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Diagnosing tuberculous pleural effusion using clinical data and pleural fluid analysis
A study of patients less than 40 years-old in an area with a high incidence of tuberculosis

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Summary
Background: Tuberculous pleural effusions (TPE) are common. The diagnosis is often problematic. As the determination of ADA is often unavailable in some countries, the aim of this study was to evaluate the diagnostic usefulness of other data from pleural fluid analysis, in young patients from populations with high prevalence of tuberculosis (TB).
Methods: We analysed 218 patients with pleural effusion (165 tuberculous, 21 infectious, 11 neoplastic, 16 miscellaneous, 3 idiopathic). We performed two regression models; one included pleural fluid ADA values (model 1), and the other without ADA (model 2).
Results: Model 1 selected two variables (ADA >35 U/L) and lymphocytes (>31.5%) and correctly classified 216/218 effusions (1 false negative, 1 false positive). Model 2 (without ADA) selected three variables: lymphocytes (>31.5%), fever and cough, and correctly classified 207/218 effusions (8 false negatives, 3 false positives). The sensitivity of models 1 and 2 was 99.4% and 95.2%, specificity 98.1% and 94.3% and accuracy 99% and 95%.

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Conclusions: In geographic areas with high prevalence of TB and a low prevalence of HIV, in young patients (≤40 years), it is possible to confidently diagnose TPE with either of the two regression tree models, with the utility of ADA providing superior sensitivity, specificity, and accuracy.

Introduction

The diagnosis of a tuberculous pleural effusion (TPE) requires a positive culture (from pleural fluid or pleural tissue) or the presence of granulomas in the pleura.[1] However, we have demonstrated that with the high diagnostic yield of adenosine deaminase (ADA), in a region like ours, with a high prevalence of TPE,[2,3] and in a specific population (less than <35 years), it would be possible to establish the diagnosis of TPE without the need for a pleural biopsy. Pleural biopsy should be reserved for patients with a low pleural fluid ADA, negative cytology and a high suspicion of a neoplasm.[4]

Although making the clinical diagnosis is more likely with the measurement of ADA, its availability may be problematic in some countries [5] and pleural biopsy is not available in many hospitals. Therefore, the aim of this study was to evaluate whether in regions with a high prevalence of tuberculosis and, at least, in young patients (less than <40 years), a confident clinical diagnosis of TPE generated can be established from clinical data and standard pleural fluid analysis, with or without a determination of ADA.

Material and methods

We analysed, prospectively, all patients admitted to our health centre, a 1000-bed teaching hospital in Santiago de Compostela, Spain from January 2000 to December 2008.

Pleural fluid and peripheral blood samples were obtained at the same visit, with the patient fasting and the closed pleural biopsy was obtained by either a Cope[6] or Abrams[7] needle. Pleural fluid samples were sent to cytology, microbiology (for Ziehl—Neelsen stain and aerobic and anaerobic cultures in Lowenstein media), and biochemistry, which included total protein, lactate dehydrogenase (LDH), cholesterol, glucose, ADA, red cell count and total nucleated cell count with differential. The same testing was performed on blood samples. All biochemical measurements were performed on a clinical chemistry analyser (ADVIA 2400, SIEMENS HEALTHCARE DIAGNOSTICS) using standard methodology. The ADA activity (U/L at 37 °C) was determined colorimetrically by the method of Galanti and Giusti.[8] The NH_4^+ released by deamination of adenosine added to the samples was quantified by incubation with phenol nitroprusside in an alkaline medium, followed by measurement of absorbance at 628 nm. The within-run precision of this method in our hands was evaluated using 30 replicate high ADA samples and 30 replicate low ADA samples. The corresponding coefficients of variation were 2.24% for low ADA samples (mean ± SD: 22.93 ± 0.5 U/L) and 2.02 for high ADA samples (102.48 ± 2.04 U/L). Between-run precision was evaluated using 17 pairs of duplicates and a coefficient of variation of 2.51% (37.29 ± 0.94 U/L) was obtained.[4] Red cell and total nucleated cell counts were determined by a Haematology analyser (ADVIA 2120, SIEMENS HEALTHCARE DIAGNOSTICS). Neutrophilic and lymphocytic effusions were defined as effusions with a neutrophil or lymphocyte count >50% of the total nucleated cell count. An effusion was considered eosinophilic if the cell count was ≥10%. Only the first pleural fluid chemistry panel was used for statistical analysis in patients with more than one thoracentesis.

