Pleura

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No Congresso da ATS *(American Thoracic Society)* foram apresentados dez trabalhos de autores brasileiros abordando aspectos clínicos e experimentais de doenças pleurais. Destes, sete foram clínicos e três experimentais.

A Universidade do Rio de Janeiro (Unirio) com o grupo do Prof. Chibante e a Universidade Federal do Rio de Janeiro (UFRJ) com o grupo do Prof. Walter Zin apresentaram um tema livre cada. O grupo de doenças pleurais da Faculdade de Medicina da Universidade de São Paulo (FMUSP) apresentou oito temas livres, sendo dois em colaboração com o *Royal Brompton Hospital* de Londres e um com o Instituto do Câncer Arnaldo Vieira de Carvalho.

Os trabalhos experimentais abordaram particularmente aspectos fisiopatológicos do desenvolvimento da pleurodese, método terapêutico utilizado em quadros pleurais recidivantes, principalmente em casos de derrame pleural maligno e em pneumotórax, quando a sínfise entre os folhetos pleurais se faz necessária.

A escolha do agente esclerosante é um fator preponderante. Há múltiplas opções de drogas, haja vista que a droga ideal ainda não foi definitivamente estabelecida. Os agentes mais utilizados incluem-se em quatro categorias: antibióticos (doxiciclina e minociclina), agentes antineoplásicos (bleomicina, mitoxantrona), imunoestimulantes *(C. parvum)* e irritantes (talco, hidróxido de sódio e nitrato de prata). Este último grupo merece uma atenção especial, pois o talco é o esclerosante pleural mundialmente mais utilizado.

O trabalho da equipe do Prof. Walter Zin insere-se em uma de suas linhas de pesquisa.

• Neste estudo, os autores relacionam histopatologia e mecânica pulmonar após pleurodese induzida por hidróxido de alumínio. São analisados parâmetros espirométricos e de mecânica respiratória após sete e 30 dias da indução de pleurodese. Os resultados mostram a presença de processo inflamatório e distúrbio ventilatório restritivo após sete dias; após 30 dias observam-se firmes aderências pleurais, caracterizando pleurodese e distúrbio ventilatório obstrutivo e restritivo, além de alterações na mecânica respiratória.

Esta pesquisa demonstra a existência de alterações funcionais pulmonares durante o estabelecimento de uma sínfise pleural eficaz. Devemos lembrar que a grande preocupação ao realizar pleurodese, principalmente, em pacientes jovens, com pneumotórax de repetição, é a preservação da função pulmonar ao longo do tempo e também a manutenção de um plano de clivagem que possa no futuro viabilizar uma cirurgia como, por exemplo, a de transplante pulmonar.

Os trabalhos experimentais da Universidade de São Paulo foram realizados com o intuito de estudar a fisiopatologia e a interferência de drogas antiinflamatórias na realização de pleurodese com nitrato de prata.

• Em trabalho preliminar estudou-se o efeito dos corticosteróides e do piroxicam (antiinflamatório não hormonal) na fase aguda da pleurodese induzida por nitrato de prata a 0,5%. Os autores concluem que o uso de antiinflamatórios concomitante à realização de pleurodese com nitrato de prata reduz o processo inflamatório pleural e altera o predomínio celular do exsudato pleural. É importante este estudo, pois muitas vezes um paciente ao ser submetido à pleurodese encontra-se em uso de drogas antiinflamatórias, quer seja corticosteróide (por outras doenças concomitantes como DPOC ou neoplasias), quer seja antiinflamatórios não hormonais (como auxiliar na analgesia pós-pleurodese).

Cinco trabalhos clínicos abordaram, fundamentalmente, métodos bioquímicos para otimizar o diagnóstico diferencial entre os derrames pleurais e marcadores imuno-histoquímicos para o reconhecimento de mesotelioma. O sexto estudo versou sobre metodologia em pleurodese.

Um dos principais objetivos em estudos do líquido pleural é a determinação de parâmetros bioquímicos que sejam por si sós capazes de determinar a etiologia dos derrames pleurais, em especial, auxiliar na diferenciação entre tuberculose e câncer.

O uso da dosagem da adenosina deaminase (ADA) no líquido pleural é bem estabelecido na literatura como medida auxiliar no diagnóstico de tuberculose. Embora não seja mundialmente utilizada, sua acurácia encontra-se acima de 90%, com reduzidos custos na execução. Apesar do custo mais elevado, a utilização do interferon gama (INF gama) no diagnóstico dos derrames pleurais tuberculosos tem demonstrado sensibilidade (> 94%), especificidade (100%) e acurácia também superior a 90%.

