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МУЛЬТИМОРБИДНЫЙ ПАЦИЕНТ С ПЕРВИЧНЫМ ИММУНОДЕФИЦИТОМ. ДИАГНОСТИКА, ЛЕЧЕНИЕ

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Multimorbid Patient with Primary Immunodeficiency. Diagnostics, Treatment

Резюме

Первичный иммунодефицит — патология иммунной системы, проявляющаяся в снижении либо отсутствии одного или нескольких звеньев системы иммунитета. Ранее считалось, что первичный иммунодефицит является редкой патологией, но последние статистические данные свидетельствуют об обратном. По этой причине врачам всех специальностей (особенно специалистам первичного звена) следует быть настороженным в вопросах диагностики и тактики ведения пациентов с данным заболеванием. Первичные иммунодефициты манифестируют различными клиническими проявлениями: инфекционными, онкологическими, аутоиммунными, аллергическими и др. Чаще всего дебют представлен рецидивирующими инфекциями и/или хронической диареей, но возможны и альтернативные варианты. В диагностике данных состояний стоит учитывать «настораживающие» признаки иммунодефицитов, а также результаты лабораторных исследований, таких как лимфо-/нейтропения, снижение сывороточных иммуноглобулинов и другие специфические тесты. Лечение первичного иммунодефицита базируется на пожизненной заместительной терапии иммуноглобулинами, а также лечении и профилактике клинических проявлений данного состояния. В статье приводится обсуждение клинического случая взрослого мультиморбидного пациента с первичным иммунодефицитом — несемейной агаммаглобулинемией. У пациента наблюдаются инфекционные (хронический бронхит), онкологические (базальноклеточный рак кожи) и другие клинические проявления заболевания (вторичная панкреатогенная энтеропатия). В разборе клинического случая делается акцент на ключевые детали в постановке диагноза «первичный иммунодефицит» у взрослых. Рассматривается вопрос ведения пациента в амбулаторных условиях с учетом основной патологии и обострения сопутствующих хронических заболеваний. Кроме этого, подчеркивается важность преемственности таких пациентов на амбулаторном и стационарном звеньях.

Ключевые слова: *первичный иммунодефицит, общая вариабельная иммунная недостаточность, агаммаглобулинемия*

Конфликт интересов

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

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Abstract

Primary immunodeficiency is a pathological condition of immune system, expressed in the absence or decrease certain parts of immune system. It was generally believed that primary immunodeficiency is a rare pathology but recent findings indicate the opposite. For that matter all types of specialists (especially family doctors) should be well informed. Primary immunodeficiency manifests with various clinical forms, like infectious, oncological, autoimmune, allergical etc. It should be well-known that primary immunodeficiency often debutes with chronic infections and diarrhea, but other sparks are also possible. As for the diagnostics, "red flags" should be taken into account, in addition to laboratory findings, such as lympho-/neutropenia, decrease in immunoglobulins and other specific tests. The therapy for primary immunodeficiency is based on substantial, vital treatment with immunoglobulins, along with prevention and treatment of comorbidities. The article discusses clinical case of an adult multimorbid patient with primary immunodeficiency, non-hereditary agammaglobulinemia with an emphasis on complexity of stating the final diagnosis in adulthood. The peculiarity of the patient is an absence of family history in immunodeficiency. He suffers from infectious (chronic bronchitis), oncological (basal cell carcinoma) and others (pancreatogenic enteropatia) clinical manifestations. It is observed, how family doctors could approach the treatment of the main pathology considering the intensification of comorbid chronic diseases. Futhermore, such patients should be managed ambulatory with full awareness of the stationary treatment and vice versa.

Key words: *primary immunodeficiency, common variable immunodeficiency, agammaglobulinemia*

Conflict of interests

The authors declare no conflict of interests

Sources of funding

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Conformity with the principles of ethics

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IgA — immunoglobulin A, IgG — immunoglobulin G, IgM — immunoglobulin M, IRAK-4 — interleukin-1 receptor-associated kinase 4, IUIS — International Union of Immunological Societies, NBN — Niymegen breakage syndrome, HIV — human immunodeficiency virus, CCH — city clinical hospital, Ig — immunoglobulin, LN — lymph nodes, FEV_1 — forced expiratory volume per 1 second, PID — primary immunodeficiency, PIDS — primary immune deficiency state, CRP — C-reactive protein, PFT — pulmonary function test, FLC — functional lung capacity, EGDS — esophagogastroduodenoscopy

Introduction

Primary immunodeficiencies (PIDs) are genetically determined life-threatening conditions, associated with defects of one or several components: cellular or humoral immunity, phagocytosis, complement system. By now, 176 hereditary disorders leading to persistent immune dysfunctions have been identified.

