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ИССЛЕДОВАНИЕ АУТОАНТИТЕЛ К 24 АНТИГЕНАМ ПРИ РАЗНЫХ ФОРМАХ ТУБЕРКУЛЕЗА И САРКОИДОЗЕ НА ФОНЕ НЕДОСТАТОЧНОСТИ ВИТАМИНА Д

© Ирина Васильевна Беляева[1,3], Леонид Павлович Чурилов[1,2], Лия Робертовна Михайлова[2], Алексей Владимирович Николаев[1], Анна Андреевна Старшинова[1,2], Петр Казимирович Яблонский[1,2]

[1] ФГБОУВО «Санкт-Петербургский государственный университет» медицинский факультет.
199034, Санкт-Петербург, Университетская наб. д. 7-9.
[2] ФГБУ «СПб НИИФ» Минздрава России. 191036, Санкт-Петербург, пр. Лиговский, д. 2–4.
[3] Санкт-Петербургский государственный педиатрический медицинский университет.
194100, Санкт-Петербург, Литовская ул., 2.

Контактная информация: *Ирина Васильевна Беляева* — кафедра патологии ФГБОУВО СПбГУ Минздрава России и кафедра патологической физиологии с курсом иммунопатологии ФГБОУ СПбГПМУ Минздрава России. E-mail: irivaba@mail.ru

Резюме. Установлена связь недостаточности витамина Д с развитием некоторых аутоиммунных и хронических воспалительных болезней, таких как туберкулез и саркоидоз. Мы исследовали пробы крови, взятой в марте-апреле (Санкт-Петербург, 59^0 северной широты) у больных с коротким и продолжительным периодом течения туберкулеза, у больных саркоидозом и у здоровых доноров. Мы измерили уровни кальцифедиола, кальцитриола и пролактина в сыворотке, кателицидина в плазме крови и индивидуальный аутоиммунный профиль больных. Уровень 25(OH) D_3 был низким даже у здоровых доноров — 19.3±1.4 нг/мл, у всех больных он был значительно ниже. Концентрация активного метаболита 1.25$(OH)_2$ D_3в сыворотке была повышена только у больных саркоидозом. В процессе инфекции активированные макрофаги конвертируют главную циркулирующую форму 25(OH) D в активную 1.25$(OH)_2$ D_3, которая интракринно вызывает выработку антимикробного пептида кателицидина. Мы не нашли ожидаемого повышения продукции кателицидина при туберкулезе и саркоидозе, видимо, вследствие низкой концентрации 25(OH) D_3. Содержание пролактина при саркоидозе не отличалось от контрольных значений, но было существенно выше у больных с инфильтративной и фиброзно-кавернозной формами туберкулеза. Уровень индивидуальной средней иммунореактивности аутоантител к 24 антигенам был значительно снижен при туберкулезе и саркоидозе по сравнению со здоровой популяцией, что указывает на поликлональную иммуносупрессию в обоих случаях. Выраженные отклонения от индивидуального уровня средней иммунореактивности обнаружены в отношении нескольких антигенов у всех больных. Однако увеличение продукции аутоантител к некоторым антигенам не сопровождалось проявлениями аутоиммунного поражения соответствующих органов. Аутоиммунным манифестациям может способствовать гиперпролактинемия. Мы выявили значительные изменения в содержании витамина Д, пролактина и аутоантител при легочных формах туберкулеза и саркоидоза, а также различия исследованных показателей в разных группах больных туберкулезом и отсутствие кателицидинового ответа на инфекцию.

Ключевые слова: аутоантитела, инфильтративный туберкулез, фиброзно-кавернозный туберкулез, саркоидоз, витамин Д.

