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Case Report

Bone Marrow Involvement by Breast Carcinoma Mimicking Blast Cells - Usefulness of CD326

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Abstract

The single cytologic analysis may be sometimes difficult in the differential diagnosis of bone marrow involvement between hematopoetic and non-hematopoietic neoplasia. Here a case of breast carcinoma involving bone marrow and mimicking blast cells is reported and illustrate the helpfulness of flow cytometry analysis using the CD326 as a discriminate marker of carcinoma cells.

INTRODUCTION

Flow cytometry (FCM) is an established method for the characterization of hematological cell, and is routinely used in the diagnosis of lymphoma and leukemia [1,2,3]. However, several reports have now demonstrated its interest to identify non-hematological cells such as carcinoma cells [4]. Multicolor FCM provides the opportunity to evaluate multiple antigens simultaneously and one of antigen interesting in non-hematopoetic neoplasms is Ber-EP4 (CD326). The CD326 antibodies binds indeed to cell membrane glycoprotein on human epithelia and a large range of epithelial tumours, including skin tumours, gastro-intestinal tumours, breast tumours, and tumours of male and female genito-urinary tract express CD326 [4-6]. Therefore, FCM appears helpful to orientate the histopathologist, who can then order a more refined panel of antibodies to precise the cell origin of the tumour.

CASE REPORT

An 84-year-old woman consulted to our institution because of fatigue increased over 2 months and bone pain. Ten years ago, the patient was treated for breast carcinoma and now considered in complete remission.

The blood count was the following: hemoglobin 102 g/L, leukocytes 2, 63 x 10^9/L and platelets 97,00 x 10^9/L. The peripheral blood (PB) smears showed few neutrophil precursors (metamyelocytes/myelocytes) and erythroblasts. Therefore, a bone marrow (BM) aspiration was realized to eliminate a secondary therapy-related hematopoietic disease. The BM smears analysis identified several isolated mononuclear cells including blast-like cells, which showed dispersed chromatin, high nuclear-cytoplasmic ratio (Figure A and B; original magnification × 60; May-Grünwald-Giemsa stain). In addition, careful screening of BM smears revealed rare cluster of neoplastic cells that argue to involvement by carcinoma cells rather blast cells (Figure C and D).

Immunophenotype by multiparameter flow cytometry (FCM) was realized on BM suspension. Data were acquired on a BD FACSCanto II cytometer and analyzed with BD FACS DIVA version 6.1 software (*Becton Dickinson, San Jose, CA, USA). The antibodies used were as follows: CD326 (clone Ber-EP4**, FITC), CD45 (clone 2D1*, APC-H7), CD33 (clone P67, 6*, PercPCy5.5), CD19 (J3-119***, PE-Cy7) and CD3 (clone UCHT-1*, APC) (**Dako, Carpinteria, CA, *** Beckman-Coulter, Hialeah, FL, USA). The strategy gating used was first CD45 and side scatter, and the populations of interest (obtained by multiparameter strategy gating) were then analyzed with the focus on identifying the expression of CD326 in CD45 negative (51% of all events) and/or CD45 positive populations (38% of all events). Interestingly, the immunophenotype has confirmed that neoplastic cells identified by cytological analysis corresponded to carcinoma cells (Figure E: carcinoma cells [black: CD45-/CD33- and CD326+; 45% of all events] and hematopoietic cells = granulocytes [pink: CD45+/CD33+/CD326-, 28% of all events], lymphocytes [CD45+/CD33-/CD326- = CD3+ T-cells (blue; 6% of all events), CD19+ B-cells (orange, 2% of all events)] and monocytes [green CD45+/CD326-; 2% of all events]). The distribution and immunological profile of different populations have been compared to these of normal BM [7]. Obviously in normal condition, no CD326 positive cells should be detected that was confirmed in 10 cases (no false positive cases).

DISCUSSION

Although the development of symptomatic BM involvement

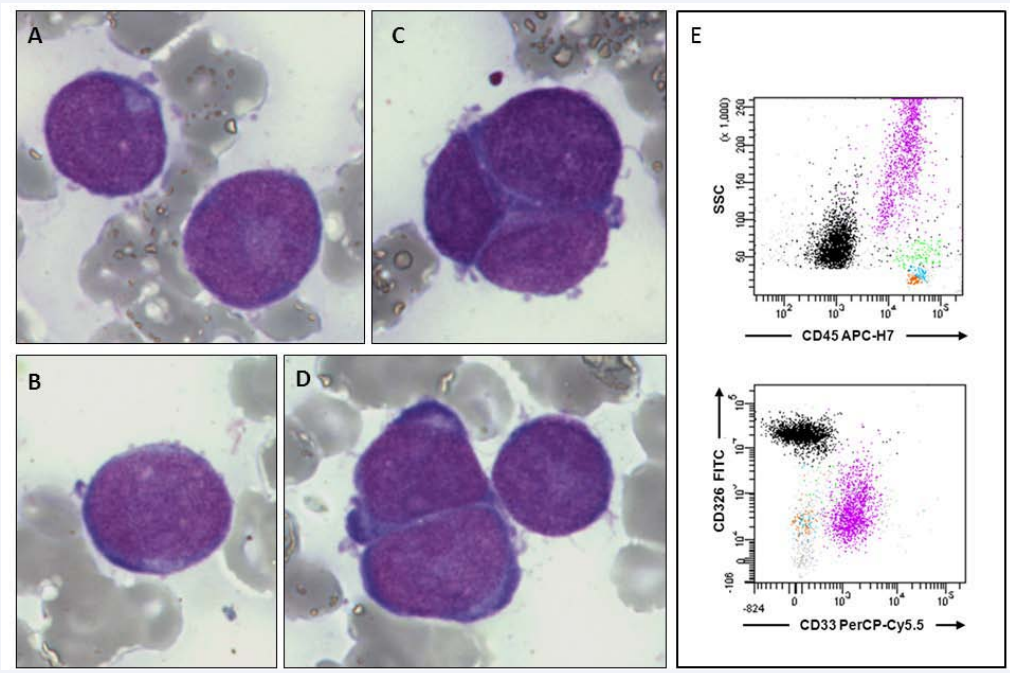

Figure 1 Bone Marrow Aspiration.

is a rare event in the course of metastatic breast cancer, the BM involvement has to be considered in breast cancer patients, in particular in those with bone metastases and otherwise unexplained cytopenia [8]. In this context, the addition of CD326 to the usual leukemia/lymphoma markers appears very helpful since (i) cytology diagnosis may be sometimes difficult and (ii) rare cases of metastatic carcinoma may dimly express the CD45 and some hematopoietic precursors are CD45- and/or dim. Therefore, FCM is a powerful tool to detect carcinoma cells and should be performed side by side with classical morphological and immunocyto (histo)-chemical studies to increase overall diagnostic accuracy. This screening of carcinoma metastasis by FCM is a sensitive, reproducible, very rapid and not too expensive method, with an excellent correlation with cytology as previous demonstrated [3]. Besides FCM will never replace conventional morphology and immunohisto-chemical in the diagnosis of non-haematopoietic neoplasms, but the value of FCM in identifying non-haematopoietic neoplasms as a way to guide subsequent studies, or evaluate potential therapeutic targets, should be considered.

CONCLUSION

Flow cytometry including the CD326 may be rapid method to screen for carcinoma metastasis, and may represent a complementary analysis to the concomitant and careful morphological analysis to avoid misdiagnosising.

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