled with the use of opioid analgesics. After written informed consent was obtained,  $^{89}\text{SrCl}_2$  therapy was planned in order to control the pain.

In December 2011,  $^{89}\text{SrCl}_2$  (Metastron; GE Healthcare UK Ltd., Little Chalfont, UK) was administered at a dose of 124.0 MBq (2 MBq/kg). Pre-treatment blood tests showed white blood cell count of  $3.2 \times 10^3/\mu\text{L}$ , hemoglobin 11.2g/dl, and platelet count  $16.4 \times 10^3/\mu\text{L}$ . No major toxicity was found that required care related to the  $^{89}\text{SrCl}_2$  injection. The patient did not receive concurrent and adjuvant

systemic chemotherapy. According to the Common Terminology Criteria for Adverse Events (CTCAE), Grade 2 anemia, Grade 1 leucopenia, and Grade 1 thrombocytopenia were found at 3–8 weeks after administration of  $^{89}\text{SrCl}_2$ , but resolved without treatment. The patient reported pain relief 2 weeks after the  $^{89}\text{SrCl}_2$  injection. Over time, the pain was further controlled.

Five months after the  $^{89}\text{SrCl}_2$  injection, a bone scan showed decreased uptake of Tc-99m HMDP consistent with multiple bone lesions in regression (Fig. 2a), and contrast-enhanced CT revealed bone tumor regression of the right 9th rib (Fig. 2b). In consistence with the shrinking of multiple bone metastases, the CEA and CA 15-3 levels decreased (Fig. 3). However, as the patient did not receive any systemic chemotherapy during this period, the liver metastases increased in size (Fig. 2b). In May 2012, pain control was satisfactory, but a second injection of  $^{89}\text{SrCl}_2$  was administered at the request of the patient, because lower back pain from bone metastases remained. One month after the  $^{89}\text{SrCl}_2$  injection, transcatheter hepatic arterial chemotherapeutic infusion (TAI) was conducted for multiple liver metastases. After the second  $^{89}\text{SrCl}_2$  injection



**Fig. 1.** Bone scan and contrast-enhanced CT images before administration of  $^{89}\text{SrCl}_2$ . (a) Bone scan showed multiple uptake of Tc-99m HMDP consistent with multiple bone lesions. (b) On contrast-enhanced CT, the right 9th rib was destroyed by a huge bone tumor (white arrow) and multiple liver metastases were found (black arrow).

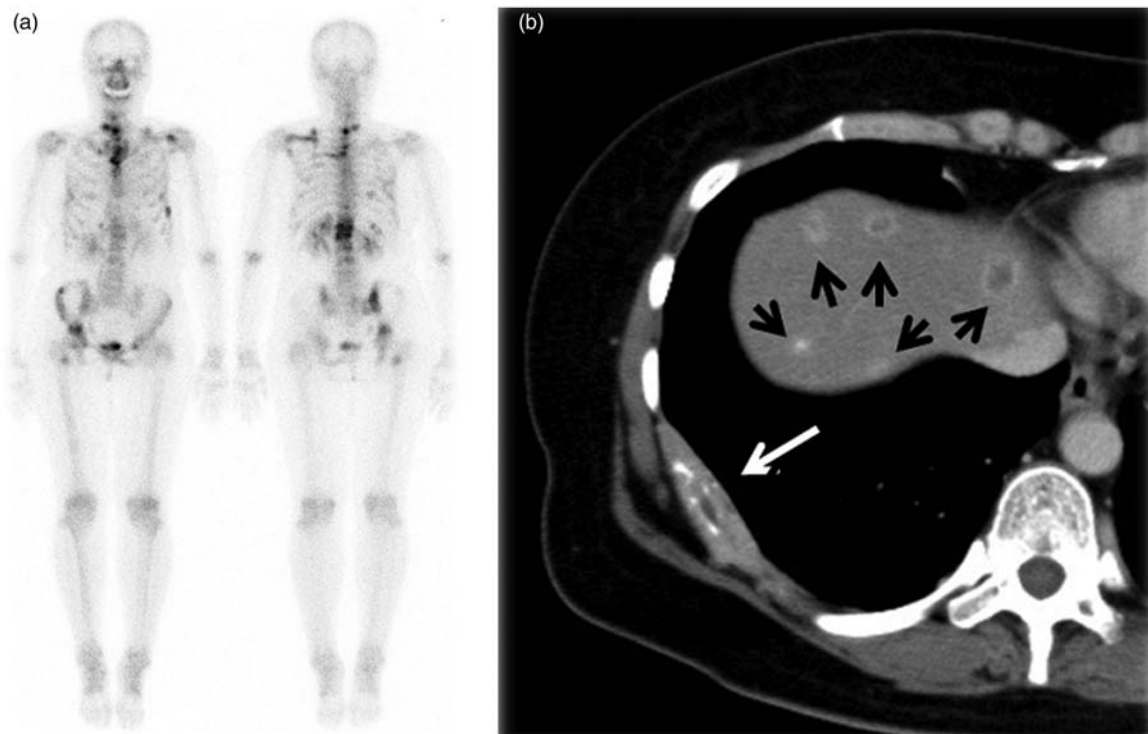
and TAI, the multiple bone metastases and liver metastases were well controlled. Currently, the patient is being treated on an outpatient basis without progression of symptoms.

