ORIGINAL PAPER
ΕΡΕΥΝΗΤΙΚΗ ΕΡΓΑΣΙΑ

ARCHIVES OF HELLENIC MEDICINE 1999, 16(4):377–379
ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 1999, 16(4):377–379

Bone marrow touch imprints for detection of epithelial tumor metastases

G. Kjurkchiev,
I. Valkov

Department of Pathology,
Medical University, Sofia, Bulgaria

Τα εντυπώματα μυελού των οστών στον καθορισμό μεταστάσεων επιθηλιακών όγκων

Περίληψη στο τέλος του άρθρου

OBJECTIVE **A total of 284 paired bone marrow biopsies and touch imprints were reviewed in order to select 21 cases with proven metastases from malignant epithelial tumors and to estimate the role of bone core touch imprints in the initial, preliminary diagnosis of metastatic bone disease.** METHOD **Eight Pappanheim stained touch imprints and eight H&E stained histological sections were prepared from every biopsy and reviewed by two pathologists independently.** RESULTS **The tumor cells were identified according to universally accepted criteria for malignancy. There was no positive touch imprint for which the biopsy was negative for tumor cells nor positive biopsy for which the cytogram was negative.** CONCLUSIONS **The method of examination of touch imprints from bone marrow trephine biopsies is rapid, reliable and sensitive. It can be used as a first step for detection of metastases from malignant epithelial neoplasms after careful examination of all cytograms.**

Key words

Bone marrow
Metastatic tumor
Touch imprints

Submitted 1.9.1998
Accepted 20.4.1999

During the past two decades bone marrow trephine biopsy has become a routine method for the diagnosis of bone marrow lesions. This is due in part to improved methods for biopsy harvesting and processing.[1] The advantages of examination of histological sections have been widely described and discussed.[1–3]

In some cases it is necessary to give a quick, preliminary description of the bone marrow cells before the final histological examination and diagnosis are made, particularly in cases with metastases from distant solid non-hematological malignancies. These are usually manifested by unexplained anemia, thrombocytopenia and weight loss which may be misinterpreted as signs of hematological malignancy. Diagnosis from histological preparations may be delayed due mainly to time taken for decalcification and processing of the biopsy cylinder but smears of bone marrow aspirate or touch imprints from the core biopsy can provide a quick picture. Advantages and disadvantages of the cytological methods are described in the literature. Bone marrow aspirate has been found reliable marrow aspirate.[4,5] Only one paper is dedicated to the role of touch imprints[6] and most cytopathologists prefer aspirates, since they provide a higher number of cells for evaluation. The purpose of this study is to assess the value of touch imprints from trephine biopsies for the rapid, preliminary diagnosis of metastases in the bone marrow from non-hematological malignancies.

MATERIAL AND METHOD

A total of 284 paired bone marrow histological sections and touch imprints were retrospectively reviewed in order to select 21 cases with metastases from solid tumors. All the specimens were retrieved from the files of the Central Laboratory of Cytopathology, Medical University, Sofia, Bulgaria. Hematopoietic malignancies were excluded from the study. The study period ran between 1 January 1994, and 1 June 1996. There was no preliminary information about the presence of malignancy in the clinical charts.

Bone marrow biopsies were obtained from the posterior iliac crest with an 8 gauge Jamshidi needle at the Department of Hematology. Immediately after delivery of the biopsy specimen in a dry sterile vial, eight touch imprints were prepared on the surface of an object glass from the sides of the cylinder by light touch. After air drying, the cytograms were stained according to the May-Grunwald-Giemsa/Pappenheim

method. The cytograms were interpreted at 400× magnification by the two authors independently. If the nature of the cells was not clear, the cytograms were examined. The preliminary conclusion was reported to the Department of Hematology for further direction of the patient. The biopsy specimen was subsequently placed in neutral buffered formaline, washed, decalcified in a water solution of hydrochloric acid for 35–40 minutes, washed again, processed and embedded in paraffin. Eight lengthwise sections from the core cylinder were stained with Hematoxylin & Eosin, van Gieson and Gomori silver staining. These histological sections were used as controls for the presence of tumor cells.

RESULTS

Of 284 paired bone marrow biopsies and cytograms, there were 21 pairs in which both cytological and histological preparations were positive for metastatic tumor cells. There were no positive touch imprints for which the biopsy was negative, nor positive biopsies for which the cytogram was negative. The origin of the primary malignancies was as follows: prostate-14 cases, female breast-4, lungs-2, kidney-1.

Epithelial tumor cells were recognized according to universally accepted criteria. They may be single, detached cancer cells or tightly packed clusters of cells (figures 1, 2). Usually they had large, hyperchromatic nuclei with rough nuclear chromatin. The nucleoli were prominent and sometimes multiple (fig. 3). The cytoplasm varied in amount and often was poorly preserved. In almost every cytogram naked nuclei with prominent nucleoli, sometimes in groups of two, three or more were found. In 15 cases the metastatic cells were identified in all eight touch imprints although in different numbers: in four of these cases scattered tumor cells were found only singly and were identified only after careful examination of the cytogram. In two cases the number of tumor cells was considerable in all the touch imprints.

