

TANATOGENESIS IN LEPTOSPIROSIS

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ABSTRACT:

During the period 1982 - 2004 in our clinic 84 patients with leptospirosis have been treated. This study dynamically compares changes of laboratory parameters in survivors and fatal cases, and reveals following post mortem founded tanatogenic factors: brain edema in 100% of non survivors, lung edema (100%), severe cardiovascular disorders with shock (100%), and hemorrhagic syndrome (80%).

Key words: tanatogenesis, acute renal failure, brain edema, lung edema, cardiovascular disorders, hemorrhagic syndrome.

Leptospirosis is an acute infectious disease of worldwide distribution caused by leptospires of complex *Leptospira interrogans*. The illness progress through an acute, septicemic phase that is followed by an immune phase. The severity of leptospirosis ranges from subclinical illness to two clinically recognizable forms: a self-limited systemic illness, and a severe, potentially fatal illness (Weil's disease) accompanied by any combination of renal failure, liver failure, hemorrhagic syndrome, cardiac and circulatory disorders, aseptic meningitis, rarely encephalitis (1, 2, 4, 6, 7, 8, 9, 10, 11, 13, 15). Mortality rate is higher in elder patients and have ranged from 5 to 40% (1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15).

AIM of this study is analysis of tanatogenesis in leptospirosis.

MATERIAL AND METHODS:

Clinical, epidemiological, and laboratory parameters have been studied retrospectively and prospectively in 84 cases with leptospirosis treated in Clinic of Infectious Diseases - Pleven (1982 to 2004).

RESULTS:

Typical for leptospirosis epidemiological history occurs in 82,14%. The mortality is 14,29%.

The illness is with acute onset with fever above 38°C, chills, headache, myalgia (specific for leptospirosis pains in calf muscles), abdominal pains, nausea and vomiting, oligoanuria.

The physical examination reveals hepatomegaly

(100%), splenomegaly (100%), jaundice (75%), cardiovascular disorders – tachycardia (59,52%), hypotension (33,33%), toxical myocarditis (20,24%), cardiac arrhythmias (11,90%); hemorrhagic syndrome (30,95%), and pulmonary disorders (19,05%). Stiffness occurs in 11,90%.

Routine laboratory parameters: leucocytosis in 73,81% (av. $14,9 \cdot 10^9/L$) with neutrophilia and left shift of granulocytes in 97,62%, increased erythrocytes' sedimentation rate in 86,90% (av. in first hour 51 mm), anemia in 73,81%, thrombocytopenia in 42,86%, increased fibrinogen in 73,81% (av. 6,4 g/L). Decreased total protein (in 29,76%; av. 65 g/L), and serum albumins (44,05%; av. 37 g/L) have been established.

Blood urea nitrogen (BUN) level is elevated in 80,95% of cases (av. 26,1 mmol/L), and serum creatinine level is elevated in 72,62% (av. 303,2 $\mu\text{mol/L}$). The comparison of these parameters in severe cases with favorable and fatal outcome reveals interesting dynamics: average BUN level of survivors in admission and before discharge is respectively 33,9 and 7,4 mmol/L. In fatal cases BUN level in admission and before the death is respectively 41,4 and 41,6 mmol/L. Average serum creatinine level of survivors in admission and before discharge is 503 and 112 $\mu\text{mol/L}$ respectively. In fatal cases serum creatinine level is av. 443 $\mu\text{mol/L}$ in admission and 283 $\mu\text{mol/L}$ before the death. Serum bilirubin is elevated in 70,24% (av. 167,9 $\mu\text{mol/L}$), with prevalence of conjugated fraction. In survivors average serum bilirubin level in admission and before discharge is 231,3 $\mu\text{mol/L}$ and 62,9 $\mu\text{mol/L}$ respectively. In fatal cases average serum bilirubin level is 333,7 $\mu\text{mol/L}$ in admission, and 303,6 $\mu\text{mol/L}$ terminally.

The levels of serum transaminases are moderate elevated and rarely exceed 200 U/L, accompanied by modest elevation of alkaline phosphatase (in 54,76% of cases; av. 358 U/L in admission and 315 U/L finally, independent of outcome).

The patients have been treated with penicillin (94,05%), ceftriaxon (5,95%), in 11,90% of cases second antimicrobial course with zinacef or ceftazidime. Pathogenical treatment includes adequate of urine output infusions of fluids (100%), corticoids (48,81%), diuretics (75%), and blood products (52,38%). Hemodiaperfusion in oliguric stage of acute renal failure is administered in 19,05% of

cases.

The postmortem examination reveals as causative tanatogenic factors brain edema (in 100% of fatal cases), lung edema (100%), critical cardiovascular disorders with shock (100%) and severe bleeding (80%).

DISCUSSION:

Leptospire enter the body through skin, mucous membranes or conjunctiva, aerosol inhalation and possibly ingestion. Once they entering in lymphatic and blood stream, leptospire are carried rapidly to organs through the body. Intensive multiplication of leptospire occurs in both blood and tissues, resulting in acute and intense organ dysfunction. The fact that there is marked peripheral leucocytosis in the absence of neutrophilic infiltration in the tissues suggests the role of toxins in the pathogenesis of the disease. The kidney and the liver are most affected by leptospire. In the kidney, leptospire cause interstitial nephritis and tubular necrosis. In the liver, there is centrilobular necrosis with a proliferation of Kupffer cells being responsible for jaundice. At severe pathological changes occur at a time when leptospire are rarely found in the lesions, it seem plausible that the toxin released by the or-

ganisms is responsible for liver injury. Leptospire are present in the cerebrospinal fluid early in the course of the disease, but meningeal symptoms appear in immune phase and meningitis is immunological in mechanism. All these pathological changes are marked in severe forms. In part of severe cases illness is with favorable course, in other – with rapid progression of toxicity, untreatable acute renal failure, appear severe bleeding, cardiovascular disorders with shock (1, 2, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15). The observed course of illness and pathological laboratory findings in our cases have been correlated with references (3, 4, 6, 8, 10, 13, 14).

CONCLUSION:

Leptospirosis has interesting and not fully clear pathogenesis, broad clinical spectrum and high mortality rate in severe cases. The illness requires correct diagnostic approach purposed to an early diagnosis and adequate treatment including early hemodiaperfusion in acute renal failure for prevention of brain and lung edema – the major tanatogenic factors. More experiments are necessary about specific factors of serotypes, and about the role of immunological changes in humans with leptospirosis, especially in severe cases.

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