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Original Article

Etiology of Pleural Effusions: Analysis of More Than 3,000 Consecutive Thoracenteses☆

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ABSTRACT

Objective: To investigate the etiology of pleural effusions (PE) in adults and the accuracy of pleural fluid (PF) cytology and cultures in malignant and infectious PE, respectively.
Patients and methods: Retrospective analysis of all consecutive patients with PE undergoing diagnostic thoracentesis during the last 19 years in a university hospital.
Results: The leading causes of PE among the 3077 patients were cancer (27%), heart failure (21%), pneumonia (19%), tuberculosis (9%), abdominal surgery (4%), pericardial diseases (4%) and cirrhosis (3%). Tuberculosis was the most common etiology in patients <34 years of age (52%), whereas heart failure predominated in octogenarians (45%). The most common primary tumors in malignant PE were lung (37%) and breast (16%) tumors. The overall accuracy of PF cytology was 59%, although it was significantly lower in mesotheliomas (27%) and squamous cell lung cancer (25%). In infectious PE, only 30% of cultures yielded positive results, a percentage which increased two-fold (66%) in purulent fluids (empyemas). Viridans streptococci were the most commonly isolated pathogens (25.5%). The sensitivity of solid media cultures of PF for *Mycobacterium tuberculosis* was low (18.5%).
Conclusions: Three quarters of patients with PE in whom a diagnostic thoracentesis was indicated had cancer, heart failure, pneumonia or tuberculosis. PF cytology and cultures give false negative results in a significant number of cases.

Etiología del derrame pleural: análisis de más de 3.000 toracocentesis consecutivas

Palabras clave:
Derrame pleural
Toracocentesis
Neumonía
Tuberculosis
Insuficiencia cardiaca
Cáncer

RESUMEN

Objetivos: Conocer la etiología del derrame pleural (DP) en pacientes adultos y la rentabilidad de la citología y del cultivo de líquido pleural (LP) en DP malignos e infecciosos, respectivamente.
Pacientes y método: Estudio retrospectivo de todos los pacientes consecutivos con DP sometidos a una toracocentesis diagnóstica durante los últimos 19 años en un hospital universitario.
Resultados: Las principales causas de DP en los 3.077 pacientes estudiados fueron: cáncer (27%), insuficiencia cardiaca (21%), neumonía (19%), tuberculosis (9%), cirugía abdominal (4%), enfermedades del pericardio (4%) y cirrosis (3%). La tuberculosis fue la etiología más común en pacientes < 34 años (52%), mientras que la insuficiencia cardiaca lo fue en octogenarios (45%). Entre los DP malignos, los tumores primarios más comunes fueron el de pulmón (37%) y el de mama (16%). La citología del LP tuvo una rentabilidad global del 59%, pero fue significativamente inferior en mesoteliomas (27%) y carcinomas escamosos de pulmón (25%). En pacientes con DP infecciosos, solo el 30% de los cultivos del LP resultaron positivos, un porcentaje que se duplicó (66%) cuando el líquido era purulento (empiemas). Los estreptococos del grupo *viridans* representaron el 25,5% del total de aislamientos. El cultivo del LP en medio sólido para *Mycobacterium tuberculosis* tuvo escasa sensibilidad (18,5%).

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Conclusiones: Las 3 cuartas partes de los pacientes con un DP en los que se indica la realización de una toracocentesis diagnóstica tienen una neoplasia, insuficiencia cardiaca, neumonía o tuberculosis. La citología y los cultivos del LP son falsamente negativos en un porcentaje significativo de casos.

Introduction

Pleural effusion (PE) is a common problem in patients seen in internal medicine and pneumology departments.[1] Etiology can vary according to geographical area, healthcare setting, patient age or the time period studied, among other factors. Knowledge of the main etiologies of PE (pre-test probability) enables clinicians to correctly choose and interpret different diagnostic tests following a Bayesian clinical reasoning model.

Only 3 studies on the etiology of PE (with 484,[2] 642[3] and 1000[4] patients) have been published in Spain in the past 25 years; the last of these was published more than a decade ago.[4] The aim of this study was to describe the causes of PE and the accuracy of some basic tests such as pleural fluid (PF) cytology and culture in over 3000 consecutive patients diagnosed in a university hospital over the past 19 years.