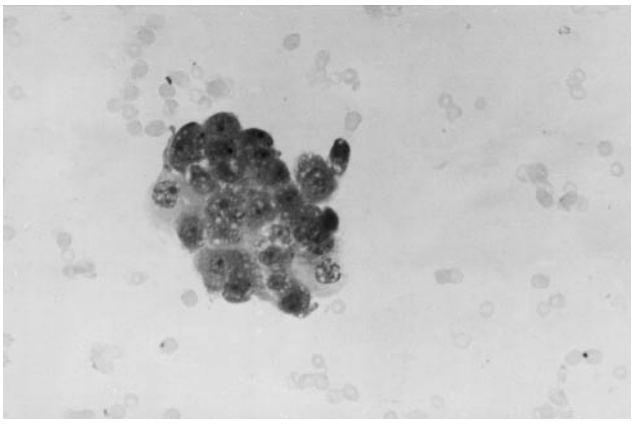

Figure 1. Cluster of malignant cells from prostatic cancer. Pappenheim staining×150.

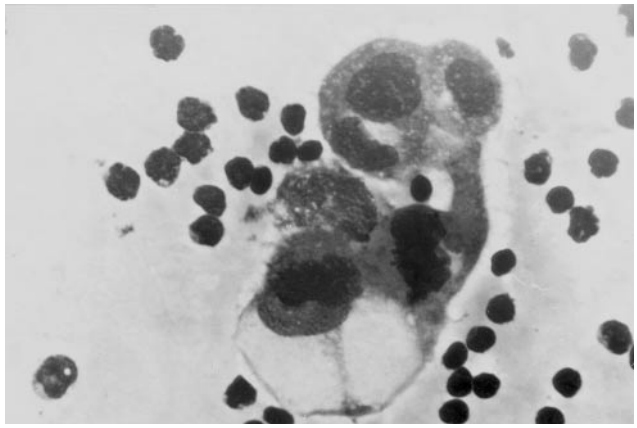

Figure 2. Cluster of malignant cells from breast cancer. Pappenheim staining×400.

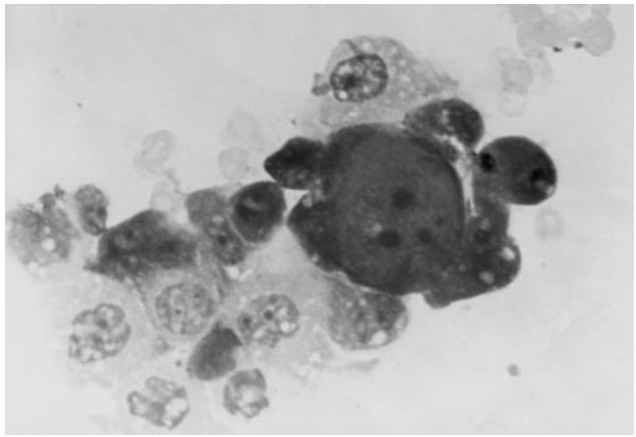

Figure 3. Metastatic cells with large, prominent nucleoli. Pappenheim staining×400.

DISCUSSION

The specificity and sensitivity of the different methods for diagnosis of bone marrow metastatic lesions have been subject of divergent views.[3–5] This may in part be explained by variation in the number of specimens reviewed, the staining methods, the extent of marrow replacement by malignant cells, the presence or absence of fibrosis and/or necrosis in the biopsy sections, the technique of preparing the cytogram, etc. Mitchell et al have found bone marrow smears alone unsatisfactory for the diagnosis of metastatic lobular breast carcinoma.[7] Some authors stress the complementary roles of bone marrow aspirate and biopsy for detection of malignancy.[8,9]

Dombernowsky et al maintain that review of cytological specimens from the bone marrow is not sufficient for the initial diagnosis of metastatic tumors.[9] Other authors emphasize the usefulness of a panel of antibodies as a reliable tool for the identification of metastatic malignancy in bone marrow.[7]

In this study it was most of the touch imprints were positive for metastatic tumor cells, although in different numbers. The small numbers of tumor cells in some cytograms may be explained by the presence of fibrosis secondary to metastasis. This finding was confirmed on examination of the histological section from the bone core cylinder. Another possible explanation for the small cell numbers is that the long period of time between biopsy harvesting and touch imprint preparation allows the drying of the surface of the bone marrow trephine. For most of the specimens in this study this period was 45–50 minutes.

Concerning efficacy, at 400×magnification the imprints with a low cell count required about twice as long for the detection of tumor cells, compared with a normocellular cytogram. The conclusion that metastatic epithelial cells are present should follow an assiduous search in the cytogram, otherwise small clusters and single cells may easily be overlooked and false negative diagnosis made.

