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FEATURES OF ALLERGIC STATUS IN A PATIENT WITH DESMINOPATHY T341P

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Abstract

Introduction. Since desminopathies represent rare or so-called “orphan” diseases, little is known about the sensitivity of their patients to allergens and physical factors. Aim. The study set out to investigate the allergic status of a patient with desminopathy T341P in a heterozygous state. Materials and methods. The retrospective study is based on a case of familial desminopathy identified in south of Western Siberia. Quantitative analysis of total and specific immunoglobulins in the blood and coprofiltrate of a proband with desminopathy was carried out by turbidimetric and chemiluminescence immunoassay, enzyme allergosorbent testing, as well as enzyme immunoassay. Results. The proband with desminopathy is evaluated as having a polyvalent allergy to plant-, food- and infectious allergens. Specific IgE antibodies to pollen of early-blooming meadow grasses and *Secale cereale*, as well as cow’s milk, *Mucor racemosus* and *Fusarium moniliforme* fungi, were found in the blood. The coprofiltrate revealed specific IgE to pollen of early-blooming meadow grasses and trees, as well as chicken eggs and casein. While, at the onset of clinical manifestations of desminopathy, the level of total IgE in the blood of the proband exceeded the reference values by two times, it has decreased by 5.5 times over the past 10 years. Over the past two years, the total concentration and average level of specific IgG4 antibodies to food allergens in the blood increased by 15%. Provocation tests for cold- and cholinergic urticaria were positive. Conclusion. A respiratory allergy, which had emerged by the age of 20, was most likely a trigger for the desminopathy T341P. Especially at this age, the proband developed ventricular extrasystole, as well as a barely perceptible decrease in physical strength. Then, from the age of 30, there was a progressive weakness of the skeletal muscles and a noticeable decrease in physical strength, followed by the full development of the disease, which began after the age of 40. In combination with excessive bacterial growth of the intestinal and oral microbiota, and an increase in endotoxin, polyvalent allergies with a high concentration of specific IgG4 antibodies and other (sub)classes can participate in the etiology and pathogenesis of desminopathy T341P.

Keywords: allergy, desminopathy, muscular diseases, disease trigger, immunity, specific IgG4.

1 Introduction

Desminopathies include hereditary myopathies [1] and cardiomyopathies [2] caused by mutations in the *DES* gene [3]. The autosomal dominant forms of such orphan diseases are typically characterized by their debut in the first three- to four decades of life [4]. To date, the triggers of desminopathy remain largely unknown, and no specific treatment is available.

The first published works on the identified case of familial form of desminopathy T341P describe its clinical manifestations in pedigree members [5], the dynamics of immune- [6], antioxidant- and biochemical statuses [7], as well as the characteristics of changes in the microbiota of saliva and feces [8].

Recent studies have shown that allergies and metabolic syndrome are associated with mitochondrial dysfunction [9], which is also observed in desminopathy [10]. Allergens cause mitochondrial dysfunction, which leads to oxidative stress, as well as the production of reactive oxygen species [9].

The immune response to allergens is accompanied by the synthesis of general and specific antibodies, whose clinical significance is complex and contradictory [11, 12]. At pathophysiological stages, various types of allergy are known to lead to inflammation, cell damage, ischaemia, tissue dystrophy, etc.

Literature data show that about 60% of the world's population suffers from a food intolerance, which can cause neurological diseases, musculoskeletal disorders [13], etc.

Unfortunately, despite the mechanisms triggered in this case having a significant potential impact on the underlying disease, or even a causal relationship with it, there is little information on the sensitivity of patients with desminopathy to the effects of allergens and physical factors.

Aim of the study. The study set out to investigate the features of the allergic status in a patient with desminopathy T341P in a heterozygous state.

2 Materials and methods

The present retrospective study is based on a case of familial desminopathy T341P identified in south of Western Siberia. The study proband is a male who, at the age of 35, according to the results of genetic studies, was diagnosed with desminopathy involving mutation in *DES* gene T341P (c.1021A> C) in a heterozygous state. At the time of writing, the proband is 45 years old. The father of the proband with desminopathy T341P had died at the age of 49 from pneumonia. The anamnestic method, including analysis of medical records, was used.

Informed consent was obtained from all subjects participating in the study. **The study was conducted in accordance with the principles of the provisions of the Declaration of Helsinki of the World Medical Association.**

The concentration of total IgA, IgG and IgM immunoglobulins in the blood of the proband was determined by immunoturbidimetry on a Beckman Coulter AU 5800 analyzer (Beckman Coulter, USA) using Beckman Coulter reagents (USA). The level of total IgE in the blood was determined by chemiluminescent immunoassay on a Siemens IMMULITE 2000 analyzer (Siemens, Germany).

In order to determine the concentration of specific IgE in the blood of the proband, food-, respiratory- and mixed allergic complexes were used. The studies

were performed by immunoblot analysis using the RIDA AllergyScreen-Biopharm (Germany) test system on the analyzer RIDA X-Screen (R-Biopharm, Germany), as well as by solid-phase immunoassay using the ImmunoCAP technique on the analyzer Phadia ImmunoCAP 250 (Phadia AB, Sweden).