Patients and Methods

Our hospital created a database in which the demographic and clinical characteristics of all consecutive adult patients undergoing diagnostic thoracentesis since 1994 have been entered prospectively, irrespective of the medical or surgical service from which they were referred. Most procedures were performed on hospitalized patients, and very few on outpatients. In this study, we analyze the etiologies of PE from January 1994 to June 2013. In total, 206 patients that had either no definite diagnosis or insufficient PF testing, imaging and clinical follow-up to establish a presumptive diagnosis or to consider the PE idiopathic was excluded. Each patient was included only once if 2 or more thoracenteses were performed for the same reason, i.e., to determine the etiology of PE. The data collection protocol was approved by the local ethics committee.

Diagnostic Criteria

Heart failure was diagnosed based on the patient's history, physical examination, chest X-ray, ECG, echocardiogram, if available, and response to diuretic therapy.

Patients were given a definitive diagnosis of malignant PE when PF cytology or pleural biopsy culture showed malignant cells. A diagnosis of probable malignancy was also accepted in patients with a known primary tumor, cytology-negative PE, and when other potential causes of PE had been ruled out.

A diagnosis of tuberculous PE was based on isolation of the tuberculosis bacillus in sputum samples, PF or pleural biopsy, or when the latter showed granuloma. Probable diagnosis was given in patients with lymphocytic exudate and pleural fluid adenosine deaminase of over >35 U/L that was resolved with empirical antituberculosis therapy.

PE was considered parapneumonic when associated with pneumonia, bronchiectasis or pulmonary abscess. The effusion was classified as uncomplicated parapneumonic PE when it was resolved with antibiotic therapy alone. Complicated parapneumonic PE were those that could not be resolved without complete drainage of non-purulent PF, insertion of a pleural catheter or surgery. The term empyema means the presence of pus in the pleural space and is, by definition, classified as complicated PE even though it is not always associated with pneumonia.

A diagnosis of pulmonary embolism was dependent on a positive CT angiography or ventilation perfusion scan performed in a suitable clinical setting. Hepatic hydrothorax was considered in all cirrhosis patients who had no heart, infectious or malignant disease that would otherwise explain the PE. Idiopathic PE cases were those in which the etiology of the condition could not be determined despite thorough testing, and which resolved during follow-up. Widely accepted clinical criteria were applied to diagnose other diseases. PE were classified as exudative or transudative according to Light's criteria cases.[5]

Statistical Analysis

Quantitative variables are expressed as percentages, and qualitative variables as medians (25th and 75th percentiles) The chi-square and Kruskal–Wallis tests, with post hoc analysis of standard residuals, or the Mann–Whitney test was used as required to compare variables from the different PE etiology groups. *P* values of <.05 were considered statistically significant. The data were analyzed using SPSS version 18.0 (Chicago, IL, USA).

Results

Causes of Pleural Effusion

A total of 3077 patients with PE were included in the study. The mean age was 69 (52–79) years; 1826 (59%) were men and 1251 (41%) were women. In total, 75% of PE were due to one of the following 4 causes (Table 1): cancer (27%), heart failure (21%), pneumonia (19%) or tuberculosis (9%). These were followed, in terms of frequency, by post-abdominal surgery PE (4%), pericardial disease

Table 1
Etiology of Pleural Effusion.

Causes	No. (%)	Age, mean (quartiles)
Cancer	840 (27)	70 (59–79)
Heart failure	640 (21)	80 (74–85)*
Pneumonia/infection	582 (19)	57 (42–73)
UPPE	202	
CPPE	216	
Empyema	164	
Tuberculosis	275 (9)	32 (25–44)**
Definite	96	
Probable	179	
Post-abdominal surgery	110 (4)	69 (53–77)
Pericardial diseases	109 (4)	68 (54–77)
Hepatic hydrothorax	97 (3)	67 (55–76)
Idiopathic	94 (3)	70 (53–79)
Trauma	77 (2.5)	71 (42–79)
Pulmonary embolism	48 (1.6)	70 (48–81)
Post-heart surgery	32 (1)	68 (60–72)
Connective tissue disease	27 (0.9)	50 (44–67)
Other[a]	146 (5)	70 (52–79)
Total	3077	69 (52–79)

CPPE: complicated parapneumonic pleural effusion; UPPE: uncomplicated parapneumonic pleural effusion.

[a] Includes, among others, hypoproteinemia (17), nephrotic syndrome (15), atelectasis (14), pancreatitis (14), trapped lung (13), volume overload (10), pulmonary hypertension (8) and uremia (8).

* Significantly higher than the other groups (*P*<.01).

** Significantly lower than the other groups (*P*<.01).