O. Bruton was the first to mention PID in the mid-20th century. His paediatric patient with recurrent infections of upper and lower respiratory tract practically had no serum protein gamma fractions. The child's condition improved after immunoglobulin as replacement therapy.

For the purpose of further studies of primary immunodeficiencies, the International Union of Immunological Societies (IUIS) was formed in the 1970s.

Globally, approximately one in every 2,000 people has PID, therefore, this condition is an orphan disease. Orphan diseases are conditions with the incidence of less than one per 2,000 newborns [1]. However, the rarity of this pathology is controversial. According to preliminary estimates, the global incidence of PID can be six million people, whereas currently there are just 27,000 confirmed cases in PID registries [2]. The incidence of these conditions varies a lot, and in some countries it is over the average rate; however, it is believed that the detectability of PID is greatly underestimated. According to specialists, in Europe the number of patients with PID is at least 638,000, but only 15,052 cases are currently registered (2.27 %). In Africa, up to 902,631 people may have PID, but the current number of registered cases is just 1,016.

In 2020 in the Russian Federation, data of 2,472 patients registered in the primary immune deficiency state (PIDS) database were analysed; most of the patients were underage (61 %) [3]. It was shown that the average incidence of all PIDs in Russia was 1.5 per 100,000 of population. The annual number of children born with PID is at least one in every 16–17 thousand newborns; and since 2010 the number of patients with confirmed PIDs has risen significantly. The lowest mortality in all PID cases is 4–5.5 %, while the highest death rate was recorded in the group of children in early years [3].

Currently, there are 415 disease entities and syndromes described and included in PIDs. Clinically, they are usually divided into nine main groups, depending on the primary damage to a component of the immune system [4]:

1) Humoral defects (including impaired antibody formation)
2) Combined cell and humoral immunity insufficiency
3) Qualitative and quantitative phagocyte defects
4) Complement system defects
5) Syndrome-like PIDS (including defective deoxyribonucleic acid (DNA) reparation)
6) PID with immune dysregulation
7) Innate immunity defects
8) Autoinflammatory diseases
9) Phenocopies

The characteristics of PID variants are presented in Table 1.

Table 1. *Classification of primary immunodeficient states based on immunological disorders according to the International Union of Immunological Societies*

Pathogenetic mechanisms	Examples of nosologies
Humoral defects (e.g. abnormal antibody formation)	X-linked agammaglobulinemia Common variable immunodeficiency IgG subclass deficiency
Combined deficiency of cellular and humoral immunity	Severe combined immunodeficiency CD40 ligand deficiency
Qualitative and quantitative phagocytic cells defects	Severe congenital neutropenia (Kostmann syndrome) Cyclic neutropenia Chronic granulomatous disease
Congenital immunity defects	Ectodermal dysplasia *Interleukin-1 receptor-associated kinase-4* (IRAK-*4*) *deficiency* Chronic mucocutaneous candidiasis
Defects of complement system	hereditary angioedema Deficiency of various components of complement
Primary immunodeficiency with immune dysregulation	Immunodeficiency with hypopigmentation Familial haemophagocytic syndrome X-linked lymphoproliferative syndrome Autoimmune lymphoproliferative syndrome
autoinflammatory diseases	familial Mediterranean fever TNF receptor associated periodic syndrome Hyper-IgD syndrome Criropyre-associated periodic syndrome
PIDS syndromic forms	Viscott-Aldridge syndrome Nijmegen syndrome Hyper-IgE syndrome DiGeorge syndrome
PID phenocopies	Phenocopies associated with somatic mutations Phenocopies associated with antibodies

Note. PID — primary immunodeficiency; PDS — primary immunodeficient states, IL — interleukins. Adapted from Bousfiha AA, Jeddane L, Ailal F, Benhsaien I, Mahlaoui N, Casanova JL, Abel L. Primary immunodeficiency diseases worldwide: more common than generally thought. J Clin Immunol. 2013;33(1):1-7. doi: 10.1007/s10875-012-9751-7 [2]

In Russia, neonatal PID screening was introduced only on January 1, 2023 (Order of the Ministry of Health of the Russian Federation No. 274n dated April 21, 2022, On Approval of the Procedure of Medical Assistance to Patients with Innate and/or Hereditary Diseases). This was a breakthrough in the area of early identification of innate immunodeficiencies and timely medical assistance to these patients; however, screenings does not take into account all possible variants of immunodeficiencies.

