Specimen FLD-06 represents a fluid from a patient with a possible malignant condition and could either be a pleural or peritoneal fluid. Two tumor markers typically ordered in such fluids include carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA 19-9), often requested to differentiate between effusions of malignant vs. non-malignant causes and to enhance cytology findings.

At the outset, it should be noted that most FDA-approved methods for CEA and CA 19-9 require the use of serum or plasma. Laboratories using such methods on other fluids (including pleural or peritoneal fluids) must verify their performance on these fluids themselves in accordance with the requirements of CLIA '88.

Serum levels of carcinoembryonic antigen (CEA), a glycoprotein produced during fetal development, are low or undetectable in healthy, nonsmoking adults but may be increased in patients with malignancies which secrete CEA into the circulation (cancers of the gastrointestinal tract, colorectal, liver, lung, breast, ovarian, pancreatic, prostate cancers , medullary thyroid carcinoma).

Analysis of CEA in pleural fluid may be useful in differentiating between a malignant and nonmalignant etiology of pleural effusions. One study found a sensitivity of 52%, specificity of 96% for pleural fluid CEA effusions caused by any type of malignancy (1). Increased pleural CEA performed best in the identification of effusions caused by cancers associated with increased serum CEA concentrations but performed poorly at identifying effusions for cancers not associated with serum CEA elevations (1). In a study of five tumor markers measured in pleural fluids, CEA was found to have the highest accuracy (85.3%) for the diagnosis of malignant vs. benign effusions, classified on the basis of definitive pathologic or cytologic diagnoses (2).

Increased pleural fluid CEA should not be used as the only basis for the diagnosis of malignancy but should be used in conjunction with cytology, imaging, other tumor markers and clinical findings. A low or negative pleural CEA may be found in malignancies that do not secrete CEA such as mesotheliomas, leukemia, lymphoma and melanomas. In addition, non-malignant disorders such as emphysema, hepatic cirrhosis and pancreatitis may be associated with increased pleural CEA (1).

Analysis of CEA in peritoneal fluid may be useful as an adjunct to cytology to differentiate between malignant and benign causes of peritoneal effusions and should be performed in all cases of suspected malignancy in which cytology is negative (3). An increased peritoneal CEA is suspicious (> 6 ng/mL) but not diagnostic of a malignancy related ascites and should not be used as the only criterion of the presence of a malignancy process but should be interpreted in conjunction with cytology and other clinical information.

Serum levels of carbohydrate antigen 19-9 (CA 19-9), a modified Lewis(a) blood group antigen, are low or undetectable in healthy adults but may be increased in patients with malignancies which secrete CA 19-9 into the circulation (pancreatic, bile duct, colorectal, liver, lung, breast, pancreatic, prostate cancers, cholangiocarcinoma). Additionally, approximately 5-10% of the Caucasian population do not

express CA 19-9 because of deficiency of a fucosyltransferase enzyme in Lewis(a) negative blood groups and such patients will have an undetectable CA 19-9 serum level.

Analysis of CA 19-9 in pleural fluid was less efficient compared to CEA with a sensitivity of 35%, specificity of 95% for the diagnosis of malignant effusions in all types of malignancies (1). CA 19-9 in pleural fluids had an overall accuracy of 71.5% for the diagnosis of malignant vs. benign pleural effusions (2). Pleural fluid CA 19-9 have been reported to be increased in patients with malignancies (stomach, cholangiocarinoma, duct, pancreatic, ovarian cancers) but may be low in cancers that do not secrete CA 19-9 (lymphoma, leukemia, melanoma and mesothelioma).

Analysis of CA 19-9 in peritoneal fluid may be useful as an adjunct to cytology to differentiate between ascites of malignant origin and benign causes of ascites. One study found a sensitivity of 19.0%, specificity of 94.5% for peritoneal CA 19-9 for malignant effusions (4). An in house study performed by Mayo Medical Laboratories found that in malignancies associated with an increased serum CA 19-9, a CA 19-9 level of > 32 U/mL is suspicious but not diagnostic of malignancy related ascites (44% sensitivity, 93% specificity) (5). For malignancies not associated with increased CA 19-9 levels (lymphoma, mesothelioma, leukemia, melanoma), CA 19-9 levels were routinely < 32 U/mL (5).

Increased peritoneal fluid CA 19-9 should not be used as the sole basis for the diagnosis of a malignant process but should be used in conjunction with cytology, imaging, other tumor markers and clinical findings.

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