AUTOANTIBODIES TO 24 ANTIGENES IN VARIOUS FORMS OF TUBERCULOSIS AND SARCOIDOSIS ON THE BACKGROUND OF VITAMIN D INSUFFICIENCY

© Irina. V. Belyaeva[1,3], Leonid P. Churilov[1,2], Liya R. Mikhailova[2], Alexey V. Nicolaev[1], Anna A. Starshinova[1,2], Petr K. Yablonskiy[1,2]

[1] Saint-Petersburg State University, medical faculty. 199034, St. Petersburg, University emb. 7-9
[2] Saint-Petersburg State Research Institute of Phthisiopulmonology. 191036, Saint-Petersburg, Ligovskiy pr., 2–4
[3] Saint-Petersburg State Pediatric Medical University. 194100, Russia, Saint-Petersburg, Litovskaya str., 2.

Contact Information: *Irina V. Belyaeva* — Department of Pathology, St. Petersburg State University, Ministry of Health of Russia and Department of Pathological Physiology, with a course of immunopathology, Federal State Budgetary Educational Institution of State Medical University, Ministry of Health of Russia. E-mail: irivaba@mail. ru

Abstract. The vitamin D deficiency is associated with several autoimmune and chronic inflammatory diseasessuch as tuberculosis (TB) and sarcoidosis (Sr). We studied blood samples taken in March — April in Saint Petersburg area (59° north latitude) from patients with different forms of pulmonary tuberculosis, sarcoidosis, and from healthy donors, distinguishing between tuberculosis patients with short either long duration of disease. We measured the levels of calcifediol and calcitriol, prolactin in sera, cathelicidin in plasma, and the individual autoimmune profile of patients. The level of 25(OH) D was low even in healthy adult donors — 19.3±1.4 ng/ml; however in all patients it was significantly lower. Active metabolite $1.25(OH)_2 D_3$ concentration in serum was increased only in the sarcoidosis patients. During infection the activated macrophages convert the main circulating form 25(OH) D into the active $1.25 (OH)_2 D_3$ which induces the antibacterial peptide cathelicidin. We saw no expected increase of cathelicidin levels in tuberculosis and sarcoidosis, apparently due to low concentration of 25 (OH) D. The prolactin content in the sarcoidosis patients did not differ from that of controls, but was significantly higher in patients with infiltrative and fibrous-cavernous tuberculosis. The individual mean immune reactivity level of autoantibodies to 24 antigens was significantly decreased in tuberculosis and sarcoidosis compared to healthy population, which indicates polyclonal immunosuppression in both diseases. Pronounced deviations from mean individual immune reactivity level were found for several antigens in all patients; the increase of the autoantibody production towards severalautoantigens could not be attributed to any clinical manifestation of comorbid autoimmune diseases in the corresponding organs. Hyperprolactinemia may contribute to autoimmune manifestations. We registered significant changes in the content of vitamin D, prolactin, and autoantibodies in pulmonary tuberculosis and sarcoidosis, as well as the difference between the studied groups of tuberculosis patients and failure of the cathelicidin response to infection in them.

Key words: autoantibodies, infiltrative tuberculosis, fibrous cavernous tuberculosis, sarcoidosis, vitamin D.

INTRODUCTION

Pulmonary tuberculosis(TB) and pulmonary sarcoidosis (Sr) both belong to chronic granulomatous inflammation and often pose difficulties for differential diagnosis having similar morphological impairments, even more so due to presence of *Mycobacterium tuberculosis* (Mtb) in many sarcoidosis patients. Sarcoidosis etiology is still unknown, but triggering role of Mtb in some cases is obvious [20]. It is possible that Tb and Sr may occur as different patterns of reaction towards the same infectious or adjuvant-like stimuli [12].

The innate immune cells primarily infected by Mtb are the alveolar macrophages. In the macrophage phagosomeMtb find favorable niche for survival and replication [21]. Human alveolar macrophages activate signaling pathways to combat bacterial replication and attract other immune cells into the site of infection [2, 33]. A number of receptors recognizing mycobacterial ligands play a role in the macrophage phagocytosis of Mtb, among them the Toll-like receptors (TLRs). The engagement of TLRs by microbial components triggers the induction of inflammatory responses, antimicrobial host defense, and the initiation of events important for the adaptive immune responses [17, 6]. Mtb interferes with the macrophage effectors and signaling pathways, inhibits phagolysosomal maturation of the dendritic cells which are important innate immune responses to intracellular infection [27, 5].

