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BRIEF ORIGINAL

Examination of cytological smears and cell blocks of pleural fluid: Complementary diagnostic value for malignant effusions

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KEYWORDS
Pleural effusion;
Cytology;
Cell blocks

Abstract
Objectives: To evaluate the independent usefulness of pleural fluid smear and cell block (CB) preparations for the diagnosis of malignant effusions.
Patients and methods: A total of 632 cytological smears and 554 CBs from 414 consecutive patients with malignant effusions were retrospectively evaluated.
Results: The diagnostic yield of a first specimen was 44% regardless of whether a smear or CB cytologic examination was performed. The use of subsequent separated specimens increased the identification of malignancy to 56%. Overall, 11% of samples found to be negative by cytologic smears showed malignant cells on CBs, whereas 15% of negative CBs were reported as positive on smear slides. Pleural fluid specimens with low red and/or white blood cell counts more frequently resulted in the generation of suboptimal CB preparations.
Conclusions: If CBs and smears are prepared and examined, the percentage of positive diagnoses will be greater than if only one method is used.

PALABRAS CLAVE
Derrame pleural;
Citología;
Bloques celulares

Examen del frotis citológico y bloque celular del líquido pleural: valor diagnóstico complementario en los derrames malignos

Resumen
Objetivos: Evaluar la utilidad independiente de frotis y bloques celulares (BC) del líquido pleural para diagnosticar derrames malignos.

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Pacientes y métodos: Se evaluaron retrospectivamente un total de 632 frotis citológicos y 554 BC de 414 pacientes consecutivos con derrame pleural maligno.
Resultados: La sensibilidad diagnóstica de una primera muestra fue del 44%, tanto en frotis como en BC. El análisis de muestras separadas ulteriores aumentó al 56% la identificación de derrames malignos. Globalmente, el 11% de muestras negativas mediante frotis mostraron células malignas en los BC, mientras que el 15% de BC negativos resultaron positivos en el estudio del frotis. Los líquidos pleurales con recuentos bajos de hematíes o leucocitos produjeron con mayor frecuencia BC insuficientes para diagnóstico.
Conclusiones: Si se evalúan frotis y BC, el porcentaje de resultados positivos es superior que si se emplean estas técnicas de forma aislada.

Introduction

Cytologic examination of pleural fluid is the easiest and least invasive way to diagnose malignant effusions, although it has limited sensitivity.[1] The routine cytopreparatory technique consists of sample centrifugation, smearing of the cell deposit and Papanicolau staining.[2] Scientific guidelines indicate that preparing cell blocks (CBs) from pleural effusion samples, in addition to smears, to allow for ''microhistology'' of the cellular solid portion may lead to greater diagnostic accuracy.[3] However, the magnitude of this diagnostic yield increase has barely been reported. Moreover, since CB methods can be time consuming and labor intensive they may not be routine in some centers, only being performed at the discretion of the pathologist or clinician. Our aim was to analyze, in the largest series reported to date, the usefulness of CBs beyond conventional cytological smears in the diagnosis of malignant effusions. Biochemical fluid characteristics predictive of the generation of inappropriate or insufficient CB material were also addressed.

Methods

The medical records of all consecutive patients at our institution between October 2010 and June 2016 whose pleural fluids had been sent for conventional cytology and/or CB examination, based on the attending physician's criterion, were retrospectively reviewed. The local ethics committee approved the study protocol.

Pleural fluid specimens were collected in heparinized tubes. For routine cytology, 5 mL of fluid were centrifuged at 2000 rpm for 10 min, the supernatant discarded, and the glass slides prepared and stained with Papanicolaou stain. For CB preparation, 10 mL of material were centrifuged as above, the supernatant decanted, and the cell button obtained (with the addition of molten agar if necessary) fixed in 10% formaldehyde, paraffin embedded and stained with hematoxylin–eosin. Immunocytochemistry panels on CB sections were applied according to the suspected tumor type and cytomorphology.

An effusion was categorized as definite malignant if malignant cells were detected upon cytological examination of pleural fluid or biopsy specimens. A diagnosis of probable malignant effusion was made on patients who met the following: (a) a known primary tumor or extrapleural metastases of undetermined origin, and (b) a pleural exudate with negative fluid cytological findings, after ruling out other potential causes of fluid accumulation by clinical data (e.g. negative pleural fluid cultures, low pleural adenosine deaminase levels), imaging (e.g. CT angiography) and, in selected cases, pleural biopsy. All patients with probable MPE were followed up long enough to determine whether alternative causes of the effusion became clinically apparent.

Sensitivity of fluid smears and CBs were calculated. The Kruskal–Wallis test was used to compare pleural fluid biochemistries (i.e., red and white blood cell counts, differential white cell count, protein, lactate dehydrogenase (LDH), glucose, adenosine deaminase, pH and C-reactive protein) between patients with representative and suboptimal CB material. The statistical significance level was set at 0.05 (two-tailed).

Results

During the study period, 632 cytological smears and 554 CBs from 414 patients (median age 70 years, 56% men) who had malignant effusions were examined. The etiological distribution of the primary tumors is displayed in Table 1. Also, there were 726 patients eventually diagnosed with a benign pleural condition for whom pleural fluid cytological analyses were ordered (a total of 945 smears and 507 CBs) and yielded negative results; all were excluded for the purpose of the study.

Although all effusions were submitted to a first cytologic examination, CBs were initially obtained from 380 (92%) specimens, but 46 (12%) yielded suboptimal material. Whether a first cytological smear or CB examination was used, both had identical sensitivity for identifying malignancy: 44% (95% CI 39–50%). Notably, of 184 cancer patients who had a first negative cytological exam, CB was diagnostic of malignancy in 18 (10%, 95% CI 6–15%). Conversely, among the 186 patients with a first negative CB examination,

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