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CLINICAL, RADIOLOGICAL AND FUNCTIONAL PULMONARY MANIFESTATIONS IN PATIENTS WITH LEPTOSPIROSIS

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SUMMARY

Twenty-four patients with leptospirosis, with liver and kidney injury, were submitted to clinical, thoracic X-ray and lung function tests. Four patients (17%) had clinical findings, six out of eighteen (33.3%) had chest roentgen changes and 75% of the patients exhibited lung function tests altered (hypoxemia and hypocapnia). Most of the patients had normal values for lung function tests after the clinical improvement. Two patients died in the acute phase of the disease. The Authors tried to establish a correlation between hypoxemia and clinical or X-ray findings, as to the oliguric renal failure, discussing the physiopathological aspects of their findings. The importance of thoracic roentgenographic examination is emphasized and, at least, one arterial blood sampling for PaO_2, $PaCO_2$ and pH analyses is recommended in these patients, to establish the diagnosis of pulmonary involvement, and the correct treatment.

INTRODUCTION

Leptospirosis, a disease caused by spirochetes of the genus Leptospira, has a pleomorphic clinical aspect, varying from slight manifestations similar to influenza until the classical form of Weil's syndrom, with fever, muscular pain, conjunctivitis, leukocytosis, variable hemorrhagic tendency and signs of acute hepatitis, nephritis, myocarditis or pneumonitis [1,5,6,8,10,13].

Pulmonary manifestations in leptospirosis have been described by several Authors as unfrequent, representing part of a general involvement of the disease [8,10,13]. Others have mentioned a hemorrhagic pneumonitis dominating the clinical picture, with dyspnea, cough, pleural pain, hemoptysis and pulmonary rales, mainly in the anicteric form of the disease [11,12].

During the last years radiological changes of the lungs have been described by many Authors, with an incidence of 15 to 70% [5,6,10,12], as SILVERSTEIN [10] and WANG et al.[12] have pointed out. These changes generally appear early, during the first 24-72 hours of the disease, and can be found even in patients without evident respiratory manifestations.

As we have no references with regard to the function of the lungs in patients with leptospirosis, we decided to study a group of patients with that disease and try to establish a relationship between the clinical, radiological and functional findings.

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MATERIALS AND METHODS

Twenty-four patients, 22 males and two females, with moderate or moderately severe icteric leptospirosis and well established hepatic and renal injury, were studied through clinical and laboratory examinations. The average age was 31.2 years, varying form 17 to 56 years (Table I).

TABLE I
Seroagglutination reaction for leptospirosis (sal) as diagnostic confirmation in patients studied

No.	Name	Age	Sex	Sal reaction	
				Beginning	Evolution
1	NCA	17	M	1:400	1:6450
2	JCS	41	M	1:200	1:1600
3	WF	17	M	Suspect	1:800
4	SJA	20	M	Negative	1:3200
5	JLS	21	M	1:400	1:800
6	JAS	23	M	1:400	1:6400
7	NF	40	M	1:200	1:3200
8	AJ	29	F	Negative	1:1600
9	CNC	22	M	1:200	1:3200
10	AAB	47	M	Negative	1:1600
11	RBE	29	M	Negative	1:3200
12	JC	45	M	1:800	Died
13	GFP	56	M	1:1600	1:1600
14	NMS	27	M	1:6400	1:25600
15	DAC	18	M	1:800	1:400
16	AS	25	M	1:800	1:400
17	LCF	27	M	1:200	1:400
18	SR	43	M	1:400	1:800
19	WPF	25	M	Negative	1:800
20	GP	34	M	Suspect	1:800
21	MS	43	M	1:400	1:800
22	AT	48	M	1:800	—
23	FFN	32	F	Negative	1:400
24	ACB	20	M	1:1600	—

In all patients the diagnosis was confirmed in some phase of the disease by the high titer of the seroagglutination reaction for leptospirosis. In all cases the agent was **Leptospira icterohemorrhagiae**; in two we had association with **Leptospira pomona**, and in another one, with **Leptospira canicola**.

General and specific laboratory tests were carried out for hepatic and renal evaluation, as well as X-rays of the lungs in the majority of cases.

The patients were admitted to the Hospital Emílio Ribas and studied in co-operation with the Laboratory of Pulmonary Function — Division of Pulmonary Diseases of the "Escola Paulista de Medicina" at the beginning of the disease. This study was repeated in a certain number of patients two weeks after beginning of treatment.

