CASE REPORT

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A CASE STUDY OF A CHILD WITH DOWN SYNDROME: A DILEMMA FOR THE ACCOMPANYING PULMONARY IMPAIRMENT

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Abstract. *This is a 12-year-old boy with proven trisomy 21 (Down syndrome). During the last calendar year, a series of severe inflammatory manifestations of the lower respiratory tract began. Before the first hospitalization, he was in a serious general condition, with a pronounced biological syndrome of inflammation (CRP – 197 mg/L), but without leukocytosis. Oxygen saturation was 60%. The performed chest radiograph showed left-sided lung destruction and a multifocal inflammatory-infiltrative process in the right lung. In the following months, an active exacerbation of the manifestations of respiratory failure and radiographic progression of pulmonary changes followed. A new chest CT scan was performed – with data on consolidation of the parenchyma in both lobes of the left lung to the extent of atelectasis. In the right lung – middle and lower lobe, extensive ground glass areas, emphysema in the right apical and dislocation of the mediastinum. The subsequent chest X-ray showed no changes compared to the previous one, except for marking the interlobe on the right. After consultation with a thoracic surgeon, a left-sided pulmonectomy was proposed. In the mycograms performed at the same time, a result was obtained proving the presence of Paecilomyces spp. Due to the negative result for Aspergillus, the treatment started with Voriconazole was changed to Itraconazole according to the obtained result. At present, the patient is at the end of the first month of his treatment cycle with itraconazole, and a new imaging study is to be conducted to assess the effect of the treatment.*

Key words: *Trisomy 21, immunoglobulins, mycosis, pneumonia, itraconazole*

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INTRODUCTION

Children with Down syndrome (DS) are called “sunshine” children due to their charisma, affection, and pure goodness radiating from them. Every year, 1 in 700 children worldwide is born with this syndrome, making it one of the most common genetic anomalies [1, 2, 3]. In Bulgaria, the number of children born with this condition is approximately 100 per year [15]. The mosaic Down syndrome, diagnosed in our patient, is the rarest genetic variation. In this type, some cells have three copies of chromosome 21, while others have the typical two copies of it. The specificity of this type is that, in most cases,

it is not inherited. Instead, it results from a random record during cell division in mitosis or meiosis [4].

Children with Down syndrome have typical facial features and body structure, reduced muscle tone, and slower physical and mental development [13, 14]. Nearly 50% of them are born with heart defects, and many cases also involve issues with hearing, vision, thyroid gland, gastrointestinal system and sleep disorders [5]. However, the syndrome manifests differently in each child, which explains why some of them require specific care throughout their lives. However, others can live independently and take care of themselves.

CLINICAL CASE DESCRIPTION

The patient is a 12-year-old boy diagnosed with Trisomy 21 Mosaic (DS).

Chronology of the illness

The first encounter with this patient was in September 2022, when, prior to hospitalization, the patient was treated ambulatorially with Cefuroxime and Acetilcisteine with unsatisfactory results. Due to the persistence of clinical symptoms (cough, mild expectoration) and the findings from the clinical examination: Wheezing with abundant medium moist rales bilaterally, RR 46/min, HR 120/min, the patient was referred for hospitalization. The conducted tests revealed the following.

The performed chest X-ray showed signs of bilateral pneumonia (Fig. 1).

Treatment with ceftriaxone, amikacin, inhalations of salbutamol, oxygen therapy at 5 l/min, antistenocardine, and furanthril led to mild improvement in the clinical condition, but with persistence of bronchopulmonary findings.

In 2023, the patient did not attend follow-up visits or undergo the recommended laboratory and imaging studies to assess their clinical condition.

In November 2024, a new hospitalization took place at the Clinic of Pediatrics. Prior to this, the patient was treated in another pediatric department without any improvement in the clinical condition. Consequently, the patient was admitted in a deteriorated general condition, with an intoxicated appearance. Moreover, moderately pronounced signs of respiratory failure were present – tachypnea up to 48 breaths/min, mixed-type dyspnea, total percussion, a short percussion tone in the left chest, and bronchial breathing, weakened at the base on the same side. The conducted tests revealed the following (Tables 3 and 4).