Clinical parameters recorded were age, sex, chest pain, cough, sputum, dyspnoea and fever. The radiological findings that were determined were: 1) pulmonary lesion and its location; 2) laterality of the effusion (right, left, or bilateral); 3) and the size of the effusion: (large if >2/3 of the hemithorax, medium if >1/3 and <2/3 of the hemithorax, or small if it was <1/3). A tuberculin skin test was performed with 2 U of RT-23 and was considered positive if the induration of the transverse axis of the forearm was ≥5 mm measured at 48—72 h. With suspected HIV, serology was also obtained. Thoracoscopy was not performed on any patient.

The pleural fluid was classified as tuberculous if the Ziehl—Neelsen stain or the Lowenstein culture was positive in pleural fluid or biopsy, or if granulomas were identified on biopsy.

An effusion was diagnosed as neoplastic only when confirmed by positive cytology in pleural effusion or pleural biopsy. An effusion was considered parapneumonic if there was bacterial pneumonia, a lung abscess or bronchiectasis or if the pleural fluid culture was positive. An empyema was diagnosed if the fluid was purulent. The other diagnoses were based on previously established criteria.[1]

Statistical analysis

Data are expressed as mean ± SD. The Student *t* test was used for the comparison of the continuous variables between TPE and the rest of the groups, and the Mann—Whitney test was used if the distributions were not normal. The chi-squared analysis was used for comparison of proportions. The results of the diagnostic tests were expressed as sensitivity, specificity, predictive values (positive and negative), positive likelihood ratio, negative likelihood ratio and accuracy, with 95% confidence intervals (95% CI). ROC (receiver operator characteristics) curve methodology was used to find the optimum cut-point.

We performed two regression tree models. The first included the ADA level in pleural fluid (model 1) while the second (model 2) did not include ADA. The statistical modelling used analysis adjusted for the following covariates: gender, fever, chest pain, dyspnoea, cough, sputum, size and location of the effusion, accompanying pulmonary lesions, tuberculin skin test, red and total nucleated cell

Table 1 Causes, gender, and age at diagnosis of pleural effusions.

	n	%	Males/females	Age, yrs[a]
Tuberculosis	165	75.7	91/74	23.9 ± 6.5
Infectious	21	9.6	16/5	31.1 ± 7.7
Neoplastic	11	5	9/2	35.7 ± 2.5
Miscellaneous	16	7.3	13/3	32.8 ± 4.9
Post-surgery	5	2.3		
Pancreatitis	4	1.8		
Pleuropericarditis	4	1.8		
Systemic lupus erythematous	1	0.5		
Pulmonary thromboembolism	1	0.5		
Liver cirrhosis	1	0.5		
Idiopathic	5	2.3	3/2	27.8 ± 5.3
Total	218	100	132/86	25.9 ± 7.3

[a] Mean ± standard deviation.

counts, lymphocytes (%), neutrophils (%), glucose, pleural fluid/serum protein ratio (P/S protein ratio), lactate dehydrogenase (LDH) and pleural fluid/serum LDH ratio (P/S LDH ratio). In the tree-based analysis, the final regression tree was derived using the CART approach.[9] This involved successive binary partitioning of the data set by identifying at each partition the explanatory variable which maximized the between groups sum-of-squares using analysis of variance. All statistical test values were two-sided, and a *P* value of <0.05 was considered to be statistically significant. Analysis was carried out using SPSS (15.0) and *R* statistical software.

Results

The 218 patients (60% males) with a mean age of 26 years and their diagnoses are listed in Table 1. A definitive diagnosis could not be established in five patients (2.3%). As expected, among our patients with pleural effusions aged <40 years, the prevalence of tuberculous effusions was high (75.7%, 165/218) compared to patients of all ages (25%) with effusions in this region.[2] The prevalence of neoplastic effusions was low at 5% (11/218) compared with 22.9% for patients of all ages with effusions.[2] The infectious effusion group consisted of the parapneumonic effusions and empyemas.