With regard to lung function, initially anaerobic samples of arterial blood were collected in all patients, breathing room air, for determination of pH and partial pressure of oxygen (PaO_2) and carbon dioxide ($PaCO_2$) in a IL 313 pH and Blood Gas analyzer. This procedure was repeated in 11 patients two weeks after treatment.

In six patients the same determinations were performed at the beginning and after treatment while breathing 100% oxygen.

From the modified formula of alveolar gas, and considering the respiratory coefficient as the unit [4] the alveolar arterial oxygen tension difference, $P(A\text{-}a)O_2$, was calculated in patients breathing room air and 100% oxygen.

From the $P(A\text{-}a)O_2$ in patients breathing 100% oxygen we calculated the fraction of cardiac output that passed through the lungs without undergoing gas exchange percent pulmonary shunt — $\dot{Q}s/\dot{Q}t\%$, of considering the oxygen arterio venous difference of 5 vol% [7].

In seven patients, at the initial stage of the disease the carbon monoxide pulmonary diffusing capacity was calculated by the steady state method [3] in a Godart Diffusion Test Apparatus, the results being given as percent of the predicted value for each patient (DCO/Pred%).

RESULTS

Most of the patients studied had at admission, fever, conjunctival congestion and generalized myalgia.

Manifestations of hepatic injury such as hepatomegaly, jaundice, choluria, hyperbilirubinemia and slightly increased levels of transaminase were found in all patients. In all patients studied, there was also leukocytosis with increased segmented forms and hemorrhagic symptoms such as petechia, epistaxis, hematuria, melena and hemoptysis in variable degrees, with predominance of the three first manifestations.

TABLE II

Relation of PaO_2 values in patients with leptospirosis, with or without pulmonar impairment, as well as with or without acute oliguric renal failure

GROUP / FREQUENCY	I NON OLIGURIC ARF WITHOUT PULMONAR IMPAIRMENT		II NON OLIGURIC ARF WITH PULMONAR IMPAIRMENT		III OLIGURIC ARF WITHOUT PULMONAR IMPAIRMENT		IV OLIGURIC ARF WITH PULMONAR IMPAIRMENT		TOTAL	
PaO_2 (mmHg)	ABSOLUTE	%	ABSOLUTE	%	ABSOLUTE	%	ABSOLUTE	%	ABSOLUTE	%
40 ⊢— 60	4	33,4	0	0,0	1	25,0	2	50,0	7	29,2
60 ⊢—⊣ 80	3	25,0	4	100,0	3	75,0	2	50,0	12	50,0
> 80	5	41,6	0	0,0	0	0,0	0	0,0	5	20,8
T O T A L	12	100,0	4	100,0	4	100,0	4	100,0	24	100,0
A V E R A G E	73,2		74,6		64,9		56,1			
STANDARD DEVIATION	18,1		7,9		8,9		17,2			

ARF = ACUTE RENAL FAILURE

Renal failure in different degrees was observed in all cases, as shown by high levels of blood urea and creatinine. Six patients had oliguria at least in one stage of the disease, and one patient developed anuria. This group was submitted to peritoneal dialysis. The remaining patients presented no significant variation in the urinary volume and developed acute polyuric renal failure. Hematuria was observed in 60% of the cases.

Electrocardiographic changes suggesting miocardial injury were observed in four patients (17%).

One patient presented symptoms of bilateral visual disturbance. And the ophthalmologic examination detected exudations and hemorrhages of the retina.

Pulmonary clinical manifestations were present in four patients (17%); two had some respiratory distress, cough and hemoptoic sputum, and the two other ones presented frank hemoptysis. These last two patients died in a short time, in spite of the support and specific treatments applied.