Table 1. Laboratory test results of the 12-year-old boy with trisomy 21

	WBC	Gran%	Lym%	Mo%	Eo%	Ba%	RBC	HGB	HCT	PLT	CRP
21.09.22	10.34	49.2	41.4	6.8	2.2	0.4	4.58	140	0.43	307	6.3

Table 2. Blood-gas analysis

	pH	pCO_2	pO_2	sO_2	BE	HCO_3
21.02.22	7.395	41.6	49	87.2	0.6	24.5

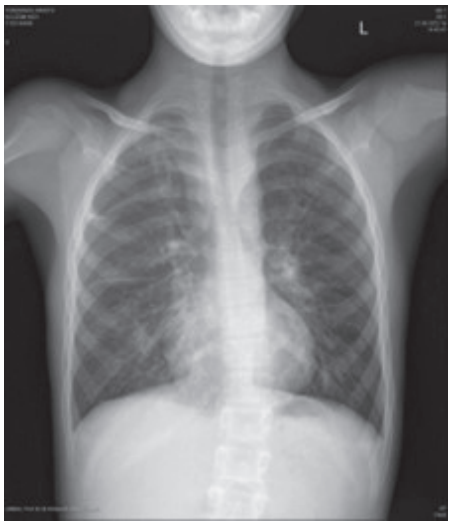


Fig. 1. Chest and lung X-ray – Presence of strip-like, network-shaped shadows bilaterally, perihilar and paracardiac. Free costophrenic angles

Table 3. Laboratory test results

	WBC	Gran%	Lym%	Mo%	Eo%	Ba%	RBC	HGB	HCT	PLT	CRP
21.11.24	12.38	82.1	12.5	5.2	0.1	0.1	4.78	147	0.46	396	1.1