Table 2 summarizes the microbiology and histology of the 165 patients who had at least one positive test for tuberculous pleural effusions. The most frequent finding (81.2%, 134/165) was the observation of caseating granulomas in biopsy tissue. In the 11 patients with a neoplastic effusion, cytology was positive in 7 (63.6%) cases and pleural biopsy was positive in 6 (54.5%).

Table 2 Microbiological and histological findings for a tuberculous pleural effusion ($n = 165$).

Criteria	*n*	%
Observation of caseating granulomas	134/165	81.2
Culture of biopsy tissue in Lowenstein medium	83/165	50.2
Culture of pleural fluid in Lowenstein medium	53/165	32.1
Ziehl–Neelsen staining of biopsy tissue	38/165	23
Ziehl–Neelsen staining of pleural fluid	8/165	4.8

Table 3 shows the clinical data and Table 4 depicts the laboratory data of the tuberculous and non-tuberculous pleural effusions.

In 95.2% of the TPE (157/165) the percentage of lymphocytes was $\geq$50%, while only one TPE had a lymphocyte percentage count $\leq$32%. Ninety-five percent (20/21) of the infectious effusions had more than 50% neutrophils, compared to only 1.8% (3/165) of the TPE. Only 4 patients (3 TPE and 1 infectious) had $\geq$10% eosinophils.

The ADA values for all the cases studied, according to diagnostics, are seen in Fig. 1. A cut-off point $\geq$35 U/L, was associated with an area under the curve of 0.909 and a sensitivity of 100% (165/165). In contrast, 42 of 53 of the non-tuberculous effusions had ADA values less than the cut-off point (specificity 79.2%; 95% CI: 68.3–90.2%). The 11 false positives were found with ten infectious effusions and one neoplastic effusion (positive by cytology and pleural biopsy). Given that the prevalence of the disease is 75.7%, the positive predictive value, positive likelihood ratio, negative likelihood ratio and accuracy for the diagnosis of a TPE were 93.8% (95% CI: 90.2–97.3%), 100%, 4.8 (95% CI: 2.8–8.1%), 0.0 and 95% (95% CI: 92%–97.9%), respectively.

Classifying a tuberculous etiology

When the ADA is included in the analysis (ADA $>$35 U/L; model 1), the regression model only selected one additional covariable for the prediction of a TPE: a percentage of lymphocytes $\geq$31.5% (Fig. 2A). With this model, 216 of the 218 effusions were classified correctly (sensitivity 99.4%, 95% CI: 98.2–100%, specificity 98.1%, 95% CI: 94.3–100%).

When ADA was excluded from the multivariate analysis (model 2), the best regression model selected three parameters for predicting a TPE: percentage of lymphocytes $\geq$31.5 and the presence of fever and cough (Fig. 2B). Applying this model, 207 of the 218 effusions studied would be classified correctly (8 false negatives and 3 false positives). This analysis resulted in a sensitivity of 95.2% (95% CI: 91.9–98.4%) and a specificity of 94.3% (95% CI: 88.1–100%). The diagnostic yield of model 1 (accuracy 99%;

Table 3 Clinical features of patients with tuberculous and non-tuberculous pleural effusions.