The concentration of specific IgG4 in the blood of the proband was determined by enzyme immunoassay using a mixed panel of 88 allergens of the Dr.Fooke (Germany) test system on the analyzer Sunrise (Tecan Austria GmbH, Austria).

The level of specific IgE and IgG4 antibodies to allergens in the coprofiltrate of the proband was tested, respectively, by an enzymatic allergen sorbent test and an enzyme immunoassay on the analyzer HumaReader HS (HUMAN Gesellschaft für Biochemica und Diagnostica mbH, Germany) using Dr.Fooke test systems. A food allergy diagnosis method was used [14].

Cold and thermal provocation tests were used to determine the proband's sensitivity to low and high temperatures, as well as to assess him for aquagenic and cholinergic urticaria according to the international guidelines for the diagnosis of urticarial [15] and the Clinical Recommendations (Urticaria 2023-2024-2025) of the Ministry of Health of the Russian Federation.

3 **Results**

The proband had been artificially fed from birth with infant formula and cow’s milk without heat treatment. By the first year of life, he had a fairly extensive scab on his cheeks, as well as around his lips and chin, which was treated with hormonal ointment for 1 month. At the age of 9, he developed dysentery, after which digestive problems began, continuing up to the age of 28 years. It was found that the proband periodically developed loose stools one hour after eating, which occurred 1-4 times a day.

From the age of 8 to 15, the proband had engaged in haymaking (south of Western Siberia) every summer in July with his father and grandfather. During the haymaking breaks, they drank untreated cow’s milk, as well eating boiled chicken eggs, wheat flour bread, and raw vegetables.

By the end of the second decade, the proband developed a respiratory allergy, manifested by allergic rhinitis and sneezing, from late June to August. The same allergic symptoms began to occur in response to damp room living conditions. Following a skin test with histamine at the age of 22, the proband gave a positive result to cereals mix pollen, *Artemisia*, *Atriplex* and *Betula alba*. Allergic rhinitis, comprising an allergy to grass and tree pollen, was diagnosed. During the exacerbation period, it was recommended that he take *Mebhydrolin*, which temporarily eliminated the allergic reactions. With age, the manifestations of allergy in the proband gradually reduced; by the age of 38, they had significantly decreased.

It should be noted that the father of the proband also had an allergy, which was also manifested by allergic rhinitis and sneezing, only less pronounced.

In the third decade of life, the proband began to note infrequent and temporary heart rhythm disturbances. In general, up to the age of 30, both the proband and his father with desminopathy T341P were physically strong. At the beginning of the fourth decade, they began to notice a weakness of the skeletal muscles, mainly the

legs. The disease progressed slowly in an ascending pattern to involve the muscles of the upper extremities. At the same time, there was a decrease in sweating, which, even in a Russian sauna at high temperatures, lessened with age. In addition to this, there was frequent itching of the scalp and a large amount of dandruff.

From the age of 35, the proband began to notice a sharp decrease in physical strength in the legs and arms with a cooling of his body, especially in winter. From the age of 40, he began to often experience cold in his legs, even in the warm season. The father of the proband had voiced the same complaints of cold at the same age and for the rest of his life.

At the age of 38, the proband began to walk with a cane; at the age of 40, using a walking frame; by the time he was 43, he required a wheelchair, as had his father.

Over the past 10 years, a change in the concentration of total immunoglobulins was recorded in the blood the proband with desminopathy: a 5.5-fold decrease in IgE, a 2.8-fold decrease in IgM, a 1.4-fold decrease in IgG, and a 2.1-fold increase in IgA (Figure 1). Moreover, at the ages of 34 and 37 years, the concentrations of total IgE exceeded the upper limits of the reference values by 2 and 1.1 times, respectively.

According to the results of extended tests of the blood of the 43-year-old proband, a significantly increased content of allergen-specific IgE antibodies to a mixture of pollen obtained from meadow cereal plants was revealed (Table 1). Separate studies recorded very high concentrations of allergen-specific IgE antibodies to *Phleum pratense, Dactylis glomerata, Lolium perenne, Festuca elatior*, high IgE to *Bromus inermis, Holcus lanatus*, as well as a moderately elevated concentration of IgE to *Cynodon dactylon.* At the same time, an increased content of specific IgE antibodies to *Secale cereale* and *Alopecurus pratensis* pollen, as well as the presence of specific IgE antibodies to cow's milk, was established. In addition, at the age of 44, specific IgE antibodies to fungal allergens *Mucor racemosus* and *Fusarium (Gibberella) moniliforme* were found in the blood of the proband.

At the age of 43 years, high concentrations (>5000 ng/ml) of specific IgG4 antibodies to 12 products were detected in the blood of the proband: egg white and yolk, bananas, mustard, soft cheese, casein, wheat and buckwheat flour, gluten, garlic, yogurt, cow's milk (Table 2). Following a three-month elimination diet, specific IgG4 was reduced in the proband's blood for buckwheat flour (by a factor of 9.3), bananas (5.9), garlic (2.5), soft cheese and egg yolk (1.5), yogurt (1.4), wheat flour (1.3), gluten (1.2). However, following the diet, the IgG4 in the blood for mustard increased by 1.4 times, while that for casein increased by 1.3 times. In addition, the change in diet increased the IgG4 of hazelnuts by 13.5 times, carp by 5.2 times, and zander by 6.1 times, the concentrations of which had previously been low. At the same time, excessively high IgG4 values for egg whites remained unchanged. IgG4 in the blood for cow's milk did not change significantly. Following the 3-month diet, he total concentration of specific IgG4 antibodies to food allergens even increased by 749 ng/ml.