Clinical presentation of primary immunodeficiencies

Clinical signs of PID can be divided into several groups. In a majority of cases, PID manifestations are similar to those of infectious diseases. There can be both unexplained chronic recurrent infections and infections caused by low-virulence or rare agents. Infections can affect skin and mucous membranes, upper and lower respiratory tract, and gastrointestinal tract. In most cases, PID starts with chronic recurrent diarrhoea [5,6]. There is also connection between PID type and clinical form of a gastrointestinal disorder. Recurrent sinopulmonary infections with encapsulated bacteria, such as Haemophilus influenzae type B or Streptococcus pneumoniae, can be typical for antibody deficiency syndrome. Frequent viral, fungal or protozoal infections can evidence impaired T-lymphocyte function. Multiple staphylococcal skin infections and fungal infections are diagnosed in neutrophil dysfunction or elevated immunoglobulin E (IgE) concentration syndrome, while recurrent Neisseria infections are a typical manifestation of deficient complement C5, C6, C7, C8, C9 components. Mycobacterial infections are typical for interleukin 12 system disorders.

Other clinical presentations of PID include malignancies. As compared to the general population, the incidence of malignancies is higher in patients with PID.

Besides, PID can manifest as various autoimmune disorders (up to 22 % of cases) [7].

PIDs manifesting as typical syndrome complexes (Table 2) need special attention.

Primary immunodeficiency diagnostics

Primary immunodeficiency diagnostics can be challenging for primary healthcare providers due to the lack of information and rarity of some forms [8]. Primary healthcare providers should be aware of manifestations of primary immunodeficiency in order to timely refer the patient to an immunologist.

The Jeffrey Modell Foundation (USA) published a guidance for practitioners titled “Ten warning signs of primary immunodeficiency”. Below are the warning signs of primary immunodeficiency in adults [8].

- Two or more cases of ear infection within one year
- Two or more complex cases of paranasal sinus infections within one year (without allergies)
- One or more pneumonia cases every year
- Chronic diarrhoea with loss of weight
- Recurrent viral infections
- Repeatedly required IV antibiotics to kill an infection

Table 2. *Syndromal forms of PID with specific symptomatic complex*

Syndromes	Defect in the immune system	Clinical features
DiGeorge syndrome	Thymus hypoplasia	congenital heart defects hypoparathyroidism facial abnormalities
Viscott-Aldridge syndrome	T- и B-lymphocytes dysfunction	Hemorrhagic syndrome (petechiae, ecchymosis, nasal bleeding, melena) eczema Recurrent infections
Louis Bar Syndrome	T- и B-lymphocytes dysfunction	Ataxia telangiectasia
Nijmegen syndrome	Mutation NBN (NIJMEGEN BREAKAGE SYNDROME) Breakdown of the synthesis of the protein nibrine, associated with double-strand repair	Microcephaly Change of facial skeleton by type “bird face” Predisposition to malignancy

- Persistent oral thrush or mycotic lesions of skin
- Severe abscesses of skin and internal organs
- Infections caused by otherwise non-pathogenic mycobacteria
- Family history of primary immunodeficiency.

Medical history and laboratory data, which should be considered in order to suspect PID and refer the patient to specific tests, are presented in Figure 1.

