Limitations of the immunocytochemical detection of isolated tumor cells in frozen samples of bone marrow obtained from melanoma patients.

Abstract:
We report on a case of a 70-year-old woman with an ocular melanoma, which was diagnosed and treated 14 years ago. The patient was referred to the hospital with a suspected lymphoma. Cytological examination of bone marrow proved a marked infiltration with melanoma cells. Because detection of isolated tumor cells in the bone marrow of patients with various types of tumors was shown to be of prognostic significance and since current tumor-staging techniques are unable to detect single disseminated tumor cells or small aggregates of tumor cells, which might be the seed for subsequent metastatic relapse, we therefore evaluated the feasibility of immunocytochemical screening of bone marrow aspirates of 36 melanoma patients in different clinical stages using three monoclonal antibodies against melanoma-associated antigens in comparison with 43 non-melanoma control patients. Two of these antibodies (HMB45 and NKI-beteb) are directed against the melanoma antigen gp100/pmel17, whereas the third one (TA99) recognizes gp75/Tyrosinase-related protein 1 (TRP-1). None of the patients demonstrated a macroscopic bone marrow infiltration as was present in our patient with metastatic ocular melanoma. Seven (20.6%) of the 34 eligible melanoma patients presented with cells in the bone marrow positive for one or more of the
above-mentioned melanosomal markers. Four of the positive patients were clinically free of tumors by the time of puncture, whereas the remaining 3 patients showed overt metastases in the subcutaneous fat (2 patients) and the brain (1 patient). On the other hand, 20 (66%) of the 29 patients with negative bone marrow findings also presented with clinical advanced disease with overt metastasis in the skin, lymph node, spleen, liver, lung, bone and brain. In conclusion, immunocytochemical screening of bone marrow samples is a feasible procedure that allows the detection of micrometastatic tumor cells in a subset of melanoma patients. Massive invasion of bone marrow with melanoma cells is a rare event even in far-advanced metastatic stages and no clear correlation between tumor load and bone marrow infiltration could be established.

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