GENERAL PATHOLOGY AND PATHOLOGICAL PHYSIOLOGY

Markers of General Pathology

V. D. Paponov, V. V. Paponov, and G. V. Baidakova

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 133, No. 3, pp. 262-264, March, 2002
Original article submitted November 28, 2001

Studies of the protein composition of leukocytes revealed markers of general pathology: 2 protein parameters (53K/H2A>0.25; 43K/H2A<1.61) differed from normal in 1627 patients with various pathologies. We compared protein parameters of leukocytes with other markers of general pathology. By the sensitivity and spectrum of associated diseases, the detected protein parameters of leukocytes can serve as the gold standard in the diagnostics of general pathology. These protein markers can be used for screening of newborns requiring therapeutic and preventive treatment, employers exposed to occupational hazards, and people inhabiting ecologically unfavorable regions, and for prevention of therapeutic complications in patients.

Key Words: *general pathology; leukocytes; proteins*

The concept of general pathology is a cornerstone for theoretical medicine. It provides general information about various diseases independently on their etiology and individual characteristics of patients [10,11]. Unfortunately, the existence asymptomatic pre- and postclinical periods in the development of each disease [10,11] is often underestimated in theoretical medicine. Specific and general diseases are characterized not only by clinical signs appearing as anatomical and physiological damages, but also by subclinical signs appearing in the early period and persisting during asymptomatic postclinical period of the disease (pre- and postclinical signs, respectively). Asymptomatic pathology can be detected by biochemical, immunological, biophysical, biomolecular and genetical methods.

This work was designed to call attention of scientists to subclinical signs of general pathology. After 20-year studies we revealed markers of general pathology unique in their sensitivity and spectrum of associated diseases [6-8]. These markers are a result of abnormal reactions of the genetic apparatus in human leukocytes to pathological conditions manifesting in abnormal content of proteins with molecular weights of 53 and 43 kDa (53K and 43K, respectively) in leukocytes.

Medical and Genetic Research Center, Russian Academy of Medical Sciences, Moscow. ***Address for correspondence:*** V_Paponov@mail.ru. Paponov V. D.

MATERIALS AND METHODS

Protein content in blood leukocytes was measured by polyacrylamide gel electrophoresis. Densitometry of gel plates stained and washed from Coomassie R-250 was performed on a Gilford spectrophotometer at 570 nm. The hight of the corresponding peaks on densitogram was measured. The relative protein parameters 53K/H2A and 43K/H2A were analyzed, where H2A is histone protein of leukocytes.

We examined 1627 patients with the following pathologies: hereditary diseases associated with gene mutations (type I neurofibromatosis and phenylketonuria; n=44); congenital chromosomal diseases associated with aneuploidy and confirmed karyotypically (syndromes of Down, Klinefelter, and Turner; n=55); multifactor diseases with genetic predisposition (psoriasis and ulcers of the stomach and duodenum; n=170); diseases accompanied by congenital and acquired im-

0007-4888/02/1333-0222$27.00

mune disorders (common variable hypogammaglobulinemia and bronchial asthma; *n*=115); tumors of the lungs, stomach, skin, larynx, intestine, mammary and thyroid glands, prostate, pancreas, liver, kidneys, urinary bladder, bones, uterus, ovaries, brain, and lymphatic and hemopoietic tissues (*n*=403); viral and bacterial infectious diseases (hepatitis, herpes, papilloma, and tuberculosis; *n*=159); diseases caused by physical factors, including ionizing radiation (radiation disease; *n*=13); diseases of the cardiovascular system (*n*=118), kidneys and urinary system (*n*=61), liver and biliary system (*n*=140), ear, throat, and nose (*n*=61), bones and joints (*n*=109), and gastrointestinal tract (*n*=179).

Previously, we established the differences between normal and abnormal protein parameters of leukocytes [7]. Values of 53K/H2A≤0.25 and 43K/H2A≥1.61 corresponded to normal.

RESULTS

The contents of 53K/H2A and 43K/H2A in leukocytes differed from normal in all patients.

The markers of general pathology were compared with other common parameters.

The following qualitative symptoms of tissue damages are used as general pathological signs [10]: edema, circulatory disturbances (plethora, anemia, hemostasis, and hemorrhage), atrophy, dystrophy, and necrosis. Compensatory and adaptive reactions to damages, including thrombosis, inflammation, regeneration, hypertrophy (hyperplasia), and immune response, also serve as signs of general pathology. Quantitative analysis of these symptoms is difficult because in various patients and at different stages of the disease they reflect pathological process or compensatory reactions. It was demonstrated at the qualitative level by D. S. Sarkisov *et al*. [10]. Moreover, we revealed quantitative manifestations of immune disturbances during psoriasis [8].

Body temperature, heart rate, respiratory rate, and blood pressure serve as quantitative clinical signs of general pathology. These symptoms accompany various pathological processes, but do not allow monitoring of patients at the pre- and postclinical stages.

