Relationship between IFN- γ Production by Blood Lymphocytes and Constitutional Personality Features of Patients with Idiopathic Mitral Valve Prolapse

I. D. Surkina, O. Yu. Sokolov, M. V. Gabaeva, K. G. Gurevich, M. V. Alfimova, E. V. Akatova*, and L. S. Pak*

Translated from *Byulleten' Eksperimental'noi Biologii i Meditsiny*, Vol. 131, No. 4, pp. 461-463, April, 2001 Original article submitted December 27, 2000

Psychological testing using Eysenck Personality Inventory and immunological testing of 75 patients with idiopathic mitral valve prolapse revealed low production of interferon-γ by blood lymphocytes and a correlation between interferon-γ production and patient's temperament. Low neuroticism and extroversion scores were found in patients with normal interferon-γ production. High neuroticism score was detected in 82% patients with lowest interferon-γ production, which refers these patients to a group at high immunological risk and prompts the use of interferon and/or its inductors in complex therapy of these patients.

Key Words: γ-interferon; neuroticism; Eysenck personality inventory; mitral valve prolapse

The course of many diseases, as well as recovery and rehabilitation processes depend on the constitutional and personality features of a patient. This has been demonstrated for patients with mental disorders, cardiovascular diseases, cancer, and many other diseases [9,11,12]. On the other hand, these processes depend on the immune and interferon status, primarily on the interferon-γ (IFN-γ) system, the key mechanism of immunity regulation. There is evidence on a relationship between functional activity of lymphocytes (serum interferon) and aggressive or inhibitory behavior under conditions of chronic psychoemotional stress in patients with borderline mental disorders [5]. However little is known on the relationship between IFN production and personality features. This prompted us to study this relationship in patients with idiopathic mitral valve prolapse (MVP), as this disease is a typical example of constitutional personality abnormalities [2]. Patients are characterized by specific personality

Laboratory of Pathophysiology, Center of Mental Health, Russian Academy of Medical Sciences; 'Department of Visceral Diseases No. 1, Therapeutic Faculty, Russian State Medical Stomatological University, Moscow. *Address for correspondence:* sokolov@rcmh.msk.ru. Sokolov O. Yu.

features; they are referred to the so-called asthenoneurotic type [7]. MVP is associated with high incidence of infections and inflammatory diseases [8], which attests to a deficiency of the immune-interferon system.

We investigated possible relationship between IFN-γ production by lymphocytes and constitutional and personality characteristics of MVP patients.

MATERIALS AND METHODS

IFN- γ production was evaluated by biological testing of the whole blood by the micromethod [4] and expressed as geometrical mean of the titer in U/ml. Seventy-five outpatients with idiopathic MVP (32 men and 43 women) aged 19-45 (31.1 \pm 1.7) years were examined.

Psychological testing was carried out using Eysenck Personality Inventory adapted for Russia [3] and intended for the diagnosis of two basic personality states, neuroticism (emotional instability) and extroversion/introversion. According to their neuroticism and extroversion scores, the examines were divided into 4 groups: melancholic (introverts with high level of neuroticism), phlegmatics (introverts with low level of neuroticism),

sanguinics (extroverts with low level of neuroticism), and cholerics (extroverts with high level of neuroticism). Psychological testing was carried out in 59 of 75 examined patients. In parallel, psychological characteristics of age- and sex-matched healthy controls (n=59) were determined by the same method.

The results were statistically processed using Statistica for Windows software. Dispersions were compared using Fisher *F* test. As normal distribution was hypothesized in all cases, the mean values in equal dispersions were compared using Student's *t* test and in various dispersions using Welch test [1]. The significance of differences expressed in percent was evaluated using Fisher f transformation [6].

RESULTS

Production of IFN- γ by blood lymphocytes in MVP patients varied from 2 to 128 U/ml. According to Epidemiological data [4] obtained on 500 donors by the same method, normal level of IFN- γ production is 64-256 U/ml, but 20% donors had very low level of cytokine production (\leq 16 U/ml). In MVP patients low level of IFN- γ production was twice more incident, and the mean level of IFN- γ production was 31.8±3.9 U/ml. Hence, in the majority of examined patients IFN- γ production was decreased compared to normal.

Psychological testing showed that 32 MVP patients (54%) had low (<12) and 27 patients (46%) high extroversion score. These data did not differ the corresponding parameters in the control group. High level of neuroticism (Eysenck score>12) was found in 33 (56%) patients vs. 44% in the control and low level of neuroticism in 26 (44%) vs. 56% in the control. Therefore, individuals with high level of neuroticism were more frequent among MVP patients than among healthy controls, but these differences were insignificant.

In cholerics and melancholics (individuals with high level of neuroticism) the level of IFN- γ production was low (Fig. 1). No relationship between cytokine production and extroversion in combination with high neuroticism was detected. In the group with low level of neuroticism, IFN- γ production depended on the level of extroversion: in phlegmatics it was significantly (p<0.05) higher than in sanguinics.