In general, during the considered age period, the total concentration and average level of specific IgG4 antibodies to food allergens in the blood of proband increased by 1.15 times. This increase was mainly due to an increase in the

concentrations of IgG4 antibodies to hazelnut by 10 times, mustard by 1.5 times, cow's milk by 2 times, gluten by 1.5 times, zander by 4.5 times, carp by 3.8 times, champignons by 6 times.

Moreover, following the 3-month exclusion diet, the absolute quantity of food allergens with a concentration of specific IgG4 antibodies in the blood from 500 to 2000 ng/ml was found to increase by 1.2 times at a concentration from 2000, by 2.5 times at 5000 ng/ml, but to decrease by 1.1 times at concentrations of more than 5000 ng/ml (Figure 2A).

Following the temporary change in the proband's diet, not a single indicator of the concentration of specific IgG4 antibodies was less than 500 ng/ml, whereas before that period 13 out of 88 indicators had been below this figure. Over the past 2 years, the absolute number of food allergens with a concentration of specific IgG4 antibodies in the blood of less than 500 ng/ml has increased by 4.4 times, and those with a concentration of 2000 to 5000 ng/ml – by 3.5 times; however, the number of allergens with a concentration of 500 to 2000 ng/ml has decreased by 5.1 times.

During the age period under consideration, the relative number of food allergens in the blood of the proband with desminopathy, to which the concentration of specific IgG4 antibodies is in the range <500 to 2000 ng/ml, decreased from 84.1% to 78.4% (Figure 2B). At the same time, there was an increase of the same value in 5.7% specific IgG4 with a concentration of 2000 to 5000 ng/ml.

The presence of specific IgE antibodies to casein, chicken egg, early-blooming meadow grasses and early-blooming trees was revealed in the coprofiltrate of the 44-year-old proband (Table 3). Specific IgG4 to chicken egg, cow's milk protein, banana and casein were found in the coprofiltrate. Blood concentrations of specific IgG4 to chicken egg, banana, casein and cow's milk were 335, 158, 100 and 83 times higher, respectively, than in the coprofiltrate.

The complex of studies is summarized in Table 4 with the indicators of specific antibodies to allergens in the biological material of the proband. Specific IgE antibodies to the pollen of early-blooming trees and early-blooming meadow grasses were detected in the coprofiltrate; antibodies to the latter allergens were also found in the blood. However, specific IgE and IgG4 antibodies are present on the chicken egg and casein in the coprofiltrate, while only IgG4 is present in the blood. Specific IgE and IgG4 to cow's milk were found in the blood, as well as IgG4 in the coprofiltrate.

At the age of 44, the proband was additionally evaluated for intestinal barrier permeability and inflammatory markers. The recorded fecal zonulin concentration of 29.5 ng/ml indicates the absence of damage to the villous surface of the intestinal mucosa, as well as the normal density of intercellular contacts. The level of eosinophil-derived neurotoxin in the feces (0.13 μg/g), which characterizes the presence of inflammation in the intestine, does not exceed the limit of reference values. The fecal calprotectin concentration of 23.8 μg/g is well below the recommended maximum (50 μg/g).

A cold provocation test for urticaria in the proband at the age of 44, involving direct contact of the skin with a piece of ice for 5 minutes (Figure 3A, D) gave a positive result. One minute after removing the piece of ice from the inside of the

proband's forearm, a red ring appeared on the skin along the outer contour of the piece of ice (Figure 3B), followed by the gradual spread of hyperemia into the cooled area until its full coverage. Further, after another 1 minute, a reaction in the form of urticaria appeared at the cooling site of the forearm (Figure 3C). Urticaria also formed on the skin of the thigh 2 minutes after removing the piece of ice (Figure 3E). During the cold provocation test, the proband reported a burning sensation when the piece of ice came into direct contact with the skin at the cooling points. Subsequently, after a period of 10 minutes, all manifested skin reactions to the cold disappeared.

In the cold test, only local reddening of the cooling areas was observed after 5 minutes of exposure when ice contacted through a plastic bag with the skin of the forearm and hip. During exposure, the proband did not report a burning sensation, but only cooling. After 10 minutes, the redness at the application sites disappeared.

During exercise in the cholinergic test, sweat secretion led to the formation of urticaria (Figure 3F), accompanied by itching and burning. Skin rashes persisted for 30 minutes. However, the results of the provocation heat test also turned out to be negative for aquagenic urticaria.

In the blood of the 44-year-old proband, the levels of cryoglobulins, histamine and serotonin are within the reference range. Nevertheless, the concentration of histamine in the proband's daily urine at the age of 35 years was 7.4 μg/day, whereas by 44 years it had increased 1.8 times to 13.0 μg/day.

4 **Discussion**

The conducted complex of studies revealed a polyvalent allergy to plant, food and infectious allergens, as well as increased sensitivity to cold and sweat in the proband with desminopathy T341P. This indicates impaired immune system function.