Markers commonly used for monitoring of diseases can serve as subclinical signs of general pathology: erythrocyte sedimentation rate, differential leukocyte count, population composition of lymphocytes characterizing cell immunity, and plasma levels of various proteins, including immunoglobulin (characteristic of humoral immunity), neopterin (early indicator of activated cell immunity) [14], acute phase proteins [9,13], and P-proteins (fragments of receptor proteins) [4]. Recently, a method for estimating conformation of human serum albumin (marker of general pathology) was developed [1].

We previously compared changes in protein parameters of leukocytes and population composition of leukocytes and lymphocytes during psoriasis [8]. Changes in the percentage of neutrophils (67%) and B cells (78%) were most pronounced in children and adults with psoriasis, respectively. The sensitivity of protein parameters was 100%.

T cell deficiency is observed in 64% patients with chronic bronchitis, 62% patients with purulent and surgical diseases, 49% patients with recurrent and long-term respiratory infections, and 37.5% patients with of ear, throat, and nose diseases [15].

The measurements of plasma immunoglobulin content allow diagnosing only certain diseases associated with disturbances in humoral immunity. The concentration of most sensitive acute-phase protein C-reactive protein remains unchanged in patients with viral infections [9].

Neopterin can serve as the marker of general pathology. Cytokines and interferon-γ released from T lymphocytes promote conversion of guanosine triphosphate into neopterin, which is secreted by macrophages [14]. Overproduction of neopterin is observed in patients with rheumatoid arthritis, ulcerative colitis, systemic lupus erythematous, multiple sclerosis, pulmonary sarcoidosis, insulin-dependent diabetes, thyroiditis, phenylketonuria, tumors, viral infections, and autoimmune disorders. However, in cancer patients the sensitivity of this marker varies from 100% (late stages of blood cancer and tumors in children) to 20% (breast cancer) [14]. By contrast, the content of 53K/H2A and 43K/H2A markers differs from normal in all patients with tumors of 18 organs mentioned above.

P-proteins are associated with various diseases, but their sensitivity is only 80% [4].

Thus, protein parameters of leukocytes 53K/H2A and 43K/H2A can serve as the gold standard for the diagnostics of general diseases (as compared to long-term observations of patients with chronic and degenerative diseases [12]).

Protein markers of general pathology hold much promise for the diagnostics of diseases in newborns (screening of patients requiring fine diagnostics and preventive treatment in the preclinical period); preclinical screening of diseases among individuals exposed to occupational hazards (physical, chemical, or biological factors) and prevention of occupational diseases; early diagnostics of diseases in people inhabiting ecologically unfavorable regions and prevention of chronic disorders and disability; monitoring of diseases, selection of adequate therapeutical methods, and prevention of complications; estimation of completeness of therapy (normal and stable content of 53K

and 43K proteins in blood leukocytes); prevention of diseases in children with hereditary predisposition; clinical tests of new medicinal preparations; and evaluation of contraindications to the use of drugs.

REFERENCES

1. *Blood Serum Albumin in Clinical Medicine* [in Russian], Eds. Yu. A. Gryzunov and G. E. Dobretsov, Moscow (1998).
2. I. V. Davydovskii, *General Human Pathology* [in Russian], Moscow (1969).
3. V. P. Kaznacheev and M. Ya. Subbotin, *Essays on the Theory of General Pathology* [in Russian], Novosibirsk (1971).
4. A. Ya. Kul'berg, *Immunologiya*, No. 2, 71 (1996).
5. *General Human Pathology*, Eds. A. I. Strukov *et al*., Moscow (1982).
6. V. D. Paponov, A. V. Simonova, E. V. Malashenkova, *et al*., *Immunologiya*, No. 2, 60-63 (1997).
7. V. D. Paponov, I. G. Suntsova, G. V. Baidakova, and V. N. Mordovtsev, *Byull. Eksp. Biol. Med*., **131**, No. 3, 310-312 (2001).
8. V. D. Paponov, I. G. Suntsova, V. V. Paponov, *et al*., *Ibid*., **132**, No. 9, 247-250 (2001).
9. D. D. Petrunin, *Laboratoriya*, No. 1, 11 (1996).
10. D. S. Sarkisov, M. A. Pal'tsev, and N. K. Khitrov, *General Human Pathology* [in Russian], Moscow (1995).
11. D. S. Sarkisov, *Byull. Eksp. Biol. Med*., **131**, No. 1, 5-10 (2001).
12. R. Fletcher, S. Fletcher, and E. Vagner, *Clinical Epidemiology. Bases of Evidential Medicine* [in Russian], Moscow (1998).
13. O. P. Shevchenko, *Laboratoriya*, No. 1, 3-6 (1996).
14. O. P. Shevchenko, G. A. Olefirenko, and O. V. Orlova, *Ibid*., No. 4, 6 (2000).
15. V. S. Shirinskii, N. M. Starostina, Yu. A. Sennikova, and O. A. Malysheva, *Allergol. Immunol*., **1**, No. 1, 62-70 (2000).