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Cytokeratin 19 (CK19) as a Tumor Marker in Pleural Effusion

Mona Z Zaghloul

Microbiology Unit, Department of Clinical Pathology, Ain Shams University Hospitals, Cairo, Egypt

Pleural effusion is a common clinical presentation. Approximately 20% of pleural effusions are due to malignancy, and 50% of these are due to primary lung cancer [1]. A malignant pleural effusion may be the initial presentation of cancer in 10 to 50% of patients [2]. Cytological examination of malignant effusion is important because it is easy and noninvasive. However, highly suspected cases of malignant effusion with repeated negative cytological findings are sometimes encountered [3]. Several tumor markers in pleural fluid have been evaluated to distinguish malignant effusion from benign e.g. carcinoembryonic antigen (CEA) [4] neuron-specific enolase [5] and cytokeratin 19 [6,7]. During the last 10 years, new immunologic and molecular analytic procedures have been developed to diagnose and characterize minimal residual cancer [8]. Malignant pleural effusions often result from malignant tumors transferring into pleural cavity. On 1998, Lockett et al. [9] had developed keratin-19, c-myc and prolactin inducible protein RT-PCR based method to identify axillary lymph node metastases in patients with breast cancer and thought it appeared to be a readily available and highly sensitive method for detecting breast cancer micrometastases.

Cytokeratins constitute the largest intermediate filament protein subgroup and represent a multigene family with more than 20 different types of polypeptides that are divided into acidic type I(CK9-CK23) and basic type II(CK1-CK8) keratins [10]. Their main function is to maintain the epithelial cell integrity and it has roles in cell signaling, stress responses, and apoptosis [11]. Cytokeratin 19 (CK19) belongs to type I cytokeratins, it is one of the most useful markers for diagnosis and management of tumors. CK19 mRNA is expressed in nearly all the epithelial malignancies as breast cancer [12], lung cancer, colorectal carcinoma [13] untreated early-stage cervical carcinomas [14] and papillary thyroid carcinoma [15]. There has been emerging evidence suggesting that CK19 mRNA detection is strongly associated with the presence of metastases or lung recurrence, particularly after surgery [16]. The detachment of cancer cells from a primary tumor is one of the early sequential events in the metastatic cascade. Therefore, surgeons always worry that the manual manipulation of a tumor during an operation might enhance the shedding of cancer cells into the bloodstream [17]. CK19 mRNA was detected in blood in benign and malignant pleural effusions by quantitative RT-PCR [17]. CYFRA 21-1 is an assay which detects the soluble fragments of cytokeratin 19 by ELISA, immunocytochemistry [13,18] flow cytometry [19] and electrochemiluminescense immunoassay on automatic analyzers [18]. On 2013, Pang et al. [19] evaluated the prognostic significance of the serum tumor markers CYFRA21-1, carcinoembryonic antigen (CEA), neuron-specific enolase (NSE), carbohydrate antigen (CA) 125, and CA 19-9 for predicting responses to different chemotherapy regimens in patients with non-small cell lung cancer (NSCLC), they had found that CYFRA 21-1 is the most sensitive of the tumor markers in predicting the response to chemotherapy.

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***Corresponding author:** Dr. Mona Z Zaghloul, Microbiology Unit, Department of Clinical Pathology,Ain Shams University Hospitals, Cairo, Egypt;Tel: 02-24023494; E-mail: monazaki_810@hotmail.com

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