Characteristics	Tuberculous ($n = 165$)		Malignant ($n = 11$)			Infectious ($n = 21$)			Miscellaneous ($n = 16$)			Idiopathic ($n = 5$)		
	n	%	*n*	%	*p*	*n*	%	*p*	*n*	%	*p*	*n*	%	*p*
Male	91	55.2	9	81.8	0.1584	16	76.2	0.1097	13	81.3	0.0798	3	60	0.8073
Fever (>37.8 °C)	146	88.5	0	0	<0.0001	21	100	0.2087	6	37.5	<0.0001	0	0	<0.0001
Chest pain	126	76.4	0	0	<0.0001	15	71.4	0.8154	6	37.5	0.0023	4	80	0.7276
Dyspnoea	62	37.6	6	54.5	0.4268	6	28.6	0.5714	3	18.8	0.2211	1	20	0.7393
Cough	105	63.6	0	0	0.0001	21	100	0.0019	1	6.3	<0.0001	0	0	0.0157
Sputum	35	21.2	0	0	0.1882	15	71.4	<0.0001	0	0	0.0856	0	0	0.5526
Massive effusions	24	14.5	1	9.1	0.9595	0	0	0.1277	0	0	0.2119	0	0	0.7903
Right-sided effusions	100	60.6	3	27.3	0.0637	12	57.1	0.9426	10	62.5	0.9049	3	60	0.6618
Bilateral effusions	0	0	4	36.4	<0.0001	2	9.5	0.0043	0	0	1.000	0	0	1.000
Lung lesion	25	15.2	0	0	0.3416	21	100	<0.0001	3	18.8	0.9855	0	0	0.7610
Tuberculin skin test	121	73.3	4	36.4	0.0201	4	19.0	<0.0001	3	18.8	<0.0001	2	40	0.2422

95% CI: 97.8—100%) was significantly higher than that of model 2 (accuracy 95%; 95% CI: 92—97.9%) ($P < 0.001$).

Discussion

The results of our study demonstrate that, in young patients (≤40 years), and in regions with a high prevalence of tuberculosis, it is possible to establish the diagnosis of TPE from clinical data and pleural fluid analysis with high ''diagnostic safety''. Although both models had a high yield (an accuracy of 99% for the ADA and 95% for the non ADA-model), the ADA-model had significantly better accuracy ($P < 0.001$).

Although the measurement of ADA in pleural fluid for the diagnosis of a tuberculous effusion is increasing, analysis of biopsy tissue is often considered obligatory for the definitive diagnosis.[10] However, in small hospitals, pleural biopsy is not always available and the patient has to be transferred to a tertiary care hospital. Following a study by our group,[4] it has been accepted that the test diagnostic value of ADA in diagnosing TPE is highly accurate and able to avoid pleural biopsy in young patients from areas with high prevalence of tuberculosis.[11—13] Since the determination of ADA is problematic in some countries,[5,14] several authors have used complex statistical models to establish the diagnosis of TPE from a series of clinical features, radiological variables, and the biochemical analysis of the pleural fluid.[14—16] We have accomplished this using a simple regression tree.

As a result of the epidemiological characteristics of tuberculosis in our region, its prevalence among cases of pleural effusion is high at 25%.[2] As was expected, given the young age of the population studied, the prevalence of TPE in our series was high (75.7%), since the mean age of TPE varies between 32 and 34 years.[2,17,18] Therefore, we reasoned that the positive predictive value of pleural fluid levels for ADA for tuberculous pleural effusions should be better than in regions of lower prevalence, particularly among patients with a low probability of neoplasia.

The diagnostic yield of each of the criteria used to establish the definitive diagnosis of TPE was similar to that in previous studies by our group.[4,18] The percentage of patients with fever (88.5%), chest pain (76.4%) and cough (63.6%) was similar to that reported in the older literature.[19] We did not find any differences in the published literature on the size and laterality of the effusions, the existence of lung lesions and the number of positive tuberculin skin tests.[18] Only one neoplastic effusion, diagnosed both by cytology and pleural biopsy, had increased ADA values. Previously, we reported that pleural biopsy should be performed in those cases where the ADA levels are lower than the cut-off point, pleural fluid cytology is negative and, in the absence any data that would lead us to another diagnosis, or if a neoplasm is suspected.[4] With this approach, those cases with malignancy with negative cytology and high pleural concentrations of ADA should not be misdiagnosed. It is necessary to stress ''should'', as it is estimated that the 66% sensitivity of cytology for neoplastic effusions is only increased to 73% if both biopsy and cytology are used.[1] It is questionable whether any of the patients representing up the 7% difference would have high pleural concentrations of ADA.