Recent investigations attracted worldwide attention to vitamin D, which besides its classical effect, is involved in pathogenesis of chronic diseases including tuberculosis and autoimmune disorders. Vitamin D deficiency is widely spread and is associated with increased tuberculosis risk in different populations [22].

The vitamin D status is based upon the serum levels of 25(OH) D. The proper level of 25(OH) D required for good health is debated, but the optimal vitamin D concentration 30–40 ng/ml 25(OH) D is associated with the most beneficial health effects including benefits against the risk of autoimmune diseases [34].

It was shown that conversion of 25-hydroxyvitamin D to active 1,25-dihydroxyvitamin D occurs in the immune cells and is essential for their antibacterial activity due to induction of cathelicidin (LL-37), a potent antimicrobial peptide [11, 19, 13]. Cathelicidin can fulfill antimicrobial, antifungal and antiviral properties through many different ways [26,1]; it plays a particular role in defense against intracellular Mtb inducing autophagy in monocytes/macrophages [37].

Vitamin D deficiency is common in patients with autoimmune diseases [7, 28] as well as in the TB patients [29]. Vitamin D supplementation restores the immune functions inducing the immature tolerogenic state, enhances the function of regulatory T cells, inhibits the Th1 functions, and affects the human B cell differentiation [24, 10]. On the other hand the microbial products aside from vitamin D deficiency can break self-tolerance and induce autoimmune disease through activation of the antigen-presenting cells [35]. Autoimmunity also is peculiar to sarcoidosis [4].

The majority of investigations of the vitamin D impact on tuberculosis did not take into account various forms of the disease. Our work partially fills that gap up. Besides, we made a comparison of

the vitamin D level and some immune and endocrine parameters in various forms of TB and in sarcoidosis. We studied the blood contents of two vitamin D_3forms — calcifediol and calcitriol, as well as concentrations of cathelicidinand prolactin, autoantibodies to 24autoantigens. Distinction was made between TB patients with short-time and long-time duration of disease.

MATERIAL AND METHODS

A total of 41 participants were enrolled in the studywith informed consent. Blood samples obtained in April-June from the in-patients of the Saint Petersburg Research Institute of Phthisiopulmonology (SPbRIP) and those of TB sanatorium near Saint Petersburg (59° north latitude). The institutional review board of the SPbRIP approved all studies involving humans. All processing of information obtained from the participants has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki).

The participants were divided into four groups, which included:

1) 33 patients with infiltrative tuberculosis (IT);
2) 22 patients with fibrous cavernous tuberculosis (FCT);
3) 16 patients with sarcoidosis (Sr);
4) 41 healthy donors.

The mean age of patients was 35.4 years (range 17–65), 73% were males. The mean age ofhealthy donors was 31.5 years (range 17–56), 44% were males. The chest X-ray findings, direct smear microscopy, mycobacterial culture results, and clinical data were abstracted from the medical records. TB manifestsin many forms. In our study two groups of TB patients had different clinical and X-ray characteristics, but all TB patients were in active phase of the disease.

The IT is the most common type of the secondary TB. In our investigation the IT patients (mean age 22.9 years, range 17–33) had 1–3 segments of the lung affected (81.4%), and more benign course of disease compared to FCT group. 38% of IT patients excreted Mtb. Physical signs of TB were absent in 49.1% of patients.

The FCT patients had progressive disease lasting from 4 to 19 years, with average 11.2 years of duration. The multiple involvement of lung segments and signs of lung destruction were observed in all FCT patients. Mtb excretion was found in 91% of them. Most patients (89%) had some manifestations of TB on physical examination. All FCT patients had multi-drug Mtb resistance and some degree of respiratory insufficiency. The mean age of FCT patients group was 47.9 (range 29–65 years).

Overwhelming majority of citizens in Russia is vaccinated with BCG, which was the case for all donors involved.