**Discussion**

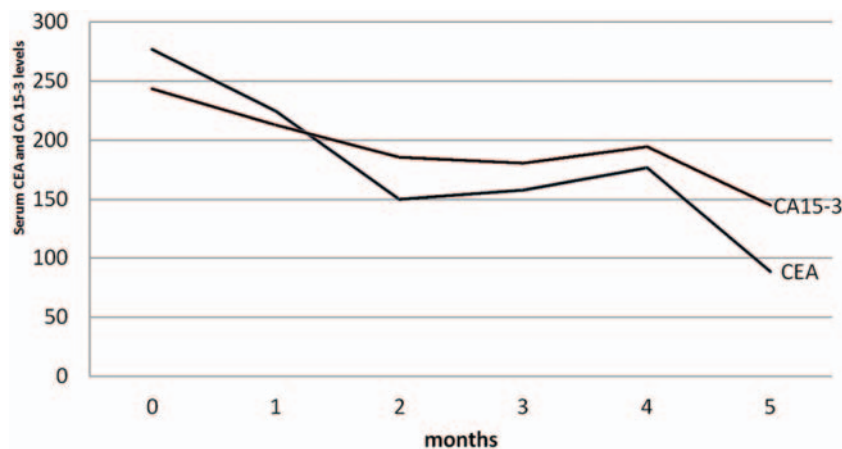
Metastatic bone tumor is a common and severe complication in advanced disease. It develops in up to 70%

of patients with prostatic cancer and breast cancer, and in up to 30% with cancers of the lung, bladder, and thyroid (6). The major complications associated with bone involvement are severe pain, spinal cord compression, and pathological fractures, all of which restrict mobility and sleep, greatly reducing the patient’s quality of life.

To relieve bone pain, analgesia and external radiotherapy have been used. However, in patients with



**Fig. 2.** Bone scan and contrast-enhanced CT images at 5 months after <sup>89</sup>SrCl<sub>2</sub> injection. (a) Bone scan showed a reduction of hot spots. (b) Contrast-enhanced CT revealed bone tumor shrinkage (white arrow) and multiple liver metastases increasing (black arrows).



**Fig. 3.** Change in tumor markers (CEA and CA15–3) after administration of <sup>89</sup>SrCl<sub>2</sub>: serum CEA and CA 15–3 levels gradually decreased after <sup>89</sup>SrCl<sub>2</sub> injection.

widespread painful bone involvement it is often difficult to control pain from multiple bone metastases. In 2007,  $^{89}\text{SrCl}_2$  (Metastron) was approved as a commercially available new drug for the treatment of multiple bone metastases in Japan.  $^{89}\text{SrCl}_2$  reaches metastatic bone sites throughout the whole body when administered intravenously as a single dose, and is therefore often employed to treat multiple bone metastases.  $^{89}\text{SrCl}_2$  is effective in providing pain relief with response rates of between 58% and 82% in patients with prostatic cancer or breast cancer bone metastasis (7,8).

$^{89}\text{SrCl}_2$  has been used as a palliative therapeutic option to relieve pain from multiple bone metastases. Its usefulness in relieving pain in patients with multiple bone metastases has been established, but few reports have described its tumoricidal effect on bone metastases (5).  $^{89}\text{SrCl}_2$  behaves like calcium; it is incorporated into the osteoid matrix adjacent to metastatic cells and emits  $\beta$ -rays. Autoradiography has revealed that the radiation dose absorbed by a metastatic tumor from  $^{89}\text{SrCl}_2$  is 1.3-64Gy (mean  $18 \pm 16\text{Gy}$ ) (9). This fact suggests that  $^{89}\text{SrCl}_2$  may have a sufficient therapeutic dose to have an anti-cancer effect depending on the site of the lesion. Turner *et al.* reported that a decrease of >50% in serum prostate-specific antigen was observed in 37% of patients with hormone-refractory prostate cancer after treatment with  $^{89}\text{SrCl}_2$  (10). Furthermore, many patients show a reduced intensity of hot spots on bone scan compared with pretreatment images (5,6). These reports suggest a possible tumoricidal effect from  $^{89}\text{SrCl}_2$ . In our case, too, a huge bone tumor of the 9th rib regressed, and a bone scan showed a reduction of hot spots after administration of  $^{89}\text{SrCl}_2$ . We assume that anti-cancer effects of  $^{89}\text{SrCl}_2$  might have contributed to tumor regression and pain relief. In the present case, serum CEA and CA 15-3 levels decreased after administration of  $^{89}\text{SrCl}_2$ , while multiple liver metastases increased. This fact, too, suggests a possible tumoricidal action.

In conclusion,  $^{89}\text{SrCl}_2$  is not only useful as a palliative therapeutic option to relieve pain from multiple bone metastases, but also has a possible tumoricidal effect on bone metastases. However, the number of reported cases is still too small to suggest an anti-cancer

effect with  $^{89}\text{SrCl}_2$ . Therefore, cases of regression of bone metastases after treatment with  $^{89}\text{SrCl}_2$  should be accumulated in the literature. Further studies are needed to address the questions of what dose and schedule to use, and which patients will respond.

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