As was reported,[19] there were 8 (4.8%) TPE cases with a percentage of lymphocytes lower than 50% and only one (0.6%) had ≤32% lymphocytes. It is possible that the time of progression of this effusion (10% lymphocytes, 70% neutrophils) was short, since neutrophils can be predominant early in these cases.[13]

When we used the regression trees, the model that included the determination of ADA (model 1) only evaluated two variables: ADA (primary variable) and the percentage lymphocytes. The cut-off points were 35 U/L and 31.5%, respectively. With this cut-points, the model with the primary variable ensured a sensitivity of 100% for the diagnosis of TPE (lowest ADA value in these effusions was 36 U/L), with the majority of neoplastic effusions also being correctly classified. With the second variable, we attempted to separate those infectious effusions that also

Table 4 Pleural fluid analysis of patients with tuberculous and non-tuberculous pleural effusions.

Characteristics	Tuberculous		Malignant			Infectious			Miscellaneous			Idiopathic		
	$x \pm SD$	Range	$x \pm SD$	Range	p	$x \pm SD$	Range	p	$x \pm SD$	Range	p	$x \pm SD$	Range	p
Pleural RBC count, 10^9/L	4574 ± 16,331	300–200,000	5829 ± 1020	4760–7560	0.7994	2599 ± 2161	390–7800	0.5810	1703 ± 2254	150–8000	0.4838	824 ± 104	700–980	0.6089
Pleural WBC count, 10^9/L	3947 ± 6694	27–77,000	1449 ± 453	780–230	0.2188	13,753 ± 16,695	2900–56,700	<0.0001	1382 ± 1506	100–5230	0.1289	2112 ± 1045	360–3000	0.5420
Pleural lymphocytes, %	79.22 ± 14.71	10–100	69.4 ± 14.5	30–85	0.0333	20.6 ± 4.4	0-70	<0.0001	50.8 ± 26.8	15–80	<0.0001	51.6 ± 25.5	23–75	0.0001
Pleural neutrophils, %	14.32 ± 12.01	1–70	17.4 ± 16.0	8–65	0.4215	68.9 ± 16.7	20-98	<0.0001	42.3 ± 26.5	16–28	<0.0001	41.0 ± 22.2	20–65	<0.0001
Pleural glucose, mg/dL	70.0 ± 12.1	9–116	87.7 ± 5.00	79–95	<0.0001	64.8 ± 11.7	42-80	0.0548	87.1 ± 6.03	76–98	<0.0001	84.6 ± 5.68	78–90	0.0085
P/S protein ratio	0.72 ± 0.12	0.13–1.60	0.68 ± 0.07	0.53–0.75	0.2766	0.75 ± 0.10	0.56–0.98	0.2739	0.58 ± 0.15	0.14–0.78	<0.001	0.67 ± 0.09	0.55–0.77	0.3575
Pleural LDH, U/L	731 ± 938	110–10,769	584 ± 631	110–2264	0.6097	1296 ± 2093	130–10,000	0.6097	323 ± 266	46–905	0.0855	313 ± 83.4	208–427	0.3219
P/S LDH ratio	3.64 ± 3.94	0.42–41.0	3.89 ± 4.21	0.73–15.1	0.8394	8.15 ± 11.9	0.86–56.6	0.0004	2.15 ± 1.78	0.30–6.03	0.1367	2.08 ± 0.56	1.38–2.84	0.3787
Pleural ADA, U/L	118 ± 40.6	36–344	19.0 ± 12.2	7.0–49.0	<0.0001	70.5 ± 67.4	21–248	<0.0001	19.6 ± 10.4	5.0–33.0	<0.0001	17.4 ± 5.03	12.0–25.0	<0.0001

RBC: red blood cell; WBC: white blood cell; P/S: pleural fluid to serum ratio.

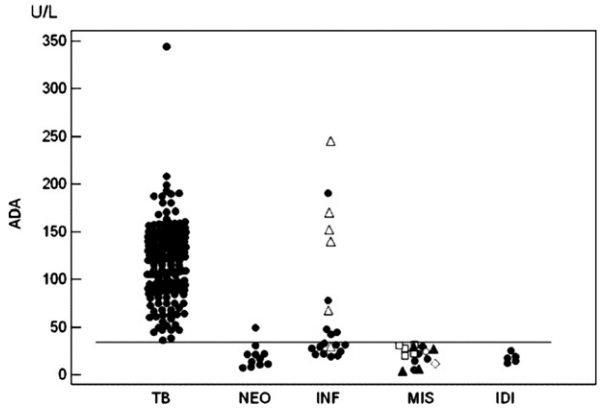

Figure 1 Concentrations (U/L) of adenosine deaminase (ADA) in 218 patients with pleural effusions. TB: tuberculous (●); NEO: neoplastics (●); INF: infectious. (●) parapneumonic, (△) empyema; MIS: miscellaneous. (□) post-surgery, (▲) pancreatitis, (●) pleuropericarditis, (◆) systemic lupus erythematous, (○) pulmonary thromboembolism, (◇) liver cirrhosis; IDI: idiopathics (●).