O estudo realizado pelo grupo do Prof. Chibante, da Unirio, demonstra a importância que vem sendo dada ao diagnóstico diferencial dos derrames pleurais.

• Neste trabalho foram avaliados líquidos pleurais de pacientes de áreas de prevalência de tuberculose e realizadas dosagens de ADA e INF gama. Os autores obtiveram resultados concordantes com a literatura, onde as medidas de IFN gama foram significativamente mais elevadas nos derrames tuberculosos que nos neoplásicos com acurácia de 95%, enquanto a dosagem de ADA mostrou ter acurácia em 92% dos líquidos pleurais.

Este trabalho mostra a importância da utilização do INF gama e da ADA no diagnóstico diferencial dos derrames pleurais, ficando a critério do serviço, na dependência da disponibilidade financeira e/ou técnica, a escolha de um dos métodos.

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Os trabalhos clínicos realizados na FMUSP procuraram diferenciar os derrames pleurais neoplásicos dos derrames tuberculosos.

• Em estudo preliminar, a avaliação lipídica no líquido pleural com dosagem de colesterol e lipoproteínas demonstrou que, em derrames neoplásicos, o valor de LDL é mais elevado que nos tuberculosos.

Numa casuística maior, enviada para o *American College Chest Physician* (1999), este grupo encontrou os mesmos resultados e também diferença estatística para a apolipoproteína A, sugerindo que a dosagem dessa lipoproteína poderá ser útil no diagnóstico diferencial dos derrames pleurais.

• A abordagem da dosagem de ADA e da colinesterase na diferenciação de derrames neoplásicos e tuberculosos demonstrou que a colinesterase não foi capaz de diferenciar estes dois grupos, comprovando mais uma vez a eficiência diagnóstica da ADA.

Com o aumento do número de casos, este mesmo grupo tem verificado que a relação entre a colinesterase no líquido pleural e no soro é mais elevada nos derrames tuberculosos, podendo ser um parâmetro útil no diagnóstico diferencial entre câncer e tuberculose. Deve-se ressaltar que a execução deste exame é simples, porém a sua aquisição ainda é restrita no mercado internacional.

• A dosagem de microalbumina no líquido pleural fundamenta-se no princípio de que ocorre nas glomerulopatias, onde a microalbumina é a primeira proteína a atravessar a membrana lesada. Desta forma, esta proteína poderia ser um marcador de lesões iniciais, permitindo a diferenciação entre os diversos exsudatos pleurais. Demonstrou-se a presença de valor mais elevado de microalbumina no líquido pleural tuberculoso, sugerindo uma maior permeabilidade, seletiva para proteínas de baixo peso molecular.

Se estes dados forem confirmados com uma maior casuística, a dosagem de microalbumina poderá ser um marcador útil no diagnóstico diferencial dos derrames exsudativos.

Um dos maiores desafios nas doenças pleurais é o diagnóstico diferencial do mesotelioma. Até o presente momento não existe um marcador especifico para esta patologia, assim como é difícil a diferenciação entre o mesotelioma maligno, hiperplasia mesotelial reativa e fibrose pleural reativa.

• No estudo da Universidade de São Paulo em colaboração com o *Royal Brompton Hospital*, os autores estudaram marcadores imuno-histoquímicos, como anticorpos para EMA, p53, e bcl2, e concluíram que o EMA parece ser um bom marcador para diferenciar o mesotelioma epitelióide e o mesotelioma *in situ* da hiperplasia mesotelial reativa. Em contrapartida, os mesmos marcadores não foram capazes de distinguir o mesotelioma sarcomatóide da fibrose pleural reativa.

• No segundo trabalho, o mesmo grupo estudou anticorpos como a trombomodulina e citoqueratina 5/6 como marcadores na tentativa de diferenciar entre mesotelioma e adenocarcinoma. Os autores concluíram que ambos os marcadores foram úteis, porém a citoqueratina 5/6 mostrou uma maior especificidade no diagnóstico diferencial entre mesotelioma e adenocarcinoma.

Estes trabalhos têm importância fundamental, pois novas pesquisa estão sendo realizadas pelo mesmo grupo, no sentido de reconhecer a existência de um marcador que possa realmente ser útil no difícil diagnóstico do mesotelioma.