Given that the above signs are typical both for primary and acquired immunodeficiency, acquired immune defi-

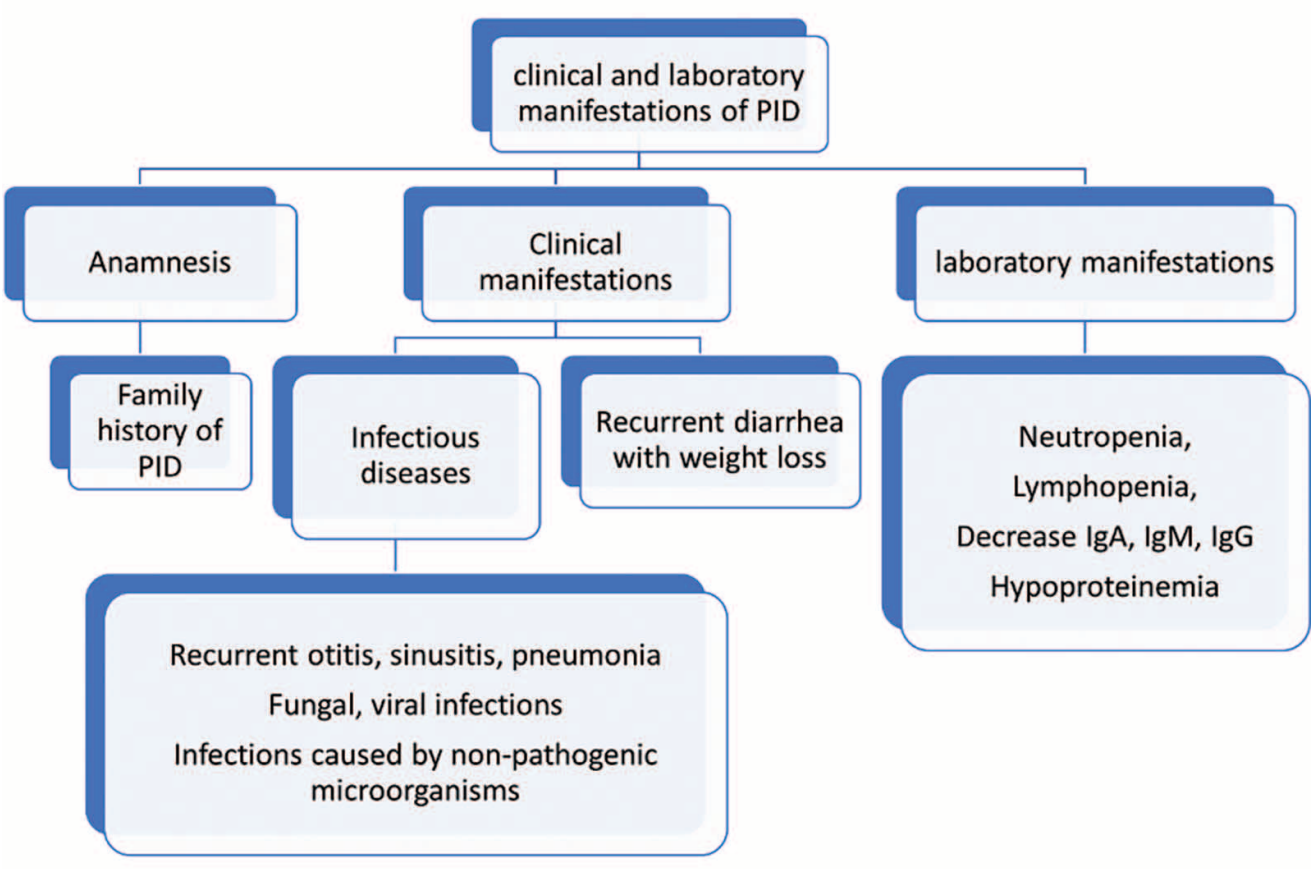

Figure 1. *Clinical and anamnestic basis for primary immunodeficiency (PID) diagnostic search*

Table 3. *Screening tests for PID detection*

Suspected immune system defect	Laboratory abnormalities that make PID suspect	Clarifying methods of diagnostics
Humoral immunity	Serum immunoglobulins (IgA, IgM, IgG) Titer of post-vaccination antibodies and/or isohemagglutinins Serum total protein level	Detection of IgG subclasses Determination of B-lymphocytes content and phenotyping with the help of monoclonal antibodies CD19 (CD20, CD21)
cellular immunity	Lymphopenia Skin Delayed Hypersensitivity Tests	T-lymphocyte count (CD4, CD8)
phagocytes	Neutropenia or neutrophilia	Nitroblue tetrazolium test (NBT test)
complement	Anemia, leukopenia, thrombocytopenia, reduction of serum immunoglobulins (IgA, IgM, IgG)	Total hemolytic capacity of serum (CH50) Content of complement components in serum

Note. PID — primary immunodeficiency; IgG — Immunoglobulin G class; IgA — Immunoglobulin A class; IgM — Immunoglobulin M class, CD19,20,21 — co-receptor proteins on the surface of B lymphocytes; CD4,8 — co-receptor proteins on T-lymphocytes

ciency syndrome (AIDS) and diabetes mellitus should be ruled out in adult patients before disease-specific tests and examinations.