Even in infancy, the proband had an allergic reaction on his skin when consuming infant formula and untreated cow's milk. Unfortunately, due to annual exposure during his youth and adolescence on the hayfield with his father and grandfather, the proband received a large dose of pollen allergens from grasses and trees, as well as consuming highly allergenic food products there. Respiratory allergy to pollen of early-blooming meadow grasses and trees appeared in the proband at the age of 20, has been ongoing for 25 years, and is seasonal from late June to August.

It is noteworthy that, at the age of 43, when another allergic rhinitis and sneezing appeared in the summer, the proband underwent a 10-day course of treatment with enterosorbent *Polymethylsiloxani polyhydras* in the form of an oral paste, which immediately eliminated allergic reactions for 1.5 months. It can therefore be concluded that intestinal microbiota contributes negatively to his allergic reactivity. At the same time, with the progression of desminopathy the proband has an excessive bacterial growth of fecal microbiota, involving a pronounced increase in transient microorganisms [8], as well as an increase in endotoxin and oxidative stress indicators [7].

At the onset of clinical manifestations of desminopathy T341P, the level of total IgE in the blood of the proband exceeded the reference values by two times;

however, it has decreased by 5.5 times over the past 10 years. As is known, in order to reduce allergic reactions and IgE, the body eventually produces specific IgG4 antibodies that bind histamine [16], whose concentration in the daily urine of the proband has increased 1.8 times over the past 9 years. However, the properties of specific IgG4 have been little studied so far [17]. There is increasing evidence that IgG4 antibodies can be pathogenic [18]. High concentrations of IgG4 are observed in a number of oncological and autoimmune diseases [19] involving damage to the central and peripheral nervous systems, gastrointestinal tract, lungs, kidneys, hematopoietic system, skin, etc.

Over the past two years, the total concentration and average level of specific IgG4 antibodies to food allergens in the blood increased by 15%. Stable high concentrations (>5000 ng/ml) of specific IgG4 antibodies in the blood per 10 food allergens were detected: egg white, cow's milk, casein, yogurt, soft cheese, wheat flour, gluten, garlic, mustard, bananas. This list is dominated by dairy products, the consumption of which by the proband currently sometimes leads to a slight itching on the hands, which however does not bother him.

In addition, after eating, the proband has a temporary decrease in physical strength; from 9 to 28 years of age, a digestive disorder was experienced. A rash appearing quite often for extended periods of time on the shoulders and thighs of the proband was also observed in his father. It should be noted that, when eating a whole chicken egg, the concentration of IgG4 in the blood for which has been excessively high from the age of 38, the proband immediately experiences a short-term heart rhythm disturbance. In this connection, it is known that IgG4 reduces the ability to transmit signals as a means of reducing the manifestation of allergic reactions [19]. With the progression of desminopathy in the proband, the heart rate gradually decreased [5] to reach 26 beats per minute during the daytime. In connection with third-degree AV block and bradycardia, a pacemaker was implanted at the age of 43. The grandfather of the proband suffered 2 myocardial infarctions at the ages of 69 and 70, dying at the age of 72 from rectal adenocarcinoma [5].

As is known, in desminopathy, pathological aggregates with mutated desmin are formed [20], whose formation can presumably be influenced by specific IgG4, as well as other allergen-specific antibodies. Moreover, IgG4 antibodies, which tend to aggregate at high concentrations, can form complexes [21].

The proband’s adherence to the elimination diet led to an increase in physical strength and muscle mass in the first month; however, over the following 2 months, the effect gradually decreased and returned to its original level. As well as leading to an increase in specific IgG4 antibodies to other foods consumed, the exclusion of some products from food did not reduce the total concentration and average level of specific IgG4 in the blood.

Of course, the presence of allergy in the proband and his father with desminopathy T341P is not a coincidence. As is known, allergic reactivity is largely determined by hereditary predisposition. Interestingly, taking even one tablet of a complex of B vitamins (B_1, B_2, B_3, B_5, B_6, B_7, B_9, B_{12}) at the age of 44 led to a temporary heart rhythm disturbance, itching on the skin, as well as muscle weakness and dizziness for up to 3 hours. In this connection, B vitamins are known to have

histamine-liberating properties [22].

The above information indicates a variety of symptoms of polyvalent allergy in the proband with desminopathy T341P: sneezing, rhinitis, rashes, itching, indigestion.

It should be noted that the proband, like his father, was born and continues to live in the rather harsh natural and climatic conditions of south of Western Siberia. At the same time, it was found that when his body is cooled, the proband's physical strength decreases sharply, and subsequently takes a long time to warm up. According to the results of provocation tests, cold and cholinergic urticaria were detected in the proband. In addition, he previously had a prolonged inflammatory reaction to skin damage, a decrease in the healing rate of damaged areas, and incomplete wound regeneration [6].

It is noteworthy that the proband's grandfather had moved at the age of 15 from the Lower Volga region, where the comparatively mild climate, featuring an average January temperature of −7.7°C and an average annual temperature of +7.3°C, to the south of Western Siberia. In the new place of residence, the average January temperature was −15°C and the average annual temperature was +2.4°C, which is 2 and 3 times lower than the corresponding air parameters in the Lower Volga region. At the same time, there was a change of natural zones from the steppe to mixed forests with completely different vegetation, as well as a significant change in the diet.

