

Journal Watch

Cytokeratin-positive cells in the bone marrow and survival of patients with stage I, II, or III breast cancer.

Braun S, Pantel K, Muller P, Wolfgang J, Hepp F, Kentenich C, et al. The New England J of Med 2000; 342(8):525-533.

Prepared by: : Dr. Robin Fainsinger

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Abstract:

Background: Cytokeratins are specific markers of epithelial cancer cells in bone marrow. We assessed the influence of cytokeratin-positive micrometastases in the bone marrow on the prognosis of women with breast cancer.

Methods: We obtained bone marrow aspirates from both upper iliac crests of 552 patients with stage I, II, or III breast cancer who underwent complete resection of the tumor and 191 patients with nonmalignant disease. The specimens were stained with the monoclonal antibody A45-B/B3, which binds to an antigen on cytokeratins. The median follow-up was 38 months (range, 10 to 70). The primary end point was survival.

Results: Cytokeratin-positive cells were detected in the bone marrow specimens of 2 of the 191 control patients with nonmalignant conditions (1 percent) and 199 of the 552 patients with breast cancer (36 percent). The presence of occult metastatic cells in bone marrow was unrelated to the presence or absence of lymph-node metastasis ($P = 0.13$). After four years of follow-up, the presence of micrometastases in bone marrow was associated with the occurrence of clinically overt distant metastasis and death from cancer-related causes ($P < 0.001$), but not with locoregional relapse ($P = 0.77$). Of 199 patients with occult metastatic cells, 49 died of cancer, whereas of 353 patients without such cells, 22 died of cancer-related causes ($P < 0.001$). Among the 301 women without lymph-node metastases, 14 of the 100 with bone marrow micrometastases died of cancer-related causes, as did 2 of the 201 without bone marrow micrometastases ($P < 0.001$). The presence of occult metastatic cells in bone marrow, as compared with their absence, was an independent prognostic indicator of the risk of death from cancer (relative risk, 4.17; 95 percent confidence interval, 2.51 to 6.94; $P < 0.001$), after adjustment for the use of systemic adjuvant chemotherapy.

Conclusion: The presence of occult cytokeratin-positive metastatic cells in bone marrow increases the risk of relapse in patients with stage I, II, or III breast cancer.

Comments:

Strengths/uniqueness: This report presents a large cohort of patients comprehensively studied and followed for four years.

Weakness: There is no discussion of whether the follow-up may have been influenced by knowledge of presence or absence of micrometastases. We are not told whether patients were informed of their micrometastases status, and the ethics of withholding this information.

Relevance to Palliative Care: The confirmation of early micrometastases (often already present in Stage I) is important information for palliative care practitioners, who frequently have to counsel distressed patients and family over issues of guilt (e.g. "I should have done self-examination/mammography") and anger (perception of failure of the health care system).