• No estudo clínico realizado pelo grupo da USP, em parceria com o ICAVC, os autores comparam a eficácia e segurança da pleurodese induzida pelo nitrato de prata 0,5% com talco em suspensão, no tratamento do derrame pleural maligno recidivante. Os resultados preliminares deste estudo demonstram que o nitrato de prata a 0,5% é tão eficaz quando o talco, sem efeitos colaterais significativos. Este estudo evidencia a eficácia e segurança do nitrato de prata em concentração de 0,5% como agente esclerosante pleural.

Se os resultados preliminares se confirmarem, poderemos antever mudanças na metodologia da pleurodese.

THE USE OF ANTIBODIES RECOGNIZING THROMBOMODULIN AND CYTOKERATIN 5/6 IN DIFFERENTIATING BETWEEN MALIGNANT MESOTHELIOMA OF THE PLEURA AND METASTATIC ADENOCARCINOMA.

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Aim: despite increased numbers of antibodies being commercially available, there is still no established marker that is specific for mesothelioma. We have therefore applied two putative mesothelioma markers, thrombomodulin and cytokeratin 5.6 (CK 5/6), to 63 cases of pleural malignant mesothelioma (MMP) and 44 cases of metastatic adenocarcinoma with known primary sites (lung = 15, breast = 21, ovary = 3, colon = 2, epididymis, kidney, pancreas = 1 case each). Results: 56 (89%) cases of MMP were positive for thrombomodulin and 57 cases for CK5/6 (90%). The number of cells showing positive staining in MMP was greater for CK5/6 than thrombomodulin, as was the intensity of staining. Only one case was negative for both markers. In the cases of adenocarcinoma, 8 (18%) cases were positive for thrombomodulin, but only 3 (7%) were positive for CK5/6. With regard to primary sites, results are shown in the table:

SITE	Lung (n = 15)	Breast (n = 21)	Others (n = 8)
THRO	40% (n = 6)	9.5% (n = 2)	0% (n = 0)
CK5/6	0% (n = 0)	9.5% (n = 2)	12.5% (n = 1)

[Others: Ovary = 3, Colon = 2, Epididymis = 1, Kidney = 1, Pancreas = 1]

Conclusions: both markers showed similar high sensitivity, but CK5/6 showed greater specificity and intensity of staining. With a false-positive rate of 7%, CK5/6 appears a useful addition to antibody panels differentiating MMP from metastatic adenocarcinoma.

IMMUNOHISTOCHEMICAL MARKERS IN THE DIFFERENTIATION OF MALIGNANT MESOTHELIOMA IN SITU, REACTIVE MESOTHELIAL HYPERPLASIA AND PLEURAL FIBROSIS.

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Aim: differentiating malignant mesothelioma of the pleura (MMP) from reactive mesothelial hyperplasia (RMH) and reactive pleural fibrosis (RPF) can be a diagnostic problem in biopsies, which is complicated by increasing recognition of mesothelioma in situ (MIS). Antibodies to EMA, p53 and bc12 have been advocated in this situation, so we have applied these antibodies to 31 cases of MMP, 34 reactive cases (RMH = 20, RPF = 14) and 4 biopsies coded as suspicious, all later proven to be MMP. Results: 30/31 (97%) cases of MMP showed positive nuclear staining for p53, with a higher incidence of positivity in epithelioid than sarcomatoid elements. 30/31 (97%) cases of MMP showed diffuse linear membrane staining for EMA, again more intense in the epithelioid elements. No cases were positive for bc12. Seven

cases contained in situ as well as invasive mesothelioma; the in situ elements showed similar staining patterns to the invasive elements 13/20 cases of RMH showed occasional nuclear positivity for p53 and 5/20 cases showed focal weak membrane staining for EMA. 3/14 cases of RPF showed positive nuclear staining for p53 and 6/14 cases showed focal membrane staining with EMA. No reactive cases stained for bc12. All 4 suspicious cases showed diffuse linear staining with EMA, but only focal staining for p53 in 3 cases. Conclusion: diffuse linear staining for EMA appears to be a good marker of malignancy when differentiating epithelioid MMP and MIS from RMH. A high incidence of nuclear staining for p53 is also suggestive of malignancy in this instance, but should not be overinterpreted. In differentiating sarcomatoid MMP from RPF, the antibodies used in this investigation are less helpful as there is greater overlap in the intensity of staining.