Besides, there are a number of laboratory screening panels to test for primary immunodeficiency, which were developed by the Working Group of the European Society for Immunodeficiencies (Table 3) [8].

Therapy of primary immunodeficiencies

The general principles of PID management are presented below:

1) Replacement therapy with parenteral immunoglobulin
2) Prevention of infectious manifestations
3) Management of non-infectious manifestations
4) Correction of immune dysregulation complications.

The case study below is an example of PID detection using clinical symptoms and laboratory test results; it also describes further patient management, both in inpatient and outpatient settings.

Patient S., 36 y.o. According to the patient, there is no history of family diseases; all his relatives are healthy. He is a father to two healthy children. As a child, he frequently had acute respiratory diseases (ARD). When he was a child, he was diagnosed with chronic rhinosinusitis with over four recurrences annually. He was successfully treated with antimicrobial drugs; however, no long-lasting remission was achieved. In 2013, the patient underwent maxillary sinus microsurgery, which resulted in long-lasting remission. The last episode of maxillary sinusitis was recorded in 2019.

Besides, since childhood he has been having 4–6 events of diarrhoea a day, at a frequency of 3–4 times a year, associated with diffuse stomachache. The symptoms were treated with intestinal antiseptic drugs, rifaximin and probiotics.

In 1998, the patient was diagnosed with hypogammaglobulimenia; the treatment was non-specific and did not result in significant improvements; no documentary evidence was provided. In 2013, genetically non-confirmed reduction in IgA, IgG, IgM levels was reported (according to the patient, he does not have any documentary evidence). Attempted immunoglobulin therapy resulted in anaphylaxis and was discontinued.

In November 2017, the patient had severe recurrence of diarrhoeal syndrome with several daily episodes of loose stool, pain in epigastric, paraumbilical and colon area, as well as bloating and occasional rises in body temperature to subfebrile values. The patient was hospitalised to the gastroenterological ward, and gluten-sensitive enteropathy was suspected. Laboratory and instrumental test results did not confirm gluten-sensitive enteropathy; the patient was transferred to the infectious disease ward with gastrointestinal salmonellosis. His condition was treated with furasolidone, intestinal sorbents and infusion therapy, however, the symptoms did not resolve.

An examination in the infectious disease ward showed absolute lymphocyte depletion, reduction in various immunoglobulin fractions, and abnormal changes

Table 4. *Patient's results of examination in infectious department in 2017*

Methods	Results
complete blood count	absolute lymphocytopenia relative monocytosis
biochemical blood test	↑CRP
Immunogramm	↓IgG
Colonoscopy with biopsy	significant diffuse inflammation with shortening of the intestinal villi; absence or reduction of plasma cells↑ interepithelial lymphocytes
Stool test for disbiosis	bacterial imbalance ↓bifidobacteria, lactobacteria ↑lactosonegative Escherichia, staphylococci, conditionally pathogenic flora, yeast-like fungi
Gliadin antibodies	↓IgA (0,2 г/л)

Note. CRP-C-reactive protein; IgG- immunoglobulins G class; IgA- immunoglobulins A class, ↓ decrease, ↑ increase

(see Table 4), which was indicative of immunodeficient conditions. Once the main symptoms were arrested, the patient was transferred to the consultative diagnostic unit for allergology and immunology at the City Clinical Hospital No. 52 (Moscow) with a referral diagnosis "Common variable immunodeficiency".

A further examination in the allergology and immunology unit showed low serum immunoglobulins; lymphocyte immunophenotyping was performed, i.e. search for co-receptor protein on lymphocytes (CD), specific for each lymphocyte family. The result was as follows: high CD3-, CD19+ levels, moderately low CD3+, CD19-; CB3+, CD4+; CD3-, CD8+ levels.