The concentration of 25-hydroxyvitamin D (calcifediol) was measured with ELISA (Immunodiagnostic Systems Ltd, UK) with the assay sensitivity 5 nmol/L.

The level of 1,25-dihydroxyvitamin D (calcitriol) was measured with ELISA (Immunodiagnostic Systems Ltd, UK). The kit was a complete assay system intended for purification of calcitriol in the human serum by immunoextraction followed by quantitation by the enzyme immunoassay. The sensitivity of the assay was 2.5 pg/mL.

Cathelicidin (human LL-37) levelin plasma was measured by ELISA (Hycult Biotech, Frontstraat 2a, 5405 PB Uden, the Netherlands). The detection limit was 0.1ng/mL.

The prolactin level was measured by the PRL AccuBind ELISA test system (Monobind Inc. 100 North Pointe Drive Lake Forest, CA 92630 USA) which had detection limit 0.15ng/mL. The prolactin, procalcitonin, T_3, T_4, TSH, and cortisol levels were measured by ELISA (Vector Best Baltica, Saint-Petersburg, Russia).

THE STUDY OF INDIVIDUAL AUTOANTIBODIES-PROFILEIN SERA

To evaluate the spectrum and relative intensity of autoimmunity, we investigated the individual serum profiles of multiple autoantibodies (AAB) and the integral autoreactivity by the method of ELI-viscero-test, (Immunculus, Russia) which is based on the ELISA technology [25].

The method allows evaluating the relative serum content of IgGAABtowards 24 major antigens simultaneously (Figure 1). For every person its average over all that antigens characterizes the individual *mean immune reactivity* (MIR). Investigations were carried out according to the instructions of the manufacturer using the computer program attached. The results of ELI-viscero-test characterize not the absolute AAB concentrations but their deviations in percentage from the individual MIR. The small quantities of AAB to different antigens are always present in the serum of healthy individuals; collectively they form the individual autoimmune reactivity profile [74]. Deviation ranges for each antigen in healthy population were established in to be between –20 and +10 percent from MIR[25].

We tested the levels of autoantibodies against the following autoantigens: the double stranded DNA (dsDNA), Fc-fragment of IgG, β2-glycoprotein, the membrane antigen of cardiomyocytes (CoM-0.2), the cardiac isoform of adrenoreceptor (betaAR), the membrane (KiM-0.5) and cytoplasmic (KiS-0.7) renal glomerular antigens, the membrane (LuM-0.2) and the cytoplasmic (LuS-0.6) lung alveolar epithelial antigens, the hepatic antigens (HMMP, HeS-08), the gastric mucosa antigen (GaM-02), the intestinal antigen (ItM-07), insulin (Ins) and its receptor (Ins-R), thyroglobulin (TG) and thyrotropin receptor (TSH-R), the adrenal medullar cell membrane antigen (AdrM-D/C), the myelin basic protein (MBP), the protein of the astroglial cell filaments (GFAP), the common antigen of the prostate cells and spermatozoa (SR-0,6), and the acid calcium-binding S100 protein (S100).

The individual relative level of the antibodies to each of the 24 antigens was evaluated as the ratio of the optical densities of the respective sera and the control serum corresponding to the population average; deviation of the mean of these 24 values from the population average expressed in per cent characterizes the individual mean immune reactivity (MIR) of a person.

STATISTICAL ANALYSIS

Statistical analysis was carried out using the Statistical Package for Social Sciences software. Mean values were compared using the t-test for the data that were normally distributed and the

Mann-Whitney test for the data that were not normally distributed. Statistical significance was set at p<0.05.

RESULTS

The peripheral blood characteristics of the two investigated TB groups were different. Both groups were characterized by monocytosis, thrombocytosis, and increased erythrocyte sedimentation rate (ESR), but in the FCT group changes were much more significant. Monocytosis was present in 76.5% FCT patients, thrombocytosis — in 85.7% patients, increased ESR — in 82.4% patients.

The vitamin D in tuberculosis and sarcoidosis.