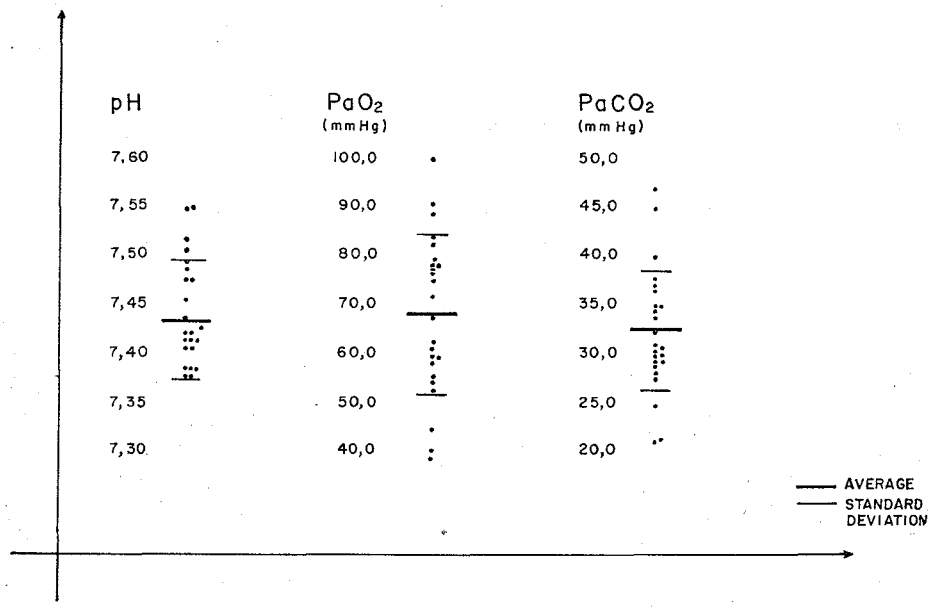
Pulmonary radiological manifestations were present in six patients out of the 18 studied (33.3%). In six cases the roentgenologic study was not possible; among these were the two patients who had hemoptysis immediately after admission to the hospital.

All patients with chest X-ray abnormalities presented disturbances in the renal function, but only three of them had oliguria during the evolution of the disease.

Chest roentgenographic features consisted of a small patchy interstitial infiltrate, localized at one basis in two cases, diffusely dispersed in both lungs in three cases, and disseminated, confluent in one case.

The pulmonary function study showed PaO_2 values below 80.0 mmHg in 75% of the patients, the average being 69.2 mmHg. The pH had normal values but alterations of the $PaCO_2$ were important, since in about 70% of the cases we had values below 35.0 mmHg, the average value being 33.4 mmHg (Diagram 1).

DIAGRAM 1



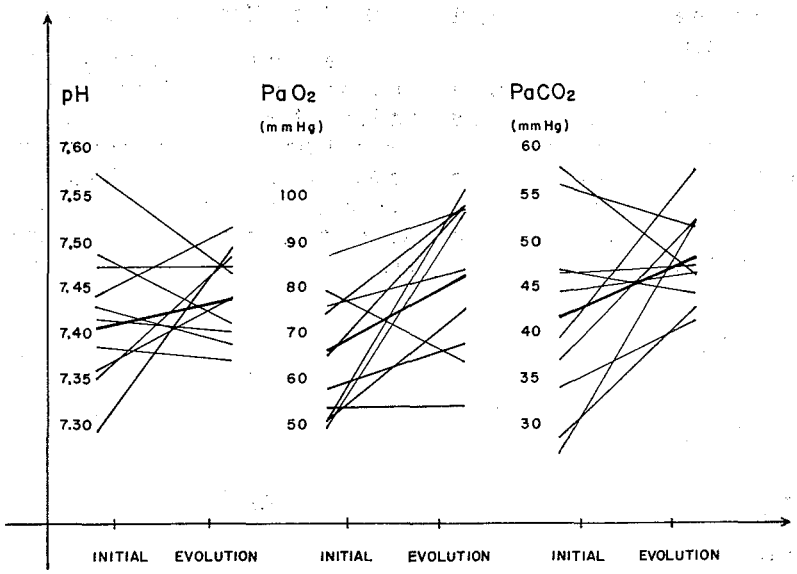
VALUES OF pH, PaO_2 AND $PaCO_2$ IN PATIENTS WITH LEPTOSPIROSIS IN THE INITIAL STAGE OF TREATMENT

Arterial blood gases and pH determinations were repeated in 11 patients two weeks later, and there was increase of the PaO_2 values in nine of them, seven with values above 80.0 mmHg. The average PaO_2 value in these 11 cases, changed from 70.1 mmHg to 81.9 mmHg. During the evolution, only one case (no. 10) presented no variation of PaO_2, and another one (no. 14), showed a decrease (Diagram 2).

We had no significant variation of pH values in the course of the disease, but in 70% of the cases we had normalization of $PaCO_2$, the average changing from 33.4 to 38.1 mmHg.