The diagnostic search allowed making the following diagnosis "Primary immunodeficiency. Common variable immunodeficiency — agammaglobulinaemia".

Recommended therapy: IV normal human immunoglobulins at a dose of 10 g of protein/day for an indefinite period of time. This therapy did not trigger any allergic reactions in the patient.

Once PID was verified during the inpatient treatment in 2017, the patient was hospitalised only once, in 2020, when he had a flare-up of his chronic bronchitis. Then the patient was followed up in outpatient settings.

In February 2018, the patient was consulted by a gastroenterologist for recurrent diarrhoea, body weight loss (10 kg from November 2017), left-sided subcostal pain. The patient underwent an outpatient examination. The following diagnosis was made: Chronic gastritis with exocrine secretion and pancreatic insufficiency; secondary pancreatogenic enteropathy with malabsorption syndrome. Excessive bacterial growth syndrome. After the diagnostic procedures, multienzyme products, mandatory course of probiotics and intestinal antiseptic drugs were prescribed. The patient takes the drugs until the temporary positive effects are achieved (normal stool for 7–8 days); a course of administration is repeated if the symptoms return. The periodic therapy resulted in significant improvement, the patient had fewer and less severe episodes of diarrhoea.

In March 2019, the patient attended his GP complaining of productive cough, especially in the morning. Sputum was from mucoid to mucopurulent. The patient had cough from time to time, starting from 2016. Given the duration of these complaints, the patient was diagnosed with chronic bronchitis. Recommendations included levofloxacin 500 mg for 10 days, in combination with ipratropium/fenoterol as nebulizer therapy. In September 2019, the patient was hospitalised to the pulmonology ward with a severe flare-up of chronic bronchitis, manifesting with fever, shortness of breath when walking less than 100 m, weakness, cough with yellow-green sputum. The patient underwent a comprehensive pulmonary function test (PFT), chest X-ray (two views); sputum culture was not performed. Chest X-ray did not show any new focal or infiltrative shadows; the lung pattern was clear in all areas. PFT did not reveal any abnormalities. The therapy included vancomycin, bronchodilators and mucolytics.

The patient was discharged after six days in the hospital with positive changes and recommendations on drugs therapy:

- Glycopyrronium bromide 50 μg for inhalation, one inhale/day, for 21 days
- Fluconazole 50 mg, two capsules in the morning after meals, for 10 days
- Amikacin 1 g + 10.0 mL saline solution — solution for nebulizer inhalations, every eight hours, for one month
- Azithromycin 250 mg, one tablet once daily, for three months [9]
- Multienzyme preparations 10,000 U, one tablet TID, for 10 days
- Trimebutine 200 mg, one capsule BID, for 2–3 weeks
- Vancomycin 500 mg, four times daily per os, as a 14-day course
- Bifidumbacterinum, 10 doses TID, for two weeks.

In case of a flare-up of chronic bronchitis, nebulizer therapy with spirometry monitoring is indicated:

- Ipratropium bromide/fenoterol budesonide, 15–20 drops per 2.0 mL of saline solution, BID
- Budesonide 0.25 mg/mL 1 nebula, or 0.5 mg/mL 1/2 nebula, BID
- Ambroxol 40 drops per 2.0 mL of saline solution, BID.

In January 2020, the patient started complaining of cough with mucopurulent sputum, subfebrile body temperature. Chest X-ray: no focal and infiltrative changes in the lung field. PFT did not show any abnormalities (forced expiratory volume per 1 second (FEV_1): 95 %, functional lung capacity (FLC): 98 %). Since the flare-up was moderate, antibiotic therapy was conducted in outpatient settings, with positive dynamics. After 2020, the patient did not visit the hospital and was not hospitalised for exacerbations of chronic conditions. He was followed up by an allergologist-immunologist, pulmonologist and ENT specialist

In January 2023, the patient came for a consultation by the skin specialist, complaining of a skin lesion on his

right cheek. Examination revealed a hollow scar up to 5 mm on his right cheek. Dermatoscopy showed dendriform vessels on the periphery of the scar. Regional lymph nodes were nonpalpable. Biopsy was performed; a histological examination verified initial stages of nodular basal cell carcinoma. Curative surgery was performed (resection). Currently, the patient is followed up by the skin specialist; he comes to scheduled monitoring visits once every six months. The tumour did not recur.