The serum level of 25(OH) D was low even in healthy adult donors constituting 19.3±1.4ng/mL (the mean±SE); but in all patients it was significantly lower, namely 13.2±1.7 in Sr (p<0.05), 11.7±1.8 (p<0.001) in IT and 8.2±1.4ng/mL (p<0.001) in FCT (Table 1).

The serum concentrationof the $1.25(OH)_2D$ was increased in the sarcoidosis patients only (50.4±16.6 vs 35.5±12.8pg/mL in healthy subjects, p<0.05) (Table 1).

CATHELICIDIN AND HORMONE LEVELS

There was no increase of the cathelicidin level in tuberculosis orsarcoidosis. The cathelicidin content was 39.8±9.7 ng/mL in healthy donors, 45.1±18.3ng/mL in IT, 50.1±32.8 ng/mL in FCT, and 39.8±8.3ng/mL in sarcoidosis patients (Table 1).

The prolactin content in the sarcoidosis patients did not differ from that of controls, but it was significantly higher in the IT (22.3±3.4 vs 7.7±0.9 ng/mL, p<0.01) and FCT (19.4±3.3 vs 7.7±0.9 ng/mL, p<0.05) groups (table 1).

The levels of procalcitonin, 3-iodotironin, thyroxin and TSH were normal in all groups; only in a few cases of tuberculosis the blood cortisol level was raised.

INDIVIDUAL SERUM AAB PROFILES

For evaluation of autoimmunity spectrum, we used the sera of 9 patients with IT, 9 those with FCT and 12 patients with sarcoidosis.

Deviation of MIR from zero reflects the individual immune system activity (Figure 1). Normal range of MIR deviations from the population average is between –25% and +5% [25].

MIR was significantly decreased in tuberculosis and sarcoidosis compared to healthy population. It was decreased in 100% patients with IT, in 67% patients with FCT, and in 91% of sarcoidosis patients.

On the background of general MIR decrease, we revealed in all patients pronounced deviations of autoantibodies towards several autoantigens from MIR level. The IT patients (Table 2) most often had increased level of AAB to the dsDNA (in 4 patients out of 9). The predominance of autoantibodies to the kidney antigens, to insulin, and to the TSH-receptor equally was (5/9).

Significant deviations of AAB from normal ranges occurred in FCT patients predominantly to both kidney antigens (7/9), and to TSH receptor (6/9) (Table 3). Negative deviations (Figure 1) indicate, according to the authors of the method, binding of AAB by the surplus of autoantigensoccurring under intensive tissue decay. Compared to IT patients, each particular patient with FCT had elevated levels of AAB towards larger number of different antigens.

The sarcoidosis patients demonstrated fewer deviations from normal MIR ranges compared to the tuberculosis patients (Table 4).

Increased levels of AAB occurred predominantly towards dsDNA (8/12) and GaM-02 (4/12).

DISCUSSION

Pulmonary tuberculosis and pulmonary sarcoidosis, the last is a disease of unknown etiology, are recognized as granulomatous disorders; they have similar X-ray, morphological, and genetic characteristics [20].

It was suggested that mycobacterial antigen(s), e.g., heat shock proteins (Mtb-hsp) can serve as causative factors; Mtb-hsp, especially Mtb-hsp65, may provide a link between infection and autoimmunity [8]. The author hypothesizes that, in genetically different individuals, the same antigens (Mtb-hsp) may induce different immune responses, leading to the development of Sr or TB.

VITAMIN D

There is no consensus on the vitamin D level ranges. We considered the vitamin D levels <20ng/mL as the deficient ones

Table 1

Vitamin D, cathelicidin, prolactin

	Healthy subjects	Sarcoidosis	Infiltrative tuberculosis	Fibrous-cavernous tuberculosis
25 (OH)D ng/mL	19.3±1.4 8	13.2±1.7 8 p<0.05	11.7±1.8 13 p<0.001	8,2±1,4 8 p<0,001
1,25(OH)2D pg/mL	35.5±12.8 10	50.4±16.6 10 p<0.05	32.1±14.7 10	40.7±19.2 11
Cathelicidin ng/mL	39.8±9.7 20	39.8±8.3 8	45.1±18.3 24	50.1±32.8 12
Prolactin ng/mL	7.7±0.9 9	9.1±1.1 9	22.3±3.4 21 p<0.01	19.4±3.3 10 p<0.05

