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

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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 (⁸⁹SrCl₂) 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 ⁸⁹SrCl₂.

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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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, 89SrCl2 therapy was planned in order to control the pain.

In December 2011, 89SrCl2 (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 3.2×10⁹/L, hemoglobin 11.2g/dl, and platelet count 16.4×10⁹/L. No major toxicity was found that required care related to the 89SrCl2 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 89SrCl2, but resolved without treatment. The patient reported pain relief 2 weeks after the 89SrCl2 injection. Over time, the pain was further controlled.

Five months after the 89SrCl2 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 89SrCl2 was administered at the request of the patient, because lower back pain from bone metastases remained. One month after the 89SrCl2 injection, transcatheter hepatic arterial chemotherapeutic infusion (TAI) was conducted for multiple liver metastases. After the second 89SrCl2 injection

**Fig. 1.** Bone scan and contrast-enhanced CT images before administration of 89SrCl2. (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 $^{89}$SrCl$_2$ 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).](image)

![Fig. 3. Change in tumor markers (CEA and CA15–3) after administration of $^{89}$SrCl$_2$: serum CEA and CA 15–3 levels gradually decreased after $^{89}$SrCl$_2$ injection.](image)
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 ± 16Gy) (9). This fact sug-
gests 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 reduc-
tion of hot spots after administration of \( ^{89}\text{SrCl}_2 \). We
assume that anti-cancer effects of \( ^{89}\text{SrCl}_2 \) might have
correlated 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 pallia-
tive 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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