Final diagnosis: primary immunodeficiency. Common variable immunodeficiency — agammaglobulinaemia. Chronic bronchitis, long-lasting remission. Chronic pancreatitis with exocrine secretion insufficiency. Secondary pancreatogenic enteropathy with malabsorption syndrome. Excessive bacterial growth syndrome. Nodular basal cell skin carcinoma, post-surgery condition.

The diagnosis was worded in mid-2023 by the GP on the basis of medical records from the skin specialist, allergologist-immunologist, pulmonologist.

At the case follow-up (September 2024), the patient complained of cough, occasionally loose stool; the management comprises the following measures:

1. Follow-up by GP, allergologist-immunologist, pulmonologist, ENT specialist, gastroenterologist, oncologist
2. Life-long replacement immune therapy with IV immunoglobulin once a month at a dose of 0.4 g/kg
3. Monitoring of pre-transfusion IgG, IgA, IgM levels once every three months (inpatient settings)
4. Routine sputum analysis, bacterial and fungal culture, chemotherapy sensitivity test once every three months
5. Spirometry, examination of diffusing lung capacity once every three months
6. Fibrocolonoscopy once a year
7. Stool culture for opportunistic and pathogenic flora in recurrent diarrhoeal syndrome
8. Complete blood count, C-reactive protein (SRP), fibrinogen, calprotectin once every three months
9. Ultrasound examination of abdomen and kidneys, retroperitoneal space, all lymph node groups once a year
10. Flu and pneumococcus vaccination.

Discussion

The characteristic of the presented case study lies in the duration and challenges with diagnosis of primary immunodeficiency with onset in an adult; and also in the development of a management strategy for these patients, causing a lot of uncertainties among healthcare practitioners.

The diagnostic challenge in this case is the absence of the family history (parents, siblings and even children of the patient did not have this pathology), as well as in late onset of the immune pathology.

For a correct diagnosis, clinical disguises of immune deficiency should be taken into account: infections, cancer, autoimmune conditions, allergies, etc. It is essential to pay attention to a common clinical sign PIDS in addition to recurrent infections, which in this case gave a hint of the correct diagnosis, namely frequent episodes of diarrhoea with stomachache. This can be explained by the fact that the large lymph system of the gastrointestinal tract, being the primary protective barrier, grows thinner and leads to the damage to jejunum villi from foreign microorganisms. It results in inflammatory and osmotic diarrhoea. The autoimmune nature of the gastrointestinal tract involvement facilitates the development of diarrhoea. Once any other known origins (human immunodeficiency virus (HIV), infectious enterocolitis, Crohn's disease, intestinal tumour and TB, pseudomembranous colitis, gluten-sensitive enteropathy, etc.) have been ruled out, PID should be suspected [6]. A typical sign of PID in complete blood count is absolute lymphopenia; immunogram — low levels of all immunoglobulin fractions; colon biopsy — short villi and an elevated level of interepithelial lymphocytes, as well as impaired bacterial balance in stool samples. For the final diagnosis of PID, a number of additional tests and examinations are required, depending on the suspected group of immune deficiencies (see Table 3). In this case study, lymphocyte immunophenotyping was performed, the results of which gave an idea of the common variable immunodeficiency.

PID therapy requires adherence to the principle of the life-long continuous replacement therapy with immunoglobulins and immunogram monitoring once every three months [10]. Besides, all comorbidities should be treated, and the patient should be hospitalised in case of severe exacerbations. It is worth mentioning that cooperation between inpatient and outpatient teams is essential for the management of patients with PIDS. Inpatient healthcare providers should verify the diagnosis of PID and offer professional services in urgent cases. In outpatient settings, the current patient's condition is corrected, and laboratory and instrumental results are monitored.