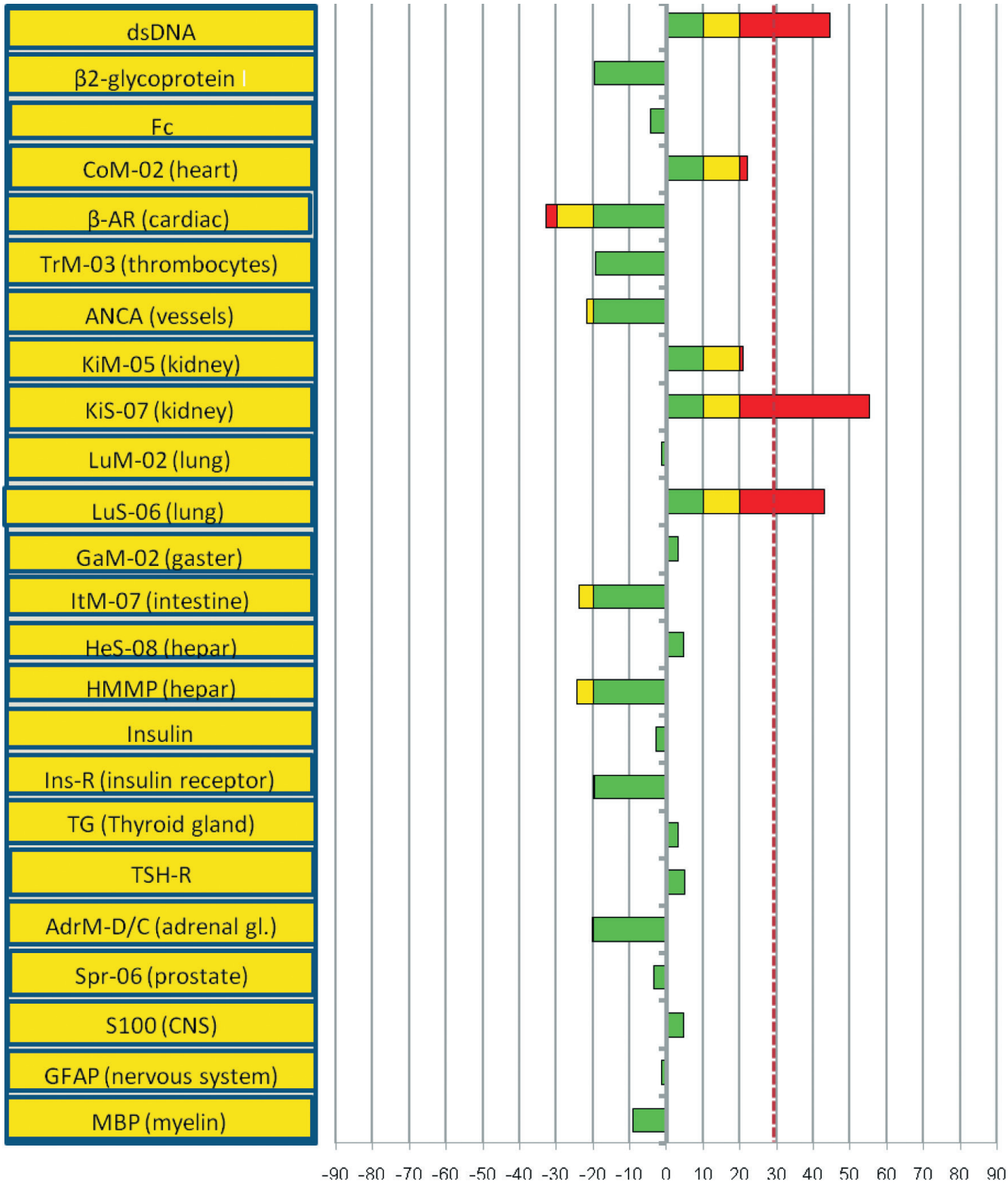

Fig. 1. Patient K., fibrous-cavernous TB. Auto-antibodies to different antigens plotted relative to individual mean immune reactivity (MIR). In four cases the increase of autoantibodies exceeds 20% and is statistically significant. For a single antigen (ß-AR) statistically significant decrease of antibodies is observed. The MIR value of K. was –29%. MIR in healthy population is shown by dashed red line