ACUTE MICROSCOPIC FINDINGS DUE TO INTRAPLEURAL SILVER NITRATE AFTER TREATMENT WITH ANTIINFLAMMATORY DRUGS.

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Previous study showed that corticosteroids interfer with talc pleurodesis (Am J Respir Crit Care Med 1998, 157). Our objective was to evaluate the acute microscopic inflammatory findings in the pleural space after intrapleural 2 ml 0.5% silver nitrate (SN) in rabbits previously treated (10 days) with IM methylprednisolone (MP) or piroxicam (P). Three groups of 7 animals were studied: a) SN alone; b) SN + MP 0.8 mg/kg/day and c) SN + P 0.33 mg/kg/day. After 3 days the animals were sacrificed and the visceral pleura analyzed. The find score is represented by the multiplication of extension (0-4) and severity (0-4) where is normal and 4 intense. ANOVA was used for the statistical study ($p < 0.05$). (* = SN x MP) (# = SN x P) (& = MP x P)

	CELLS	P <	SN	SN + MP	SN + P
Pleura	Inflammation	* #	11.4 + 4.2	3.9 + 2.4	7.7 + 3.9
	Eosinophils	* &	4.8 + 2.2	1.9 + 1.0	3.7 + 2.1
	Neutrophils		6.0 + 2.8	3.6 + 3.6	4.6 + 1.5
	Macrophages	* #	10.6 + 3.7	3.6 + 1.6	5.5 + 1.3
Lung	Inflammation	* &	10.9 + 5.6	4.3 + 1.4	7.3 + 3.4
	Eosinophils	*	9.3 + 4.5	3.0 + 2.0	6.6 + 4.6
	Neutrophils	* #	3.6 + 1.6	1.0 + 1.4	1.6 + 1.4
	Macrophages	* #	12.3 + 4.9	5.6 + 1.8	6.3 + 3.7

Methylprednisolone and piroxicam reduced the pleural inflammatory process. Apparently this findings reflect the systemic and no the local effect of the drugs. The chronic use of antiinflammatory may reduce the effectiveness of pleurodesis.

SILVER NITRATE VERSUS TALC SLURRY FOR PLEURODESIS IN PATIENTS WITH MALIGNANT PLEURAL EFFUSIONS.

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We evaluated the security and efficacy of 0.5% silver nitrate solution versus talc slurry for pleurodesis in patients with malignant pleural effusions. From March to September 1998, 21 patients with symptomatic recurrent malignant pleural effusions were submitted to chemical pleurodesis with 0.5% silver nitrate solution or talc slurry, with random distribution. We performed simple chest tube drainage under local anesthesia, followed by instillation of 20 ml-0.5% silver nitrate solution or 5 g of talc in 50 ml of saline solution (slurry) and drain closure for 1 hour. Patients were evaluated regarding dyspnea relief, no need or further thoracocentesis and radiological lung expansion. 16 patients were female (76%), median age was 63 years (range: 41-74); 10 patients had right side (47.7%), 7 had left side (33.3%) and 4 (19%) had bilateral pleural effusions. Primary malignancy was breast cancer in 11 patients (52.5%), non-small cell lung cancer in 8 patients (38%) and ovarian carcinoma in 2 patients (9.5%). Twelve patients were allocated in the talc group (57%) and nine (43%) in the silver nitrate group. Seventeen patients (81%) had dyspnea relief and no pleural effusion recurrence after 30 days of follow-up; ten in talc group (83.3% of success) and seven in silver nitrate group (77.7% of success). We had no serious complications related to the therapy with talc or silver nitrate. 0.5% silver nitrate solution was as effective as talc slurry in promoting pleurodesis with no complications in this preliminary results.

ANTIINFLAMMATORY DRUGS IN ACUTE PHASE OF SILVER NITRATE PLEURODESIS.

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Corticosteroids inhibit the inflammatory response and effectiveness of talc pleurodesis (Am J Respir Crit Care Med 1998, 157). The aim of this study was to evaluate the acute inflammatory response of the pleural space after intrapleural 2 ml 0.5% silver nitrate (SN) in rabbits previously treated with IM methylprednisolone (MP) or piroxicam (P) for 10 days. Three groups of 7 animals were studied: a) SN with no previous treatment, b) SN + MP 0.8 mg/kg and c) SN + P 0.33 mg/kg. After 3 ANOVA was used ($p < 0.05$). SN + MP and SN + P induced a significant increase in the total nucleated cells and leukocytes when compared to SN alone. Among leukocytes the neutrophils were significantly predominant (MP > P > SN) whereas eosinophils were significantly decreased in the MP group (MP < P < SN). Lymphocytes and macrophages were not statistically different.