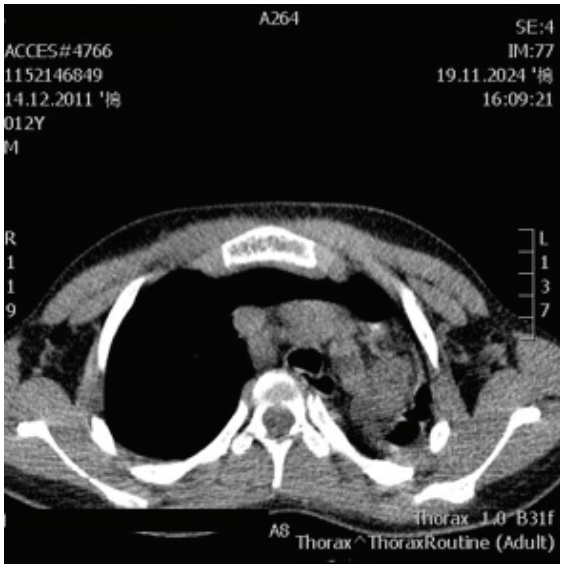
Table 4. Blood-gas analysis

	pH	pCO_2	pO_2	sO_2	BE	HCO_3
21.11.24	7.38	39.8	55.6	85.8	-0.9	23.4

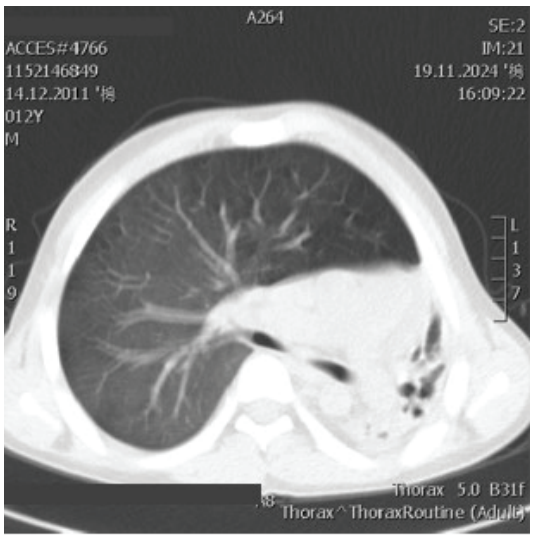
During the previous calendar year, he suffered a series of lower respiratory tract infections. In November 2024, the patient was hospitalized for the first time, in a severe general condition, with laboratory signs of manifested biological inflammatory syndrome (CRP – 197 mg/L), but without leukocytosis. The following symptoms were present: respiratory failure, mixed tahidyspnea, total retraction, dull percussion tone, bronchial breathing in the left chest half and desaturation up to 74%. Virus detecting tests were conducted with the following results: RT-PCR COVID-19 (negative), RSV (negative), Adenovirus DNA -not detected, RT-PCR Rhinovirus – not detected, Influenza virus A/B – not detected.

The applied treatment involved antibiotics (meropenem, ciprofloxacin), dexamethasone, inhalations with salbutamol, and an antimycotic drug – fluconazole resulted in partial clinical improvement.

Due to the unsatisfactory effect of the ongoing treatment and the persistence of bronchopulmonary changes, a chest CT scan was performed (22/11/24). The results were as follows: parenchymal consolidation in the two lobes of the left lung, atelectasis in the middle and lower lobes of the right lung – extensive ground-glass opacity areas, emphysema in the right upper lobe and mediastinal dislocation; pericardial effusion – 8 mm axial size at the level of the right atrium (Fig. 2 – images A, B, C, D).



A



B

Fig. 2. (Images A, B) – Chest CT scan results

Moreover, an echocardiography was performed. The results were as follows: structurally and functionally normal heart, pericardial effusion in front of the right atrium – 12 mm, in front of the right ventricle – 8 mm; behind the left ventricle – 8 mm (Fig. 3).

Due to the unsatisfactory effect of the ongoing treatment, a follow-up chest X-ray was performed. The conducted X-ray showed a shaded left lung with mediastinal and tracheal deviation to the left; inflammatory changes and atelectasis in the left lung; the cardiac shadow was completely displaced to the left (Fig. 4).

The following tests were performed in dynamics: Quanti FERON test, through which the possibility of tuberculosis was ruled out (20); COVID-19 test – negative; sweat test (Na – 57.5 mmol/l, Cl – 37.5 mmol/l); immunoglobulin G – 10.01 g/l; immunoglobulinA – 1.45 g/l. Blood cultures were tested a few times with no bacterial flora isolated.

On 01.12.2024, the patient was admitted again for hospitalization (following previous treatment in another pediatric department). The patient was admitted in a severely compromised general condition with manifest signs of respiratory failure: tachypnea of the expiratory type, shortened percussion tone in the left chest half, and bronchial breathing in the same chest half. In the right lung base, vesicular breathing was auscultated with the presence of cracles. Respiratory rate (RR) 48-52/min, heart rate (HR) 100/min. The following changes were noted in the laboratory tests (Tables 5 and 6).

After that, an X-ray was performed (12/24), and no dynamic change was detected compared to the previous results, with the exception of the marked interlobe on the right. This required a consultation with a thoracic surgeon at the UMHATEM "N.I.Pirogov," who recommended performing a pneumonectomy, which the parents declined (Fig. 5).

Treatment with vancomycin, salbutamol inhalation, and oxygen therapy was administered. Due to the prolonged periods of antibiotic treatment, therapy with voriconazole was started. A sample was sent for cultural testing for Aspergillus niger, and the result was negative. The patient was discharged in a stabilized general condition.