Table 2

Infiltrative tuberculosis

№№	73	77	94	85	46	23	42	90	86
dsDNA				+48	+30	+30			+90
β2-GPI			+28						
Fc									
CoM-02		+37	+36		+25				
βAR									
TrM-03									
ANCA									
KiM-05–40									
KiS-07	+80	+55				+64			+87
LuM-02								+21	
LuS-06	+31						+32		
GaM-02									
ItM-07									
HeS-08									
HMMP									
Insulin	+26	+23	+55					+59	+58
Ins-R									
TG							+35		
TSH-R		+28	+30	+29			+38	+39	
AdrM-D/C									
Spr-06									
S100	+44								
GFAP									
MBP									
MIR	-46	-33	42	-51	-31	-34	-51	-36	-43

and founddeficiency of the vitamin D in our study in patients with pulmonary Sr and especially with TB. The FCT patients with long progressing TB with many phases of exacerbation and remission and considerable lung lesion, had the deepest drop of the vitamin D level. Indeed, these patients were altered by multiple factors influencing their vitamin D status such as medicines (Rifampicin), long staying in hospital, and avoiding the sun exposure. It looks unlikely that the FCT patients had initially, before the TB disease onset, such a low level of vitamin D (8.2±1.43ng/mL); it is perhapsmore probable for thosefew patients who had comorbid chronic hepatitis. It seems that the low level of vitamin D is the result of interactions between Mtb and the host macrophages. A novel subset of genes was identified [5], whose regulation was affected specifically by infection with mycobacteria. This subset includes genes involved in response to vitamin D. The mean level of $1.25(OH)_2D$ was increased only in sarcoidosis patients probably due to its excessive production by the macrophages of Sr granulomata [3].

CATHELICIDIN

There were no significant changes in concentration of cathelicidin (LL-37) in the TB and Sr patients compared to healthy donors, probably due to the low concentration of 25(OH) D in both diseases. In patients with acute septic and non-septic infection the cathelicidin level was markedly enhanced and correlated with vitamin D status, but there was no correlation in the case of TB [36]. The authors of that work revealed higher LL-37 concentrations in TB patients. However the level of 25(OH)D in that study was higher than in our TB patients, besides the investigations were performed in the serum samples and not in plasma received from freshly taken blood. In that case during the procedure of plasma receiving, neutrophils may degranulate to be the source of LL-37. We found, as well as the authors of this study, high prevalence of thrombocytosis in TB patients but it correlated with the disease severity, monocytosis, and enhanced RSR and not with the cathelicidin level. We can find some support to our data in the report that demonstrated an association between low cathelicidin levels and the history of bacterial

Table 3

Fibrous cavernous tuberculosis

№№	169	82	27	78	69	67	81	76	90
dsDNA	+36		+37		+67				
β2-GPI									
Fc									
CoM-02	+56				+40			+33	
βAR							+25		
TrM-03									
ANCA						-35	+30		
KiM-05–40				+22		+29			
KiS-07	+29	+42		+57					
LuM-02									
LuS-06				+50					+28
GaM-02			+39	+48		+60			
ItM-07									
HeS-08									
HMMP									
Insulin		+60				+60		+90	+63
Ins-R					-36	-33			
TG							+49		
TSH-R	+26	+27	+28		+41		+31	+30	+47
AdrM-D/C		-33							
Spr-06					-33				
S100					-38	-35			
GFAP									
MBP					+31				
MIR	-39	-33	-31	-10	-8	-25	-31	-43	-54

pneumonia in the study of 650 individuals[18]. In the case of an intracellular pathogen like Mtb the intracrine mechanisms of defense are especially important and dependent on the vitamin D status.