In this study all the histologic sections used as controls were positive for metastatic tumor cells. It is beyond the scope of this study to compare these two approaches but it can be noted that the touch imprint is at least as sensitive as the standard histological preparation from the same biopsy specimen. In the rapid preliminary diagnosis no attempt was made to determine the location of the primary malignancy, but only to establish whether the cells were epithelial or not. The location of primary tumor was established after processing and examination of histological sections.

In conclusion, the examination of touch imprints from bone marrow trephine biopsies is a rapid, reliable and sensitive method which can be used as a first step for the detection of metastases from malignant epithelial neoplasms.

ΠΕΡΙΛΗΨΗ

Τα εντυπώματα μυελού των οστών στον καθορισμό μεταστάσεων επιθηλιακών όγκων

G. KJURKCHIEV, I. VALKOV

Department of Pathology, Medical University, Sofia, Bulgaria

Αρχεία Ελληνικής Ιατρικής 1999, 16(4):377–379

ΣΚΟΠΟΣ Από 284 παράλληλες βιοψίες και εντυπώματα μυελού των οστών επιλέχθηκαν 21 περιπτώσεις με αποδεδειγμένες μεταστάσεις κακοήθων επιθηλιακών όγκων, με σκοπό τη διερεύνηση του ρόλου των εντυπωμάτων του μυελού των οστών στην αρχική διάγνωση των μεταστατικών όγκων των οστών. **ΥΛΙΚΟ-ΜΕΘΟΔΟΣ** Από κάθε βιοψία παρασκευάστηκαν 8 εντυπώματα, που χρώστηκαν κατά Pappenheim, και 8 ιστολογικές τομές, που χρώστηκαν με αιματοξυλίνη-ηωσίνη και εξετάστηκαν ανεξάρτητα από δύο παθολογοανατόμους. **ΑΠΟΤΕΛΕΣΜΑΤΑ** Τα κύτταρα των όγκων αναγνωρίστηκαν σύμφωνα με τα διεθνώς αποδεκτά κριτήρια κακοήθειας. Δεν παρατηρήθηκαν θετικά εντυπώματα που να αντιστοιχούσαν σε βιοψία αρνητική για κύτταρα όγκου ούτε βιοψίες, τα αντίστοιχα εντυπώματα των οποίων ήταν αρνητικά. **ΣΥΜΠΕΡΑΣΜΑΤΑ** Η εξέταση των εντυπωμάτων του μυελού των οστών είναι ταχεία, αξιόπιστη και ευαίσθητη και μπορεί να χρησιμοποιείται ως πρώτο βήμα για τον προσδιορισμό μεταστάσεων κακοήθων επιθηλιακών

Λέξεις ευρετηρίου: Εντυπώματα μυελού των οστών, Μεταστατικοί όγκοι, Μυελός των οστών

References

1. JAMSHIDI K, SWAIM WR. Bone marrow biopsy with an unaltered architecture: a new biopsy device. *J Clin Lab Med* 1971, 77: 335–341
2. CECI G, FRANCIOSI V, NIZZOLI R, FIORITO D. The value of bone marrow biopsy in breast cancer at time of diagnosis: a prospective study of 280 biopsies. *Hum Pathol* 1994, 25:714–718
3. CONTRERAS E, ELLIS L, LEE R. Value of the bone marrow biopsy in the diagnosis of metastatic carcinoma. *Cancer* 1972, 29:778–783
4. GARRETT TY, GEE TS, LIEBERMANN PH. The role of bone marrow aspiration and biopsy in detecting marrow involvement by non-hematologic malignancies. *Cancer* 1976, 38:2401–2403
5. HIRSCH R, HANSEN HH, HAINAV B. Bilateral bone marrow examination in small cell anaplastic carcinoma of the lung. *Acta Pathol Microbiol Scand Secta* 1979, 87:59–62
6. BEARDEN JD, RATKIN GA, COLTMAN CA. Comparison of the diagnostic value of bone marrow biopsy and touch imprint in neoplastic disease. *J Clin Pathol* 1974, 24:738–740
7. MITCHELL A, FIORITTO D, CORKILL M, HUFFER W, STEMMER S. Bone marrow involvement by lobular carcinoma cannot be identified reliably by routine examination alone. *Hum Pathol* 1994, 25:781–788
8. ATAC B, LAWRENCE C, GOLDBERG N. Metastatic tumor: the complementary role of the bone marrow aspirate and biopsy. *Am J Med Sci* 1991, 302:211–213
9. DOMBERNOWSKY P, WORM AM, HAINAW B. Problem of tumor cell identification in the bone marrow. *Cancer* 1966, 19:1527–1533

Corresponding author:

G. Kjurkchiev, Medical University, Department of Pathology, 2 Zsrave street, 1431 Sofia, Bulgaria