Summarizing the obtained information, the following conclusions can be drawn. A respiratory allergy, which had emerged by the age of 20, was most likely a trigger for desminopathy T341P. From the age of 20, a latent period of desminopathy began, which lasted 10 years. Especially at this age, the proband developed ventricular extrasystole [5], as well as a barely perceptible decrease in physical strength. Then, from the age of 30, there was a progressive weakness of the skeletal muscles and a noticeable decrease in physical strength, followed by the full development of the disease, which began after the age of 40.

Previous reports of temporary improvement (for 1–3 months) in the physical condition of the proband with desminopathy T341P after taking antibiotics [8] are most likely associated with a weakening of the immune response to allergens and physical factors, as well as a decrease in endotoxin levels.

In general, polyvalent allergy with a high concentration of specific IgG4 antibodies and other (sub) classes, in combination with excessive bacterial growth of the intestinal and oral microbiota, and an increase in endotoxin, can participate in the etiology and pathogenesis of desminopathy T341P.

5 **Conclusion**

The conducted complex of studies on the patient with desminopathy T341P revealed a polyvalent allergy to plant, food and infectious allergens, as well as increased sensitivity to cold and sweating. With the progression of desminopathy, a decrease in the level of total IgE in the blood is observed with an increase in the total concentration and average level of specific IgG4 antibodies to food allergens. A respiratory allergy, which had emerged by the age of 20, was most likely a trigger for the desminopathy T341P. In combination with excessive bacterial growth of the

intestinal and oral microbiota, and increased endotoxin, a polyvalent allergy with a high concentration of specific IgG4 antibodies and other (sub) classes can participate in the etiology and pathogenesis of desminopathy T341P. Thus, the reported work opens up completely new approaches to the prevention and future treatment of desminopathy T341P.

ТАБЛИЦЫ

Table 1. Levels of specific ige antibodies to allergens in the blood of the proband with desminopathy t341p at the ages of 43 and 44 years.

<table>
<tr><th>Allergen</th><th>Concentration of IgE antibodies at 43 years old, IU/ml</th><th>Allergen</th><th>Concentration of IgE antibodies at 44 years old, kU/l</th></tr>
<tr><td rowspan="7">Meadow grass plants (pollen): Alopecurus pratensis, Anthoxanthum, Arrhenatherum elatius, Bromus inermis, Cynodon dactylon, Dactylis glomerata, Elytrigia repens, Festuca pratensis, Holcus lanatus, Lolium, Phleum pratense, Secale cereale</td><td rowspan="7">8.07</td><td>Phleum pratense</td><td>25.20</td></tr>
<tr><td>Dactylis glomerata</td><td>22.40</td></tr>
<tr><td>Lolium perenne</td><td>21.40</td></tr>
<tr><td>Festuca elatior</td><td>17.70</td></tr>
<tr><td>Bromus inermis</td><td>14.00</td></tr>
<tr><td>Holcus lanatus</td><td>13.70</td></tr>
<tr><td>Cynodon dactylon</td><td>0.83</td></tr>
<tr><td>Alopecurus pratensis</td><td>2.01</td><td>Mucor racemosus</td><td>0.59</td></tr>
<tr><td>Secale cereale (pollen)</td><td>1.04</td><td rowspan="2">Fusarium (Gibberella) moniliforme</td><td rowspan="2">0.42</td></tr>
<tr><td>Cow's milk</td><td>0.02</td></tr>
<tr><td colspan="4">There were no specific IgE to allergens:</td></tr>
<tr><td colspan="4">Alnus, Alternaria alternate, Amoxicillin, Anthoxantum odoratum, Artemisia, Aspergillus fumigatus, Atriplex canescens, Atriplex lentiformis, Betula alba, Candida albicans, Cladosporium herbarum, Corylus, Dermatophagoides farinae, Dermatophagoides pteronyssinus, Penicillium notatum, Plantago, Pyridoxine, Quercus, Thiamine, almonds, apple, baker's yeast, banana, beef, carrots, casein, cat, celery, chicken, cod, crab, dog, egg whites, egg yolks, garlic, guinea pig, hamster, hazelnuts, horse, lamb, mustard, orange, peanuts, pork, potatoes, rabbit, rye flour, sesame seeds, soybeans, tomatoes, walnuts, wheat flour</td></tr>
</table>

Table 2. Change in the levels of specific igg4 antibodies to allergens in the blood of the proband with desminopathy t341p.

Allergen	**Blood concentration (ng/ml) of specific IgG4 antibodies at the age of the proband**			
	43 years	**43.3 years (after 3 months of diet)**	**44 years**	**Change (44-43)**
Egg white	>50000	>50000	>50000	0
Egg yolk	10198	7016	4564	-5634
Cow's milk	5159	5252	10567	5408
Beta-lactoglobulin	548	604	609	61
Casein	7307	9577	10980	3673
Blue cheese	894	925	583	-311
Goat milk	2710	1718	4284	1574
Yogurt	6654	4842	6502	-152
Soft cheese	10772	7261	10927	155
Cod	886	4894	2824	1938
Herring	736	2243	2573	1837
Trout	532	632	517	-15
Shrimps	532	577	<500	-32
Salmon	<500	570	<500	0
Squid	<500	584	<500	0
Mackerel	510	672	518	8
Carp	1187	6169	4513	3326
Zander	1307	8026	5901	4594
Caviar (red and black)	568	808	<500	-68
Wheat flour	10677	7963	7111	-3566
Rye flour	552	634	678	126
Oat flour	865	884	781	-84