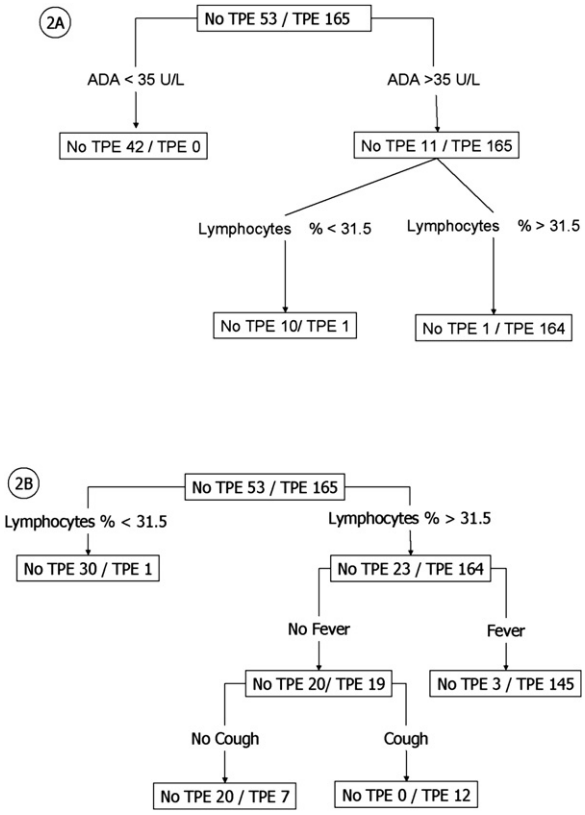

Figure 2 Regression trees for predicting tuberculous pleural effusions (TPE). Model 1 includes ADA (A) and model 2 excludes it (B). Figures are number of patients at the terminal nodes. The statistical modelling used in the above analysis adjusted for the following covariates: gender, fever, thoracic pain, dyspnoea, cough, sputum, effusions (location and size), lung lesion, tuberculin skin test, red and white blood cell counts, lymphocytes (%), neutrophils (%), glucose, P/S protein ratio, LDH and P/S LDH ratio. In model 1, ADA and lymphocytes (%) were the covariates kept in the final tree regression model. In model 2, lymphocytes (%), fever and cough were the covariates kept in the final tree regression model.

had a high ADA, as they are typically predominantly neutrophils. The only neoplastic effusion in our series that had a high ADA value also had a lymphocyte percentage of 30%, which was correctly classified with the second variable. With this model, only two effusions were erroneously classified: a tuberculosis effusion with a low percentage of lymphocytes and a parapneumonic that had both high ADA and lymphocyte values. It is likely that the false negative effusion was sampled early in its course which would explain the low percentage of lymphocytes; in this case the fluid culture and the pleural biopsy were diagnostic. The false positive (a parapneumonic effusion with increased ADA and percentage lymphocytes) could not be diagnosed by pleural biopsy. This parapneumonic most likely was sampled late in its course when the infection was regressing. The diagnostic yield of this model was very high (sensitivity 99.4%, specificity 98.1%, and accuracy 99%). This regression tree is supported by the studies of Burgess and co-workers[20] and Diacon and colleagues,[21] as these authors used the same variables to establish the diagnosis of TPE in their series.