The $P(A\text{-}a)O_2$ with patients breathing room air, in the 11 cases studied, was initially higher than 15.0 mmHg in more than 70% of them. During the evolution we had a reduction of this values in 10 patients. The initial

DIAGRAM 2



VALUES OF pH, PaO_2 AND $PaCO_2$ IN PATIENTS WITH LEPTOSPIROSIS IN THE INITIAL STAGE AND TWO WEEKS AFTER TREATMENT

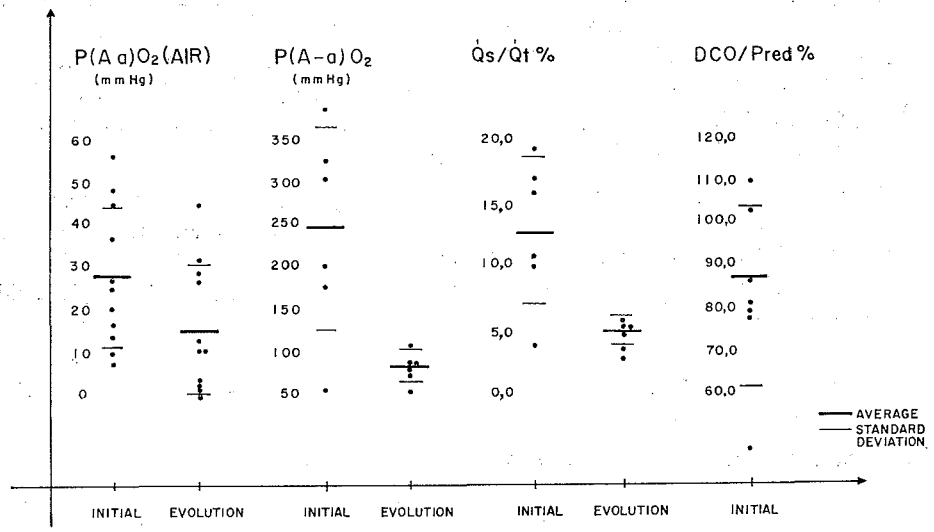
and evolutive averages presented a change from 29.2 mmHg to 16.7 mmHg (Diagram 3).

The $P(A\text{-}a)O_2$ with patients breathing 100% oxygen was calculated in six cases, initially and after treatment. At the initial period, five had $P(A\text{-}a)O_2$ above 100.0 mmHg, with an average of 250.4 mmHg. During the evolution these values decreased in all cases, only one remaining with $P(A\text{-}a)O_2$ above 100.0 mmHg, with an average of 90.4 mmHg (Diagram 3).

The analysis of the percent of pulmonary shunt $\dot{Q}s/\dot{Q}t\%$ in six patients, showed that five on them presented values higher than 10%, with an average value of 13.1% initially. After treatment all patients presented $\dot{Q}s/\dot{Q}t\%$ values lower than 10%, with an average of 5.2%.

The DCO/Pred% was measured in seven patients, and presented values above 80% in five of them. Only one patient had a value

DIAGRAM 3



VALUES OF P(Aa) O_2 IN PATIENTS WITH LEPTOSPIROSIS BREATHING AIR AND O_2 AT 100%, PERCENT OF PULMONAR SHUNT ($\dot{Q}s/\dot{Q}t$%) AND CAPACITY OF PULMONAR DIFFUSION RELATED TO THE PREDICTED VALUE DCO/Pred %

lower than 50% of the predicted, the average being 88.4% (Diagram 3).

In Table II we established the relationship between the PaO_2 values of patients with leptospirosis, and both the occurrence or not of pulmonary impairment and the incidence or not of acute oliguric renal failure.

DISCUSSION

Our leptospirosis patients presented the classical picture of universal capillaritis which characterizes this disease, with systemic injury and important hemorrhagic manifestations, as mentioned before.

Anicteric forms of leptospirosis were not included in this study due to the difficult diagnosis among us. No case was recorded during the period covered by our observations.

The liver injury was of the collangiolar type, with direct hyperbilirubinemia and slightly increased blood transaminase levels.

Renal impairment was evident but transitory in almost all patients studied, the oliguric period being brief or absent. Most presented normal or polyuric diuresis, in spite of high blood levels of urea and creatinine. Some patients developed oliguria in some stage of the disease and only one case had acute renal failure with anuria.

Other hemorrhagic manifestations of the skin and mucous membranes were also frequent in our material.

There is still much discussion with regard to the incidence of respiratory symptoms and roentgenologic occurrence. While some Authors mention low frequency of the same [8,10], others such as WANG et al. [16], refer incidence of respiratory manifestations and hemoptysis in 50.0% of 168 patients, and chest roentgen changes in 66.7% of 93 patients studied in the acute stage of the disease.