CELLS	SN	SN + MP	SN + P
Nucleated cells	1747 ± 1231	4473 ± 2047	3309 ± 792
Macrophages	958 ± 750	597 ± 343	1035 ± 520
Leukocytes	719 ± 501	3849 ± 2162	2238 ± 976
Neutrophils	145 ± 226	3500 ± 2163	1647 ± 1179
Eosinophils	314 ± 258	40 ± 43	105 ± 73
Lymphocytes	219 ± 143	216 ± 102	438 ± 383

MP and P induce leukocytosis in the pleural space with neutrophil predominance and reduction of eosinophil migration.

CHOLINESTERASE (CHS) AND ADENOSINE DEAMINASE (ADA) IN PLEURAL FLUID.

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Pleural fluid cholinesterase with emphasis to pleural fluid to serum ratio have been suggested as accurate parameters for the separation of transudates and exudates. The measurement of ADA activity has been helpful for the diagnosis of tuberculosis. However, it is not clear the relationship between these parameters in lymphocytic exudates. The aim of this study was to evaluate CHS level. CHS pleura/serum ratio and ADA levels in lymphocytic (> 66%) pleural effusions. Pleural fluid secondary to cancer (n = 16) was confirmed by cytology or biopsy and to tuberculosis (n = 13) by pleural biopsy. Unpaired test (*$p < 0.05$) was used for statistical analysis. ADA levels were significantly higher in pleural tuberculosis than in cancer. No differences were and in 33% with tuberculosis the ratio was < 0.45, demonstrating an evident overlap between the group (Garcia-Pachon E, Rev Clin Esp 1997; 197:402).

	Cancer	p	Tuberculosis
Cholinesterase	3148 ± 1186		3236 ± 1270
Cholinesterase PI/S	0.37 ± 0.12		0.45 ± 0.07
ADA	20.7 ± 8.9	0	129.2 ± 67.8

We conclude that ADA is useful to the diagnosis of tuberculosis and that cholinesterase does not have discriminative function to recognize the pleural effusions due to cancer or tuberculosis.

MICROALBUMIN AND PROTEIN ELECTROPHORESIS IN TUBERCULOSIS AND CANCER PLEURAL FLUID.
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Among exudative pleural effusions, cancer (CA) and tuberculosis (TB) are predominant. The objective of this study was to evaluate microalbumin and protein electrophoresis in the differentiation of CA and TB effusions. Cancer (n = 16) was confirmed by fluid cytology or pleural biopsy and TB (n = 13) by pleural biopsy. Unpaired t-test (*p < 0.05) was used for statistical analysis. Microalbumin globulin, 2-globulin and -globulin were significantly higher in TB when compared to CA effusions.

	Cancer	p	Tuberculosis
Microalbumin	12.8 ± 6.7	*	25.8 ± 16.6
Proteins	4.7 ± 1.1		5.3 ± 0.8
Albumin	2.7 ± 0.8		2.5 ± 0.9
Globulin	2.0 ± 0.8	*	2.6 ± 0.6
1-globulin	0.2 ± 0.1		0.2 ± 0.1
2-globulin	0.3 ± 0.1	*	0.4 ± 0.2
-globulin	0.6 ± 0.2		0.6 ± 0.3
-globulin	0.9 ± 0.6	*	1.2 ± 0.4

We conclude that microalbumin could be considered a marker to differentiate between cancer and tuberculosis pleural effusions. We also hypothesize that microalbumin level in tuberculosis is higher due to the presence of inflammation determining a more selective permeability to protein of low molecular weight.

LIPIDIC EVALUATION OF PLEURAL FLUID.
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Cholesterol has been suggested as adjuvant in the differentiation of transudates and exudates. However, the complete pleural fluid lipid analysis has been underevaluated. The aim of this study was to determine the value of cholesterol and lipoproteins in the differentiation between cancer (CA) and tuberculosis (TB). Cancer (n = 16) was confirmed either by find cytology or pleural biopsy and tuberculosis (n = 13) by pleural biopsy. Unpaired t-test (*p < 0.05) was used for statistical analysis. The only statistical difference was observed in the LDL level, which was almost 4 times higher in the cancer group.