On 09.01.2025, the patient was readmitted for treatment in a severe general condition, having received

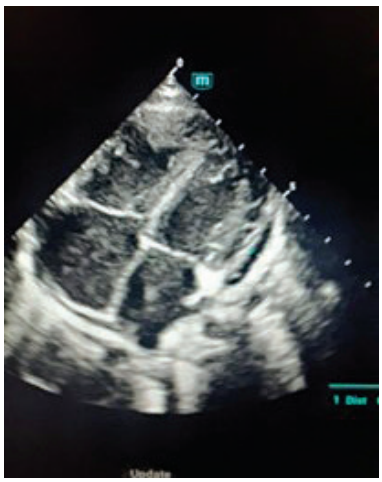


Fig. 3. Heart ultrasound-pericardial effusion

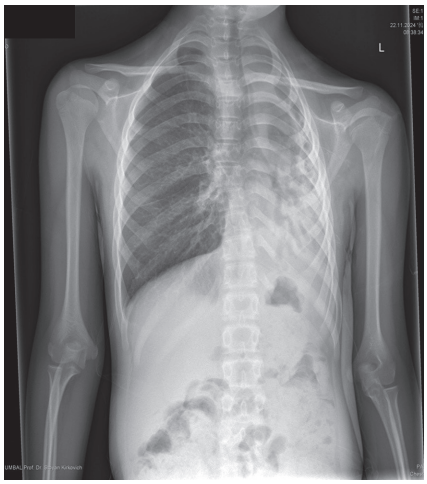


Fig. 4. Chest X-Ray

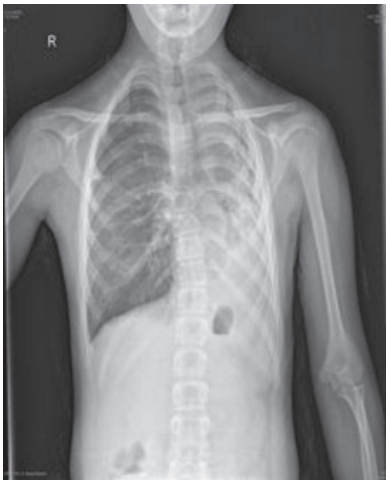


Fig. 5 . Chest X-Ray

Table 5. Laboratory test results

	WBC	Gran%	Lym%	Mo%	Eo%	Ba%	RBC	HGB	HCT	PLT	CRP
01.12.24	10.6	87.9	7.2	4.9	0.0	0.0	4.37	135	0.42	218	197

Table 6. Blood-gas analysis

	pH	pCO_2	pO_2	sO_2	BE	HCO_3
01.12.24	7.33	30.6	42.2	74.8	-8.4	15.9

prior treatment at another medical facility. Upon hospitalization, the patient presented with signs of manifest respiratory failure, total exhaustion, tachypnea up to 66/min, and fever. Heart rate and blood pressure was normal.

The following laboratory tests were conducted (Tables 7 and 8).

The condition was assessed as critical, with readiness for mechanical ventilation. However, after the initiation of aggressive conservative treatment with zavicefta, methylprednisolone, salbutamol, furanthril, infusion of glucose-saline solutions, frizobin,amino acids crystalline, oxygen therapy at 10L/min, acid-base state correction with $NaHCO_3$ in accordance with the results from the blood-gas analysis. Consequently, an improvement in the overall condition occurred within a few hours, along with improvements in the parameters of the acid-base balance (Table 9).

The negative result for Aspergillus presence and the treatment with Voriconazole, the medication was changed to Itraconazole due to the positive result for Paecilomyces spp. (Fig. 6) [19]. The decision was based on the patient's condition and studies confirming the effectiveness of the medication after a year of treatment, followed by an invasive surgical intervention (pulmonectomy) [9, 16].

Currently, the patient is at the end of his first month of medical treatment with Itraconazole. The next imaging examination is scheduled to assess the effectiveness of the treatment.