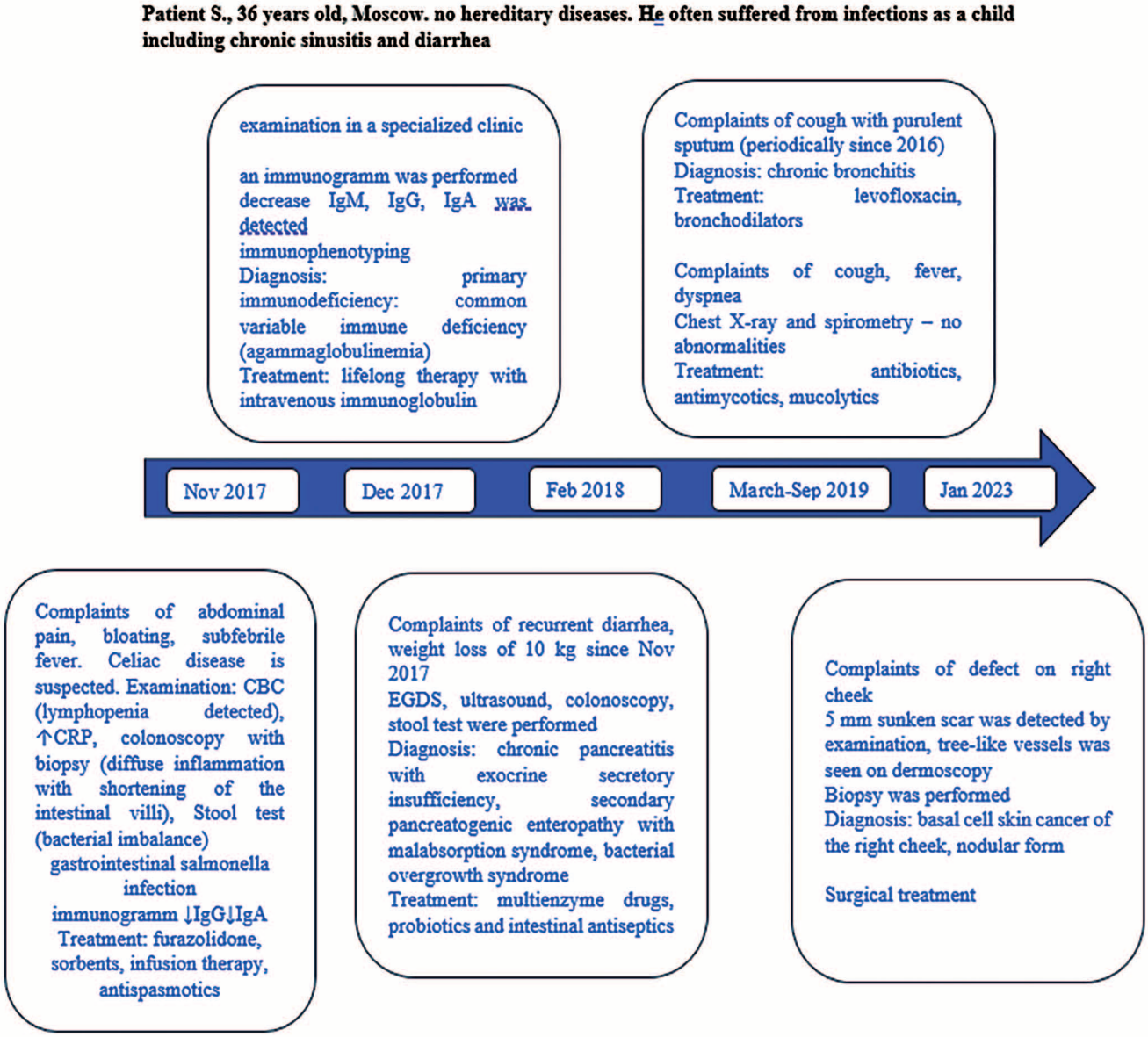

Figure 2. *Timeline of observation of a patient with primary immunodeficiency*
Note. Ig — immunoglobulin, CBC — clinic blood cells, CRP — C-reactive protein, EGDS — esophagogastroduodenoscopy

In this patient, the prognosis is favourable due to an optimal level of serum immunoglobulins maintained with monthly intravenous infusions; there are no reports of any serious flare-ups of chronic conditions; and the patient is highly compliant with the therapy.

Conclusion

An approach to the diagnosis and management of PIDS is a complex cross-disciplinary task. One should not forget about late onset of the disease, possible disguises of this pathology, compulsory life-long replacement therapy with immunoglobulin and serum immunoglobulin monitoring, as well as regular follow-ups by healthcare providers involved in the therapy of comorbidities.

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