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Title: 1,25-dihydroxyvitamin D in malignant and non-malignant pleural effusions

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Body: Background: Vitamin D (VitD) is a key modulator of host immune response and is raised in patients with lung cancer. However, there are no studies evaluating the levels of VitD in malignant pleural effusions. Objectives: To evaluate the diagnostic role of VitD levels in pleural effusions of various etiologies. Methods: Prospective study of consecutive patients with a new diagnosis of pleural effusion. Exclusion criteria included previous diagnostic/therapeutic attempts or no definite diagnosis after at least 6-month follow up. Pleural fluid and serum samples were collected, protected from light exposure and immediately stored in -20°C until testing for VitD with Chemiluminescent Immunoassay. Results: Fifty patients were studied. Pleural VitD was higher than serum VitD ($p < 0.001$). Pleural VitD did not differ between exudates and transudates ($p = 0.31$) but was significantly higher in malignant compared to benign effusions ($p = 0.037$). VitD levels > 11.6 ng/ml were diagnostic for malignant effusions (Sensitivity=68%, Specificity=73%, PPV=81%, NPV=58%). Malignant effusions with positive cytology had higher levels of VitD than those with negative cytology ($p = 0.007$). Pleural VitD did not differ between effusions caused by lung cancer versus non-lung cancer ($p = 0.72$). VitD levels in malignant effusions above the upper quartile (i.e. 24.5 ng/ml) were related to better survival during the 6-month follow up compared to lower levels ($p < 0.001$, log rank test). Conclusions: Malignant pleural effusions present increased levels of VitD and higher levels of pleural VitD were associated to positive cytology, plausibly reflecting a greater local immune response. Increased levels of VitD were associated with better survival in this small population.