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Table 2 (continued)

Allergen	Blood concentration (ng/ml) of specific IgG4 antibodies at the age of the proband			
	43 years	43.3 years (after 3 months of diet)	44 years	Change (44-43)
Rice	631	596	<500	-131
Buckwheat flour	6093	653	<500	-5593
Corn (grain)	582	616	<500	-82
Gluten	8166	6954	12577	4411
Millet	656	599	<500	-156
Champignon	511	616	3069	2558
Peas	713	594	<500	-213
Sesame	<500	594	<500	0
Soybeans	<500	621	<500	0
Pork	1571	632	<500	-1071
Beef	584	675	<500	-84
Chicken meat	548	624	<500	-48
Mutton	645	619	<500	-145
Orange	<500	609	520	20
Mandarin	1407	621	<500	-907
Garlic	9490	3787	12110	2620
Bulb onions	521	596	<500	-21
Celery	589	723	<500	-89
Mustard	14838	20771	22221	7383
Tomato	519	611	<500	-19
Carrot	550	596	<500	-50
Potato	<500	594	<500	0
White cabbage	542	614	<500	-42

Table 2 (continued)

Allergen	Blood concentration (ng/ml) of specific IgG4 antibodies at the age of the proband			
	43 years	43.3 years (after 3 months of diet)	44 years	Change (44-43)
Cauliflower	521	594	<500	-21
Cucumber	502	563	<500	-2
Beetroot	599	664	<500	-99
Eggplant	597	577	<500	-97
Pumpkin	502	565	<500	-2
Cabbage mixture	769	592	<500	-269
Olives (green and black)	549	554	<500	-49
Peanut	530	568	<500	-30

Walnut	<500	570	<500	0
Hazelnut	1054	14267	10440	9386
Almond	655	700	<500	-155
Pistachios	542	614	<500	-42
Bananas	17450	2954	19758	2308
Pear	654	584	511	-143
Apple	638	672	572	-66
Peach	<500	606	<500	0
Pineapple	<500	584	<500	0
Kiwi	<500	565	<500	0
Apricot	552	700	<500	-52
Strawberry	548	666	<500	-48
Cherry	573	587	658	85
Raspberries	552	570	<500	-52
Currants (red and black)	511	577	<500	-11

Table 2 (continued)

Allergen	**Blood concentration (ng/ml) of specific IgG4 antibodies at the age of the proband**			
	43 years	**43.3 years (after 3 months of diet)**	**44 years**	**Change (44-43)**
Melon and watermelon	511	599	<500	-11
Grapes (white and black)	<500	559	<500	0
Black tea	545	552	<500	-45
Green tea	547	629	<500	-47
Rosehip (fruit)	580	561	<500	-80
Brewer's yeast	<500	545	<500	0
Hops and malt	957	572	<500	-457
Baker's yeast	503	570	<500	-3
Chocolate	2149	1670	2711	562
Coffee	<500	568	<500	0
Lecithin	518	580	<500	-18
Glutamate	526	632	<500	-26
Aspartame-HSA	587	587	<500	-87
Honey	1676	1429	1049	-627
Sugar	654	543	<500	-154
Mixture of peppers (hot red, sweet ground paprika, chili, allspice, green pepperoni, cayenne)	510	637	<500	-10
Mixture of peppercorns (white, green, black)	524	655	<500	-24

Spice mixture 2 (bay leaf, dill, parsley, parsley root)	501	672	<500	-1
Candida albicans	598	757	611	13
Ascaris lumbricoides	522	729	<500	-22
Average value	2374,5	2383,0	2724,3	349,8
Sum	208956	209705	239739	30783

Table 3. Levels of specific antibodies to allergens in the coprofiltrate of the proband with desminopathy t341p at the age of 44 years.

Allergen	**Concentration of specific antibodies in the proband's coprofiltrate**	
	IgE, IU/ml	**IgG4, ng/ml**
Chicken egg (whole)	0.38	149.30
Casein	0.49	108.95
Cow's milk protein	<0.35	127.20
Banana	<0.35	124.90
Early-blooming meadow grasses (*Dactylis glomerata*, *Festuca elatior*, *Lolium perenne*, *Phleum pratense*, *Poa*)	0.41	<100
Early-blooming trees (*Alnus*, *Corylus*, *Ulmus*, *Salix alba*, *Populus*)	0.37	<100
There were no specific IgE and IgG4 to allergens:		
Wheat and rye flour, pork, baker's yeast, gluten, gliadin, a mixture of household allergens (mites, epithelium of cats, dogs, *Aspergillus fumigatus*, *Cladosporium herbarum*), late-blooming trees (*Acer negundo*, *Betula alba*, *Fagus sylvatica*, *Quercus*, *Juglans regia*), *Amoxicillin*, *Tetracyclinum*		

Table 4. Specific antibodies to allergens in biological material of a proband with desminopathy t341p.