Despite the administered treatment with antibiotics, the improvement in clinical and X-ray follow-ups was inconsistent and inconclusive. Paecilomyces spp was isolated during the performed mycogram of sputum. As studies have determined, lens implantation is the most common predisposing factor for ocular mycosis [13]. Moreover, skin and subcutaneous infections that most often occur in recipients of organ and bone marrow transplantations are also predisposing factors, as is the primary or acquired immunodeficiency.

Table 7. Laboratory test results

	WBC	Gran%	Lym%	Mo%	Eo%	Ba%	RBC	HGB	HCT	PLT	CRP
09.01.25	7.8	82	11.1	6.9	0.0	0.0	4.06	118	0.4	263	12

Table 8. Blood-gas analysis

	pH	pCO_2	pO_2	sO_2	BE	HCO_3
09.12.24	6.8	53.2	41.7	67	-32.5	5.6

Table 9. Blood-gas analysis

	pH	pCO_2	pO_2	sO_2	BE	HCO_3
09.12.24	7.19	30.6	49.2	74.8	-8.4	15.9

Fig. 6. Mycosis culture

DISCUSSION

Nowadays, it is widely accepted that children with Down Syndrome suffer more often from infections of the respiratory tract [12]. Our case confirms the latter statement. Moreover, it is believed that the absence of heart function impairment is not a determining factor for the increased risk of infections. Amongst children with Down Syndrome, there is a high risk of deterioration of the general condition and worsening the course of infection towards acute respiratory distress syndrome (ARDS) [17]. While the genetic condition is associated with a low mortality rate, there is a hypothesis of abnormal regulatory mechanisms of infection in such children, such as antioxidant imbalance and oxidative stress, which leads to apoptosis in lung tissue [18].

In the differential diagnostic plan, the nosological entities with chronic pulmonary damage were discussed: tuberculosis (excluded due to the negative result from QuantiFERON test), cystic fibrosis of the pancreas (negative sweat test and absence of other cardinal symptoms), non-Hodgkin lymphoma (absence of polyadenopathy), and bronchiectatic disease (presence of dynamic change in the pulmonary findings).

The tendency for recurrence of the respiratory tract infections suggests disruption of humoral immunity. However, since this wasn't confirmed with the patient in question, the other possibility was a decrease in the various subgroups of lymphocytes, i.e., the possibility that the number of T- and B-cell subgroups was below the 10th percentile of the norm. Unfortunately, in our case, the assessment of the cellular immunity disruption was hindered due to the lack of family consent.

Studies have confirmed that children with Down Syndrome have decreased T-cell receptor excision circles (TREC), which are byproducts of DNA TCR recombination and reflect the production of new T-cells in the thymus [7]. It has been reported that the level of the lymphocytic proliferative response to phytohemagglutins is significantly low in children with Down Syndrome [6, 8], while anomalies in IgG levels are not detected in all such children [9]. However, a difference in neutrophil chemotaxis has been confirmed [10, 11]. A number of studies have reported a low level of NK cells. In addition, some sources suggest disturbed secretion of cytokines and interleukins, such as IL-2, IL-7, IL-10 [12] and a deficiency of mannan-binding proteins [13]. It is believed that they are connected with the increased susceptibility to infections [14].

CONCLUSION

Despite the lack of the usual congenital complications of the cardiovascular system and the theoretical possibility of a quadruple higher risk of malignant hemopathies, in this case study, the challenge was determined by compromised cell immunity, which caused periodic exacerbation of severe lower respiratory tract infections. The administered etiopathogenic antibacterial treatment didn't succeed in improving the clinical status of the patient and caused additional complications with severe and rare mycosis (Paecilomyces spp.).We believe that in such cases, the only aim in therapy is to limit the mycotic infection followed by a life-saving pulmonectomy.

Conflict of Interest Statement: *The authors declare no conflicts of interest related to this work.*

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Ethical statement: *This study has been performed in accordance with the ethical standards as laid down in the Declaration of Helsinki.*

Consent for publication: *Consent form for publication was signed by the parent/guardian and collected.*

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