In our material, the incidence of respiratory symptoms with hemoptoic sputum or hemoptysis occurred in four of the 24 patients studied (17%) while the roentgenographic examination of the chest performed in 18 cases, in the acute stage of the disease, showed abnormal appearances in 6 (33.3%).

Functionally most of the cases had alveolar hyperventilation, with hypocapnia in the arterial blood. Hypoxemia was also observed frequently (75% of the cases), probably due to pulmonary veno-arterial shunts in impaired pulmonary areas, as indicated by the high values of $\dot{Q}s/\dot{Q}t\%$ and $P(A\text{-}a)O_2$ in patients breathing room air and 100% oxygen.

No significant change of the DCO/Pred% was found in our patients, only one presented a value below 50% of the predicted, suggesting that the distributive inequalities are the most important factor in the development of hypoxemia.

With the clinical and radiological improvement, also PaO_2, $PaCO_2$, $P(A\text{-}a)O_2$ and $\dot{Q}s/\dot{Q}t\%$ values became normal in most of the patients.

We tried to establish a relation between the values of PaO_2 and the occurrence or not of clinical and X-ray lung manifestations, and the incidence or not of acute oliguric renal failure (Table II). Although the statistical analysis showed no significant difference between groups, we observed that: a) the average values of PaO_2 were higher in patients with acute non oliguric renal failure (Group I and II); b) the only five patients with PaO_2 higher than 80.0 mmHg were in Group I, i.e., patients without oliguric renal lesion and without chest X-ray changes or hemoptysis; c) the patients presenting acute oliguric renal failure and pulmonary abnormalities (Group III) had lower average values of PaO_2; d) all patients with chest roentgenographic manifestations had PaO_2 values lower than 80.0 mmHg.

We present two physiopathologic hypotheses to explain the lung functional disturbances found in our patients. First it is an hemorrhagic pneumonitis, sometimes with few clinical and radiological manifestations, due to the liberation of toxins of the leptospire itself, causing, as in other organs, diffuse hemorrhagic capillary lesions. As a consequence, important distributive disturbances occur at alveolo-capillar level, leading to hypoxemia with increase of $P(A\text{-}a)O_2$ and pulmonary shunt. To support this hypothesis we have the occurrence of hemoptoic sputum and hemoptysis in a certain number of patients not only in our material but also in other studies [8,10,11,12]. The second possibility, already described by other Authors [2,14], including one of us [9], is a pulmonary impairment associated with acute renal failure with hypervolemia, although the majority of our patients did not have important hydric retention.

Finally, we call attention upon the relatively frequent clinical and roentgenologic changes of the lungs in the icteric form of leptospirosis, as well as the high incidence of disturbances in arterial blood gases (hypoxemia and hypocapnia) even in patients without other manifestations of pulmonary involvement.

In our opinion, the disturbances found could be due to the association of the two etiopathogenic processes as described above, and it is not possible to identify the predominant factor in this study.

RESUMO

Manifestações clínicas, radiológicas e funcionais pulmonares em pacientes com leptospirose

Estudo clínico, radiológico e funcional pulmonar foi realizado em pacientes com Leptospirose com comprometimento hepático e renal estabelecido. As manifestações clínicas ocorreram em apenas 4 (17%) dos 24 pacientes estudados, as radiológicas em 6 (33,3%) dos 18 pacientes submetidos a este exame, enquanto as alterações funcionais pulmonares (hipoxemia e hipocapnia) foram bastante mais freqüentes (75,0% dos casos).

A maioria dos pacientes apresentou normalização dos parâmetros de função pulmonar com melhora do quadro clínico. Dois deles evoluiram para óbito na fase aguda da moléstia.

Foi tentada correlação dos níveis de hipoxemia com a ocorrência ou não de comprometimento pulmonar clínico ou radiológico, assim como com a incidência ou não de insuficiência renal aguda oligúrica, e formuladas hipóteses para as alterações fisiopatológicas encontradas.

NERY, L. E.; PAULA, A. B. de; NAKATANI, J.; SANTOS, M. L. dos & RATTO, O. R. — Clinical, radiological and functional pulmonary manifestations in patients with leptospirosis. **Rev. Inst. Med. trop. São Paulo 19**:366-373, 1977.

Ressaltamos a importância do exame radiológico de tórax, assim como de pelo menos uma dosagem gasométrica de sangue arterial destes pacientes não só para diagnóstico de comprometimento pulmonar associado, como para orientação terapêutica adequada.

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