Types of bone metastases in women with breast cancer undergoing systemic treatments

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Dear Editor,

We read with great interest the article published in your journal by Quattrocchi et al. presenting a retrospective analysis of the computed tomography (CT) appearance of bone metastases in breast cancer patients [1]. A higher incidence of osteosclerotic bone metastases was reported in the period 2001–2005 compared with the period 1996–2000. More specifically, during the 1996–2000 period, CT evaluation revealed that 53.6% of patients had lytic, 32.1% mixed and 14.3% sclerotic bone metastases. The corresponding values for the 2001–2005 period were 9.4%, 71.9% and 18.7%, respectively. No significant correlation was found between the radiological appearance of bone metastases and histological type or grade or systemic treatments such as chemotherapy or antiestrogens. The higher prevalence of osteoblastic lesions in the years 2001–2005 was attributed to the use of zoledronic acid treatment [1].

We recently published two studies in which CT was used to group patients according to type of bone metastases (recruitment period 2003–2006) [2, 3]. Of these patients, 34 suffered from metastatic bone disease due to breast cancer, and the percentage of patients with lytic, mixed and sclerotic bone lesions was 26.5%, 44.1% and 29.4%, respectively. From these patients, 29/34 had undergone hormonal therapy in the past, and all had received at least one cycle of chemotherapy. None of the patients had received bisphosphonates prior to the baseline evaluation with CT. These results suggest that systemic treatments such as chemotherapy and hormonal therapy may also alter the radiological appearance of bone metastases. This is also suggested by other literature data, as Bonadonna et al. found that breast cancer patients who received chemotherapy had mostly mixed or sclerotic bone metastases, which were asymptomatic in 66% of cases [4]. In contrast, 66% of breast cancer patients with metastatic bone disease who had not received chemotherapy had lytic lesions, and 70% were symptomatic [5].

Another important aspect that should be noted is that the above results show that the level of bone resorption at metastatic bone sites correlates with patient morbidity levels, something that was also revealed in the study investigating the correlation between types of bone metastases and patients’ clinical status [2]. Consequently, systemic treatments may not only modify the radiologic appearance of bone metastases but also the level of suffering. It would be very interesting if the authors of the study on which we are commenting could provide data on patients’ symptoms (pain) for the years 1996–2005. We agree with the authors that further studies are required to assess the impact of systemic treatment on the radiologic appearance of bone metastases.

Yours sincerely,

Vassilios Vassiliou and Dimitrios Kardamakis.
We are grateful for the interest our work has generated and for the observations that have been made. Bone metastases represent the very advanced phase of the breast cancer disease, and the radiological appearance of bone metastases is affected by exposure to different hormonal and chemotherapeutic drugs and radiation therapy. Moreover, other factors such as duration of bone disease and histological type of primitive breast cancer may influence the radiological appearance of bone metastases.

Our study [1] was carried out by retrospectively reading computed tomography (CT) examinations. The relative prevalence of osteolytic, osteosclerotic and mixed bone metastases that we observed should be considered spurious due to the retrospective nature of our work, with consequent methodological limits as stated, especially in the association of radiological appearance of bone metastases with symptoms such as pain or with exposure to specific drugs. The only evidence of a specific possible association we observed was that regarding zoledronic acid, because it was administered to all candidate patients in our oncology department beginning in 2003.

To overcome the limitations of that retrospective study, we recently prospectively evaluated the effect of zoledronic acid on the radiological appearance of bone metastases, showing a net effect of zoledronic acid towards bone sclerosis over an observation period of 12 months [2]. Even though it was not possible to compare the study population with a control group without zoledronic acid, we never observed a decrease in bone density in our patients. Increased density was documented in both patients with partial extraskeletal response (responder) and with disease stability or progression (16/23) (nonresponder) [2]. The correlation of radiological appearance of bone metastases with the clinical status of patients is mandatory, and Vassiliou et al. [3, 4] recently provided interesting data. In our prospective study, we observed patient’s skeletal-related events (SRE) in 12 out of 23 patients as an objective clinical measurement. To determine the effect of zoledronic acid on clinical response, we assessed the frequency of SREs and time to the first SRE and found no correlation with increased bone density, at least in our small group of patients. In this regard we are continuing to collect data.

Moreover, we are oriented towards removing the “mixed” definition in the CT classification of bone metastases, using, in our opinion, a more consistent denomination of predominantly lytic or predominantly sclerotic bone metastases, on the basis of the average bone density measured at CT. The mixed definition, in fact, is a qualitative measurement, making difficult any comparison between studies performed in different institutions.

In summary, we still have not found a clear impact of i.v. zoledronic acid administration on skeletal clinical response in patients with bone metastases. Further studies will be necessary to find functional imaging measurements, particularly to assess the biological effects of bisphosphonates on the vitality of tumour cells at bone metastatic sites.

Response

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