Model 2 of the regression trees (without ADA) used 3 variables; the percentage of lymphocytes (cut-off point 31.5%) as primary variable and the presence of fever and cough. With the primary variable, the model attempts to separate the effusions of infectious, non-tuberculous origin, which should have a low percentage of lymphocytes (only one false negative was observed with this variable) and, with fever should eliminate the non-tuberculous effusions that usually do not present with fever. A total of 20 of the 23 non-tuberculous pleural effusions (three false positives: a parapneumonic effusion, lupus pleuritis and pleuropericarditis) and 19 out of 164 tuberculous pleural effusions did not have fever. Lastly, the third variable (cough), served to correctly classify the 20 non-TPE that did not have a fever and the 12 TPE that were febrile. There did not appear to be an association between cough and the presence of a pulmonary lesion on chest radiography, as only 2 of 12 had cough. Seven TPE were not associated with fever or cough (7 false negatives). The pleural biopsy did not appear to support the diagnosis in the false positives, although it was positive in the eight false negatives.

It is surprising that the model did not take the tuberculin skin test into account to discriminate between both groups; there may be two explanations. As a primary form of tuberculosis in our region, the tuberculin skin test may be negative in a high percentage of patients (26.7%). Secondly, with a high prevalence of tuberculosis, a significant percentage of patients without a TPE have a positive skin test. This method correctly classified 207 of the 218 effusions (three false positives and eight false negatives) with a high diagnostic yield (sensitivity 95.2%, specificity 94.3%, accuracy 95%), although it was significantly inferior to the model that included the ADA ($P < 0.001$).

Carrion and colleagues[15] performed a discriminant analysis using 47 variables (not including ADA) for the diagnosis of TPE. They studied 78 patients with TPE and 111 with non-TPE. The predictors for the diagnosis of TPE were

age, white cell count, tuberculin skin test and bloodstained exudates; with a sensitivity of 90%, a specificity of 87% and an accuracy of 88%. Porcel and co-workers[14] studied 106 tuberculous and 286 neoplastic effusions. In one model that included ADA, four variables predicted a tuberculous etiology: ADA >40 U/L, age <35 years, temperature >37.8 °C and RBC count $<5 \times 10^9$/L. In a second model that excluded ADA, the absence of previous malignancy in the clinical history and a PF/serum LDH ratio >2.2 was added to the latter three variables of model 1. A proportional score was applied to the magnitude of the coefficients of the logistic equations, with a cut-off point of >5 in model 1 and >6 in model 2. The two models had a sensitivity of 95% and 97%, a specificity of 94% and 91% and an area under the ROC curve of 0.987 and 0.982, respectively. Recently Sales et al.[16] established two predictive models for the diagnosis of pleural effusions secondary to tuberculosis, based on the numerical score of Porcel and co-workers.[14] These authors propose a model including ADA, globulins and the absence of malignant cells in the pleural fluid; and another model including ADA, globulins and fluid appearance, with similar results in both models (accuracy of 97.7% versus 96.6%).

Our study had three important methodological differences. The studies by Carrión,[15] Porcel[14] and Sales[16] were performed on a general population, which is why one of the discriminant variables was age. Also, in the studies of Porcel[14] and Sales,[16] the authors tried to differentiate tuberculous from neoplastic effusions, without considering other effusions. The model by Carrión and others[15] calculated the final discriminant function using an impractical equation; whereas the models by Porcel[14] and Sales[16] applied a scoring system that, although proportional to the magnitude of the coefficients of the logistic equations, was arbitrary. In a similar way, Dheda et al. have used a bioclinical scoring rule by assigning a relative score or points to each of the variables included in the final multivariate model for pleural tuberculosis diagnosis.[22] However, our regression tree enables the physician to classify an effusion into TPE or non-TPE using an easy to perform algorithm. Further studies are needed to confirm our results; but in theory, they should be reproducible, since all the variables that were used had a frequency similar to those previously described, and the yield of ADA was even lower than in previous studies.[4]

This study may have some limitations, taking into account that these results correspond only to a young population where the likely proportion of TPE cases is very high, and with low prevalence of HIV infection. Thus, the high predictive value of the strategies is reflected by the high prevalence of the disease within the population. These results may be different in an older population.

In conclusion, in geographic areas with a high prevalence of tuberculosis and in young patients (<40 years), it is possible to safely diagnose TPE with either of the two models that we have studied, although using the ADA is superior.

Conflict of interest

The authors have not any financial or other conflict of interest.

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