	Cancer	Tuberculosis	p
Cholesterol	82.0 ± 28.1	79.4 ± 21.3	
Triglycerides	31.6 ± 15.1	35.7 ± 17.2	
HDL	18.6 ± 23.4	14.6 ± 13.5	
LDL	137.8 ± 41.7	33.5 ± 11.3	*
Apo A	40.4 ± 16.5	45.6 ± 18.0	
Apo B	40.4 ± 9.6	47.5 ± 16.5	
Alfa lipoprotein	42.8 ± 17.7	37.5 ± 14.4	
Beta lipoprotein	53.1 ± 15.2	59.0 ± 16.5	
Pre lipoprotein	45.9 ± 19.1	53.1 ± 24.0	

The classic tendency of higher levels of cholesterol in cancer effusions probably is due to the elevation of LDL. The factor involved is suggested to be the reduced lymphatic removal of large particles through the parietal pleura in cancer disease.

COMPARATIVES STUDY BETWEEN INTERFERON-GAMA AND ADENOSINE DEAMINASE IN THE DIAGNOSIS OF PLEURAL EFFUSION IN A HIGH PREVALENCE AREA OF TUBERCULOSIS.
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The interferon-gamma (IFN-gamma) is a cytokine that helps macrophages to eliminate the bacilli from the intracellular cells and is usually elevated in patients with tuberculosis. Studies in pleural fluid proved its utility with sensitivity ranged from 94 to 100% and specificity from 92 to 100%. Our goal is to test IFN-gamma and adenosine deaminase (ADA) utility in the diagnosis of pleural effusion in a high prevalence area of tuberculous. Method: we studied 42 pleural fluid samples of different patients: 32 with tuberculosis, 5 with neoplasic disease and 5 transudates. The concentration of IFN-gamma was determined by ELISA and ADA values by the method of Giusti. Results: using a cut off value of > 750 pg/ml (5º percentile for the tuberculosis group) the accuracy was of 95%, with sensitivity of 94% and specificity of 100%. The values of IFN-gamma were significantly higher in tuberculosis (median of 4931.23 SD 7591.16, varying from 155 to 40364 pg/ml) than those non-tuberculosis (median 140 SD 147, varying from 45 to 546). ADA activity was verified in 39 patients with an accuracy of 92% (sensitivity of 90% and a specificity of 100%), using a cut-off value of > 45 U/l. There was no correlation between individual values of INF-gamma and ADA in the tuberculosis group. Conclusion: the IFN-gamma level is simple and helpful to distinguish tuberculosis from neoplasic in pleura, in a high prevalence area of tuberculosis.

PLEURODESIS INDUCED BY ALUMINIUM HYDROXIDE: A MECHANICAL AND HISTOPATHOLOGICAL STUDY.
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The ideal agent to produce pleurodesis has not been identified. Spirometry, mechanics, histopathology and immunohistochemistry were analyzed 7 and 30 days after intrapleural instillation of saline (S, 2 ml) or albuminium hydroxide [P, 2 ml (0.15 g/ml of 0.9% NaCl)] in rats. The animals were anesthetized and spirometric parameters determined by forced expiration. The rats were then paralyzed and respiratory system (rs), lung (L) and chest wall (w) resistive (P1) and viscoelastic/inhomogeneous pressures (P2), and static elastance (Est) were measured by end-inflation occlusions. The thorax was resected in block and fixed in 10% neutral-buffered formalin. Pleurodesis was confirmed by histologic and immunohistochemical techniques. After 7 days pleurodesis lead to a restrictive impairment of lung function, while after 30 days an obstructive/restrictive pattern was observed. P2, w and Est, w were larger in P7 than in S7. All mechanical parameters were higher in P30 than in S30. In P7, the presence of thin adhesion easily lysed with blunt dissection, diffuse or sparse nodules constituted by the xanthophylic hystocytes, necrosis and neovascularization were observed. In P30, xanthomatous nodules, proliferation of fibroblasts in the submesothelial tissues, an increase in the ratio type I/type III collagen, thick bands between visceral and parietal pleural leaflefts and a completely obliterated pleural space were evident. Intrapleural instillation of aluminium hydroxide had very little effect on the underlying lung. Immunohistochemistry indicated that the observed xanto-granulomatous reaction was promoted by macrophages. In conclusion, this model yields pleural inflammation 7 days after aluminium hydroxide instillation, while at 30 days, marked pleural adherence was found.