

# New Dimensional Perspectives on Differential Diagnosis of Pleural Effusion

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To the Editor: We appreciate the attentive and interesting article “clinical value of tumor markers for determining cause of pleural effusion” written by Gu *et al.*<sup>[1]</sup> The authors have nicely shown the tumor markers in tuberculous pleural effusion (TPE) differ significantly from those in malignant pleural effusion (MPE) especially when detected in pleural fluid, and there is still no single tumor marker with high sensitivity and specificity in differential diagnosis of pleural effusion (such as TPE and MPE); the combined detection of tumor markers can improve diagnostic sensitivity. Therefore, the authors explored the differential diagnostic value of five tumor markers, including carbohydrate antigen 125 (CA125), carbohydrate antigen 199 (CA199), carcinoembryonic antigen (CEA), neuron-specific enolase (NSE), and squamous cell carcinoma-associated antigen in patients with TPE and MPE. Especially, the discussion section of this article has given readers some inspirations. We can develop new perspectives on the differential diagnosis of pleural effusion from these three aspects of specimen types, inspection methods, and test items.

The authors mentioned the difference of the serum and pleural fluid concentrations of CA125, CA199, CEA, and NSE in MPE and in TPE. Obviously, they were dramatically higher in MPE than in TPE ( $P < 0.05$ ). With the description of “a diagnostic model that involves five tumor markers in serum and pleural fluid” researched by former study, it is clear that the study particularly emphasizes the detection of tumor makers in pleural fluid has high specificity (100.00%) and accuracy (86.92%). Therefore, whether pleural fluid can be used as a specimen type to better distinguish TPE from MPE? This problem requires us to reflect on Trapé *et al.*<sup>[2]</sup> which mentioned that tumor marker concentrations in fluid from patients with malignant effusions were significantly higher than those obtained in benign fluids or serum. However, there are two types of tumor markers: those released/secreted by normal mesothelia such as CA125 and cytokeratin 19 (higher levels in benign fluids than in serum) and non released/secreted tumor markers (low concentrations in benign fluids) such as CEA. Thus, in the differential diagnosis of pleural effusion, could we choose pleural fluid as the specimen type instead of serum?

Wang *et al.*<sup>[3]</sup> reported that the medical thoracoscopy is an effective and safe method for diagnosing pleural effusions of undetermined causes. Medical thoracoscopy should be definitely helpful and

useful in the differential diagnosis of TPE especially in areas with high tuberculosis prevalence. In addition, the authors listed the current available data which indicated that thoracoscopy under local anesthetic is popular among the techniques with the highest diagnostic ability. Meanwhile, it cuts the possibility of aspiration cytology revealing negativity for exudative PE. The method has about 88–96% diagnostic sensitivity for malignant pleural disease. However, such invasive examinations cannot be performed on the elderly, or on those in poor physical conditions. Then, in the selection of inspection methods, do we choose “minimally invasive” or “invasive?”

In the differential diagnosis of pleural effusions, do we choose “traditional” or “novelty” test items? Traditional test items are generally divided into physical and chemical tests, cytological examination, biochemical testing, tumor marker detection and the like. The authors reported that cytological examination is routinely performed. However, the positive diagnostic rate of this technique is about 50% in patients with MPE. In addition, based on the fact that there is no single tumor marker with high specificity and sensitivity, many researchers have shown that tumor markers may help differentiating TPE from MPE. Furthermore, a combination of several tumor markers may improve the diagnostic rate and accuracy for MPE, and an ideal diagnostic combination of tumor markers would have high specificity and sensitivity. Therefore, the author selected tumor markers for better detecting such as joint detection of five tumor markers mentioned in the article for the differential diagnosis of TPE and MPE. Recently, Wang *et al.*<sup>[4]</sup> proposed that accurate differentiating diagnosis is essential for choosing treatment for exudative pleural effusions and exploring diagnostic accuracy of interleukin 27 for TPE. Interleukin 27 as a new test item can be used to diagnose TPE in a high prevalence setting, and a negative result can also be reliably used to rule out TPE in all prevalence settings. In particular, the sensitivity and specificity of interleukin-27 diagnosis of TPE were as high as 92.7% and 99.1%, respectively. Therefore, should we choose

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“traditional” or “novelty” test items for the identification of pleural effusions?

In a word, the efforts of selecting the biological markers and effective diagnostic tools for determining causes of pleural effusion, which are made by clinical medical, have not stopped. Therefore, how do we choose the appropriate type of specimens, inspection methods, and test items for the effective differential diagnosis of benign pleural effusion and MPE such as TPE and MPE are the issues we need to concentrate and consider at the moment.

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### Conflicts of interest

There are no conflicts of interest.

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