The prolactin levels were raised in both TB group patients, but not differed from Sr patients. It was suggested that the prolactin level is a marker of the autoimmune processes [23].

INDIVIDUAL SERUM AAB PROFILES

Our interest to the AAB in the TB patients was motivated by the growing number of evidence that the autoimmune processes are triggered by infections like TB, because chronic presence of Mtb can be regarded as an endogenous adjuvant [29]. The important question is whether the AAB presence leads eventually to overt autoimmune disease. We studied two groups of patients with short-time and long-time course of TB and patients with Sr, which is a disease with an autoimmune component of pathogenesis, to clear this.

Individual mean immune reactivity (MIR) was significantly decreased in TB and Sr compared to healthy population, which indicates polyclonal immunosuppression [25]. Immunosuppression in pulmonary TB was demonstrated previously by other methods [14]. The immune responses in TB may increase the spontaneous and the Mtb antigen-induced apoptosis of T cells [15].

We saw that patients with TB and Sr had increased content of AAB to different antigens in spite of general background of immunosuppression. It is worth mentioning that evaluation of the relative AAB level with respect to MIR demonstrates the increase of the AAB production with greater sensitivity than the standard method of measuring their absolute content, under significant immunosuppression peculiar both to TB and Sr.

The increased level of AAB most often occurred with respect to the dsDNA (in IT and Sr). The TB patients also demonstrated enhanced level of AAB to different antigens, but AAB to the kidney antigens, to insulin, and to the TSH-receptor were prevailing. Our data are consistent with data of other reports; the TB patients' mean serum levels of several AAB were significantly increased compared with the controls [9]; a common anti-DNA idiotype in sera of patients

Table 4

Sarcoidosis

№№	49	117	118	130	132	123	124	141	202	203	205	206
dsDNA		+44			+28	+51	+43	+55		+82	+27	+60
β2-GPI				+23					+28			
Fc						+51						+29
CoM-02									+34			
βAR				+27								
TrM-03												
ANCA										+39		
KiM-05–40												
KiS-07												
LuM-02			+30		34							
LuS-06				+31								
GaM-02	+31						+26		+22	+23		
ItM-07												
HeS-08									+28			+23
HMMP				+23								
Insulin											+24	
Ins-R												
TG									+34			
TSH-R			+24									
AdrM-D/C						+32						+36
Spr-06												
S100			-38			-32						
GFAP	+22	+22										-35
MBP			23									
MIR	-56	-28	-56	-27	-46	-23	-29	-52	-41	-33	-52	-32

with active pulmonary tuberculosis was discovered [32]. Several reports demonstrated the presence of different AAB in the serum of the active TB patients [16, 30].

In our studythe Srpatients demonstrated fewer deviations from normal MIR ranges compared to the TB patients. It seems important that the change patternsin the IT, FCT and Sr groups were different. There were no corresponding clinical symptoms and signs of the autoimmune diseases involving the organs to which AAB were found. Despite high prevalence of AAB to the thyroid gland and the TSH receptor in TB patients we found no changes in concentrations of thyroid hormones and TSH. The authors of paper [30] who demonstrated the presence of AAB to different antigens in the TB patients, suggested that AAB are reactive in TB instead of being pathognomonic, and do not require immunosuppressant therapy. We tend to accept this interpretation, because 1) the most common anti-dsDNA autoantibodies were characteristic both for TB and Sr; 2) the FCT patients suffering from a more severe form of TB than the IT patients, had higher prevalence and a different set of AAB.

We registered significant changes in the content of AAB, vitamin D, and prolactin, in pulmonary TB and Sr, as well as the difference between the studied groups of TB patients and failure of the cathelicidin response to infection in them.

The data of this study testify the role of vitamin D deficit in poor cathelicidin response in TB and Sr. Both TB and Sr are accompanied by significant changes of autoimmune profile, which can be related to status of vitamin D and cytokine regulation in these patients.

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