In order to evaluate possible relationship between neuroticism and IFN- γ production in MVP patients, the patients were divided into 3 groups with different levels of IFN- γ production: 1) below 16 U/ml (n=30), 2) 16-64 U/ml (n=9), and 3) 64 U/ml and higher (n=20) and the percentage of patients with low and high levels of neuroticism were evaluated for each group (Fig. 2).

Analysis of the results showed an intricate relationship between IFN- γ production by lymphocytes and the level of neuroticism in patients with MVP

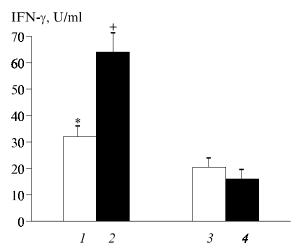


Fig. 1. Production of IFN- γ in MVP patients: sanguinics (1, n=12), phlegmatics (2, n=14), cholerics (3, n=15), and melancholics (4, n=18) with low (1, 2) and high (3, 4) levels of neuroticism. Light bars: extroverts; dark bars: introverts. *p<0.01 vs. cholerics and melancholics; †p<0.05 vs. all other groups.

(Fig. 2). In group 1, a high neuroticism score according to Eysenck scale was detected in 82% patients and a low score only in 18% (p<0.05). The same tendency was observed in group 2. In group 3 the percentages of patients with high and low neuroticism scores were similar. Hence, in patients with idiopathic MVP and decreased production of IFN- γ the level of neuroticism negatively correlated with the immune and interferon status, while in MVP patients with high production of IFN- γ no such relationship was found observed.

Possible physiological mechanisms responsible for the observed relationship between the immune IFN system and personality features are unknown. Serotoninergic system involved in the regulation of mental

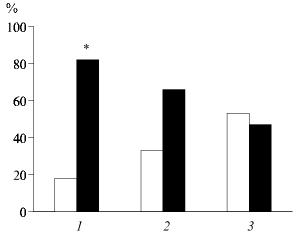


Fig. 2. Distribution of patients with low (light bars) and high (dark bars) level of neuroticism in relation to production of IFN- γ . Production of IFN- γ : 1) below 16 U/ml (n=30), 2) 16-64 U/ml (n=9); 3) above 64 U/ml (n=30). *p<0.05 vs. patients with low neuroticism score in the same group.

I. D. Surkina, O. Yu. Sokolov, et al.

and immune processes can play a role [10,13]; the sympathetic nervous system also affects IFN- γ production, and changes in this system are typical of patients with MVP [14,15]. Involvement of other regulatory mechanisms is also possible.

These data allow us to conclude that low level of neuroticism and extroversion (phlegmatic temperament) are most favorable personality features for the function of the immune interferon system. High neuroticism is the most unfavorable feature and can be regarded as a immunological risk marker irrespective of the level of extroversion.

Presumably modulation of the immune interferon system can affect many processes accompanying MVP. This indicates the advisability of including IFN- γ and/or its inducers into complex therapy for patients with MVP with high level of neuroticism.

REFERENCES

- 1. A. Afifi and S. Eizen, *Statistical Analysis: Computer Approach* [in Russian], Moscow (1982), p. 488.
- A. P. Vein, A. D. Solov'eva, and A. V. Nedostup, *Kardiologiya*, No. 2, 55-58 (1995).

I. N. Gil'yasheva, Clinical Methods of Psychological Diagnosis and Correction [in Russian], Leningrad (1983), pp. 62-81.

391

- 4. F. I. Ershov, *Interferon System in Health and Disease* [in Russian], Moscow (1996), p. 239.
- N. N. Naidenova, M. V. Mishenev, V. Ya. Semke, et al., Zh. Nevrol. Psikhiatr., No. 5, 74-76 (1994).
- 6. N. A. Plokhinskii, *Biometry* [in Russian], Moscow (1970), p. 360.
- 7. Ya. A. Storozhakova, *Psychovegetative Syndrome in the Structure of Borderline Mental Disorders in Patients with Mitral Valve Prolapse in an Outpatient Psychiatric Setting.* Methodological Recommendations [in Russian], Moscow (1992).
- 8. V. M. Yakovlev, A. V. Glotov, and G. I. Nechaeva, *Ter. Arkh.*, No. 5, 79-83 (1994).
- F. Bonaguidi, M. G. Trivella, C. Carpeggiani, et al., G. Ital. Cardiol., 24, No. 6, 745-753 (1994).
- 10. H. Boudoulas, A. Kolibash, and P. Balker, *Am. Heart. J.*, **118**, 796-816 (1989).
- S. Cohen and T. B. Herbert, Annu. Rev. Psychol., 47, 113-142 (1996).
- 12. R. Dantzer, Encephale, 21, No. 7, 3-9 (1995).
- J. Elenkov, D. A. Papanicolau, R. L. Wilder, and G. P. Chrousos, *Proc. Ass. Am. Physicians*, **108**, No. 5, 374-381 (1996).
- 14. M. Kubera, G. Kenis, E. Bosmans, et al., Neuropsychophar-macology, 23, No. 1, 89-98 (2000).
- 15. A. Roy, J. Affect. Disord., 52, Nos. 1-3, 247-249 (1999).