Allergen	**Presence (+) or absence (-) of specific antibodies to allergens in the biological material of the proband**			
	blood		**coprofiltrate**	
	IgE	**IgG4**	**IgE**	**IgG4**
Cow's milk	+	+	-	+
Chicken egg	-	+	+	+
Casein	-	+	+	+
Banana	-	+	-	+
Baker's yeast	-	+	-	-
Pork	-	+	-	-
Wheat flour	-	+	-	-
Rye flour	-	+	-	-
Garlic	-	+	?*	?*
Early-blooming meadow grasses	+	?*	+	-
Early-blooming trees	-	?*	+	-
Secale cereale (pollen)	+	?*	?*	?*
Mucor racemosus	+	?*	?*	?*
Fusarium (Gibberella) moniliforme	+	?*	?*	?*
Candida albicans	-	+	?*	?*

Note. ?* - not studied

РИСУНКИ

Figure 1. Change in the concentration of total immunoglobulins in the blood of the proband with desminopathy T341P.

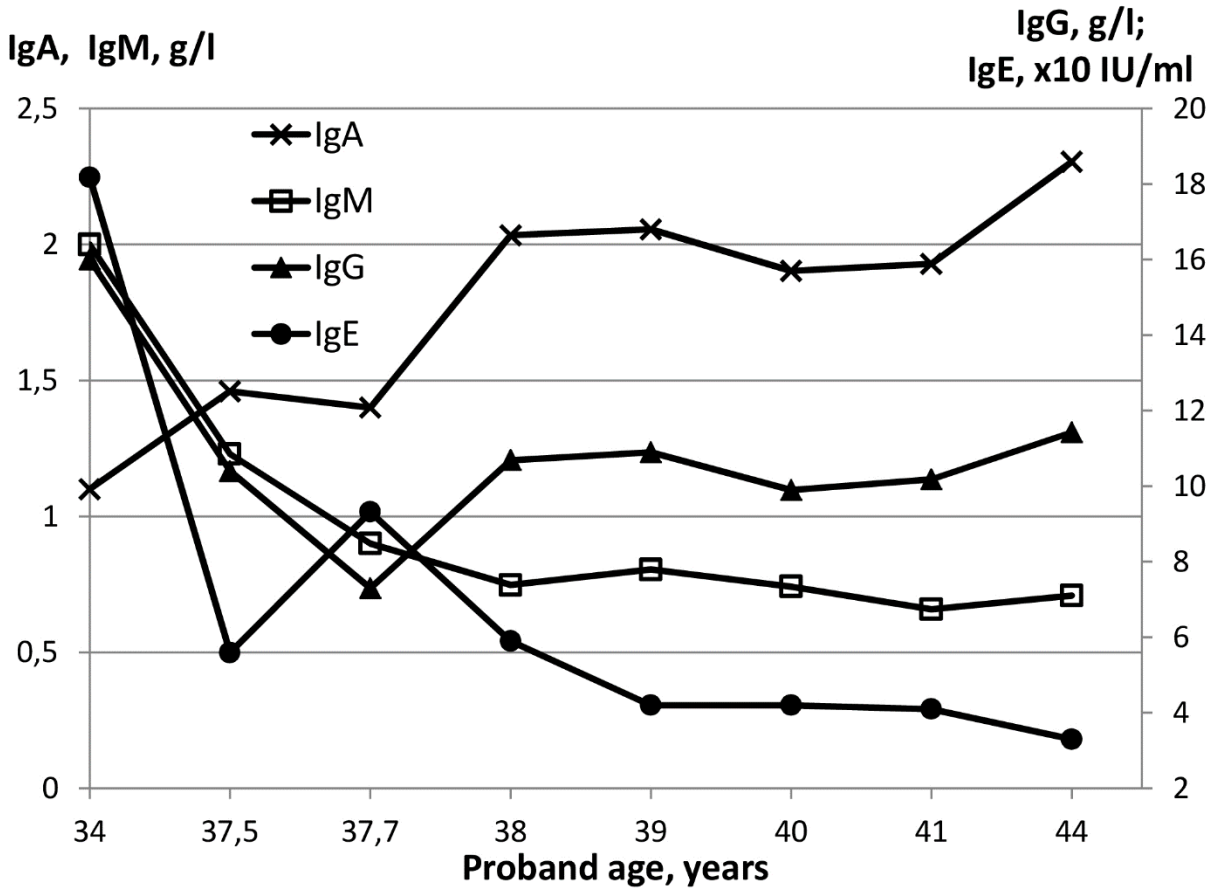


Figure 2. Change in the absolute (A) and relative (B) amount of food allergens depending on the concentration of specific IgG4 antibodies in the blood of the proband with desminopathy T341P.

