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REVIEW ARTICLE

Prostate cancer is not breast cancer

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ABSTRACT

Cancers of the prostate and breast are hormone dependent cancers. There is a tendency to equate them and apply same algorithms for treatment. It is pointed out that metastatic prostate cancer with bone-only disease is a potentially fatal condition with a much poorer prognosis than metastatic breast cancer and needs a more aggressive approach.

Key words: *Bone-only disease, metastatic prostate cancer, prognosis*

INTRODUCTION

Solid tumors, when metastatic, are incurable. Exceptions such as testicular tumors and gestational trophoblastic disease do exist, but this is, unfortunately, true for the vast majority of cases. This leads to caution on the part of medical oncologists who prefer minimal therapy striving for good quality of life over aggressive chemotherapy with curative intent. Wait and watch is one option; hormone dependent tumors (a percentage of breast cancers and all prostate cancers) provide a good opportunity to play around with less toxic drugs in an effort to delay administration of chemotherapy for as long as possible.

This is reflected in the current guidelines for management of metastatic breast cancer (MBC),[1] where the bar for aggressive treatment has been further raised recently by defining "visceral crises" as not the mere presence of visceral metastasis, but metastasis to visceral organs compromising organ function.

The same reluctance to start chemotherapy is carried on to the management of prostate cancer with chemotherapy recommended only when the tumor becomes castrate resistantly. The availability of newer hormonal agents (abiraterone, enzalutamide) has pushed this option further back. However, there is a danger in equating prostate cancer with breast cancer. I believe that by unconsciously equating bone disease in prostate with that in breast cancer, just because hormonal therapy is available for both, we are doing our patients of metastatic prostate cancer a disservice.

There is evidence that bone metastasis of prostate cancer is not as "benign" as bone disease of breast cancer. Other than the obvious blastic versus lytic difference, which could lie at the molecular level,[2] bone metastasis in prostate cancer is deadlier than that in breast cancer.

First, bone metastasis is common, but not inevitable in breast cancer, in sharp contrast to prostate cancer where metastatic disease usually starts in the bone and has a poor outcome. A population based study from Denmark (1999 to 2007) of 23,087 patients of prostate cancer[3] showed that 5 years survival was 3% in the group with bone metastasis (vs. 56% in those without). A similar study[4] showed a higher 5 years survival (8.3%) in breast cancer with bone metastases; this despite more associated visceral disease (For instance, a seminal study from Guys Hospital[5] from 1979 to 1984 showed that only 70% of women dying of MBC will have bone metastasis (while, by definition, all had metastases elsewhere).

Secondly, visceral disease is much less common in prostate cancer, even in terminal stages. A retrospective study from Royal Marsden, UK showed that visceral metastasis in prostate cancer appears late;[6] the frequency of radiologically detected visceral disease 3 months before death was only 32%. Thus, 68% of prostate cancer patients die without ever developing visceral disease. In fact, survival can be predicted by the degree of bone involvement at detection of visceral disease, varying from 6.1 months in men with more than six bone metastases to 18.2 months in men with no bone metastases ($P = 0.001$). It is the bone disease that determines survival; waiting for visceral metastasis is fatal, literally. Death is a paraneoplastic

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syndrome in prostate cancer, in the sense that patients can die without involvement of vital organs.

Two recent trials show the "it's only bone disease, we can wait" approach to prostate cancer is the wrong approach; attacking bone metastasis improves survival. First, the Alpharadin in symptomatic prostate cancer trial[7] with radium Ra 223 that used an alpha transmitter specific to bone, which targets tumor cells with radioactivity showed an increase in survival. This underlines the fact that bone disease in prostate cancer does determine survival. Simply improving bone strength (such as by bisphosphonates and denosumab) does not change survival.

The other trial, CHAARTED,[8] showed improved survival of 17 months in high volume disease (defined as visceral disease, or more than 4 bone lesions with at least one beyond pelvis and vertebral column) in hormone sensitive metastatic prostate cancer exposed to chemotherapy right at the beginning (The negative French trial GETUG AFU15 had mainly low volume disease).[9] In this trial, only about a third of patients had visceral metastasis, again underlying the futility of waiting for visceral metastasis as a trigger for starting chemotherapy (387 of the 514 patients with high volume disease had bone metastasis only; the other 125 had bone and visceral metastasis; the forest plot clearly shows the benefit for bone-only disease).

Hence here is a plea to fellow medical oncologists. Please don't equate bone-only metastatic prostate cancer with MBC. Don't wait for visceral metastasis in prostate cancer, and definitely not for visceral crises. The correct time to start chemotherapy in metastatic prostate cancer is upfront, in a fit, hormone sensitive patient with high volume disease (by which I mean 4 or more bone metastasis).

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Conflicts of interest

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