Zoledronic acid-induced regression of multiple metastases at nonskeletal sites

Bisphosphonates have been shown to reduce skeletal complications in individuals with bone metastases secondary to a wide range of solid tumors including lung, breast, and prostate cancer [1]. They are widely administered as palliative agents together with chemotherapy, hormonal therapy, or irradiation [2]. In addition, several types of cancer cells including hematologic malignancies respond to bisphosphonates in vitro, with such effects having been attributed, at least in part, to inhibition of the Ras-signaling pathway [3]. We now report an unusual case in which tumors in visceral organs and soft tissues responded markedly to treatment with the bisphosphonate zoledronic acid (ZA) alone, with the performance status of the patient improving in the absence of chemotherapy.

A 69-year-old man with no significant past medical history presented with pain in his left hip joint at our hospital in January 2007. X-ray examination revealed an osteosynthetic change in his left femur, and a metastatic tumor in his left thigh bone was indicated. Positron emission tomography with 2-[fluorine-18]fluoro-2-deoxy-D-glucose (FDG–PET) revealed uptake of the tracer at multiple sites including the left femur, right rib, left scapula, bilateral adrenal glands, s.c. tissue of the right gluteal region, and abdominal lymph nodes (Figure 1A, left panel). Concomitant computed tomography (CT) revealed tumors of various sizes at multiple sites corresponding to those of tracer uptake, with enlargement of the left adrenal glands apparent from a diameter of 50.2 mm. Biopsy specimens were obtained from the putative tumor on the left femur and the s.c. nodule of the right buttock. On the basis of the morphological and immunohistochemical staining characteristics of the specimens, a histopathologic diagnosis of spindle cell carcinoma was made, but the primary site of the tumor was not determined. The patient’s general condition was poor, and he had an Eastern Cooperative Oncology Group performance status of three at the time of diagnosis. Systemic chemotherapy was therefore not selected, and palliative care was commenced. Together with prescription of narcotics and 20 Gy of radiation...
to the left femur, ZA (4 mg/body) was administered i.v. every 4 weeks to reduce bone pain. After 6 months, his general condition was dramatically improved and follow-up FDG–PET revealed decreased uptake of the tracer in metastases not only in bone including the right rib, which was not irradiated, but also in the adrenal glands, abdominal lymph nodes, and s.c. tissue of the right buttock (Figure 1A, right panel). Unexpectedly, CT revealed that tumors in the adrenal glands had shrunk markedly, with the diameter of the left gland having decreased from 50.2 mm (Figure 1B, left panel) to 26.4 mm (Figure 1B, right panel), and the s.c. tumor in the right buttock was no longer detectable.

As far as we are aware, there have been no other reports of a tumor at a nonskeletal site responding to bisphosphonate treatment alone. ZA was recently shown to have efficacy as a preventive agent for cancer recurrence in premenopausal women with early-stage breast cancer [4]. This previous study suggested that ZA was able to prevent cancer recurrence not only in bone but also in nonskeletal organs including the contralateral breast, lung, and liver. The present case supports the notion that ZA targets not only osteoclasts, a major contributor to the tumor microenvironment in bone, but also tumor cells themselves, as has been shown in preclinical studies [3]. Further clinical evaluation of ZA for treatment of cancer is warranted.

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Figure 1. Positron emission tomographies with 2-[fluorine-18]fluoro-2-deoxy-D-glucose before (A, left panel) and after (A, right panel) zoledronic acid treatment, and the corresponding computed tomographies before (B, left panel) and after zoledronic acid treatment (B, right panel) are shown.