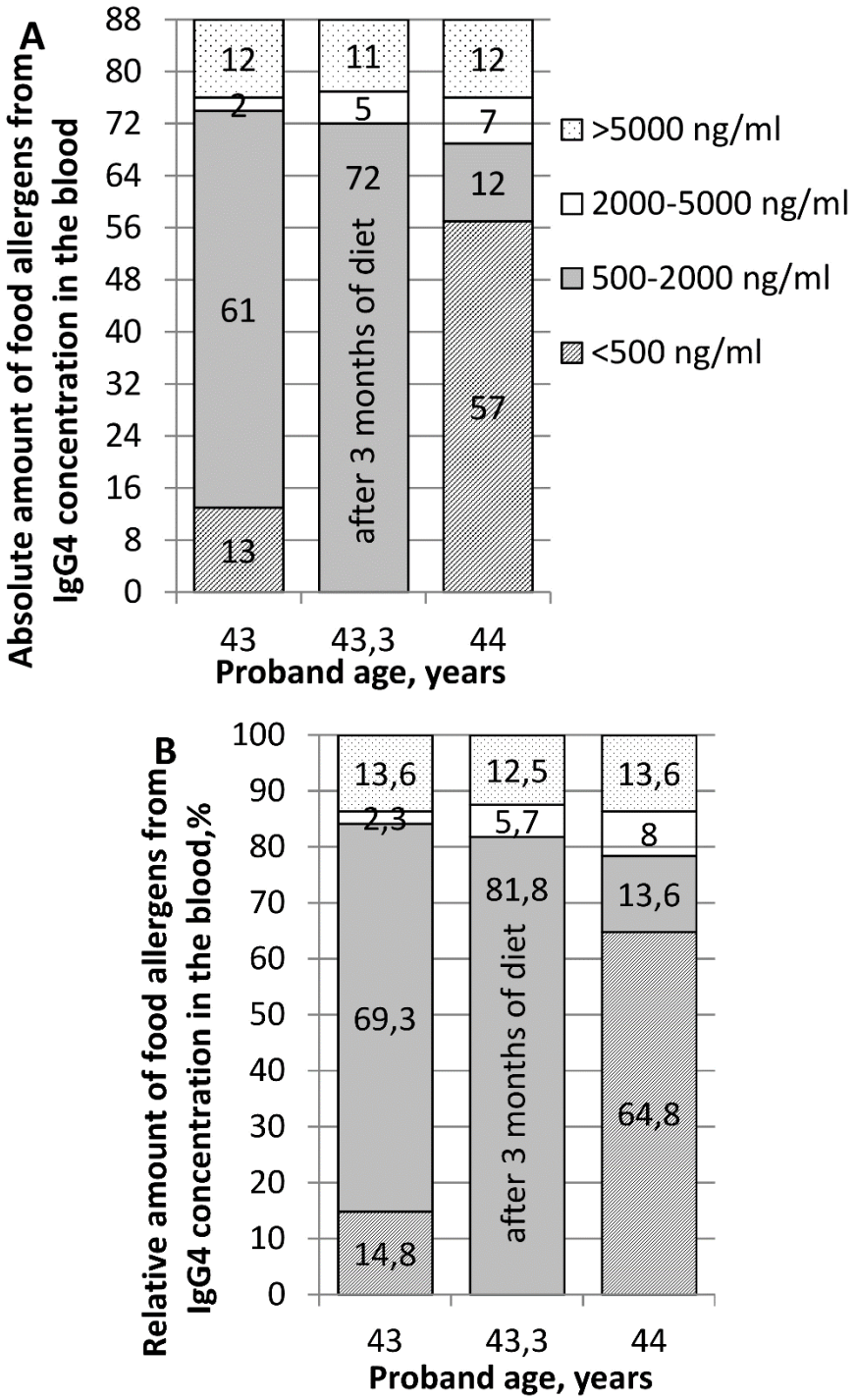
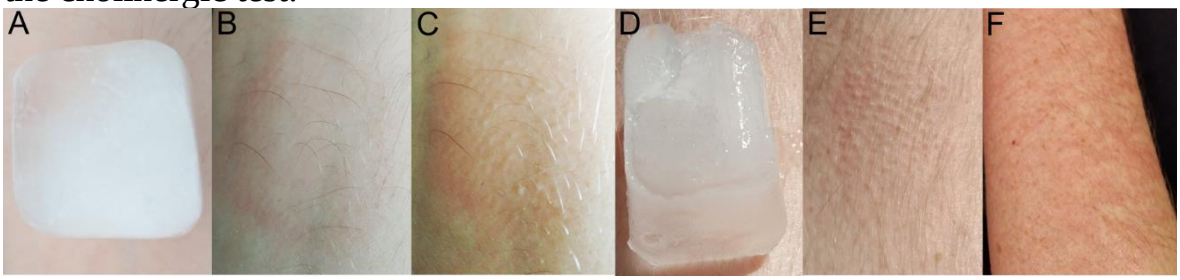


Figure 3. Results of cold and cholinergic provocative urticaria tests in the proband with desminopathy T341P at the age of 44: A - piece of ice on the forearm; B - forearm 1 minute after ice removal; C - forearm 2 minutes after ice removal; D - piece of ice on the hip; E - thigh 2 minutes after ice removal; F - forearm following the cholinergic test.



ТИТУЛЬНЫЙ ЛИСТ_МЕТАДАННЫЕ

Блок 1. Информация об авторе ответственном за переписку

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Блок 2. Метаданные статьи

FEATURES OF ALLERGIC STATUS IN A PATIENT WITH DESMINOPATHY T341P

Сокращенное название статьи для верхнего колонтитула:

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Keywords: allergy, desminopathy, muscular diseases, disease trigger, immunity, specific IgG4.

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Порядковый номер ссылки	Авторы, название публикации и источника, где она опубликована, выходные данные	ФИО, название публикации и источника на английском	Полный интернет-адрес (URL) цитируемой статьи или ее doi.
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