

Case report

Imunodeficiência comum variável pediátrica com hipogamaglobulinemia e resposta vacinal heterogênea: relato de caso

Pediatric common variable immunodeficiency with hypogammaglobulinemia and heterogeneous vaccine response: a case report

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Abstract

Objective: To describe the clinical course, diagnostic investigation, and therapeutic management of a pediatric patient with hypogammaglobulinemia, recurrent infections, and a heterogeneous vaccine response who was being followed for suspected common variable immunodeficiency. **Case report:** A 12-year-old male patient, born late preterm at 34 weeks of gestation, had a history of recurrent respiratory and gastrointestinal infections since early childhood, multiple hospitalizations, and frequent corticosteroid use. In July 2023, an allergy and immunology evaluation revealed hypogammaglobulinemia (IgG: 640 mg/dL; IgM: 53 mg/dL) and initially non-protective antibody titers against hepatitis B (anti-HBs: 2 IU/L) and the evaluated pneumococcal serotype (serotype 4: 1.1 µg/mL). After booster vaccination, an assessment performed in March 2024 demonstrated protective antibody titers against multiple pneumococcal serotypes, indicating a heterogeneous vaccine response over the course of follow-up. Because of persistent infections, prophylaxis with trimethoprim-sulfamethoxazole was initiated. In February 2025, intravenous human immunoglobulin therapy was indicated and subsequently initiated at an approximate dose of 0.4 g/kg every three to four weeks. Following the first infusion, self-limited systemic adverse events occurred and were managed symptomatically. During follow-up, a reduction in infectious manifestations and an increase in serum IgG levels were observed, with dose adjustments based on body weight and clinical and laboratory findings. **Conclusion:** This case highlights the complexity of investigating children with hypogammaglobulinemia and recurrent infections, particularly in the presence of heterogeneous vaccine responses over time. In this patient, immunoglobulin replacement therapy was associated with clinical and laboratory improvement during the follow-up period.

Keywords: Primary Immunodeficiency Diseases. Hypogammaglobulinemia. Common Variable Immunodeficiency.

Resumo

Objetivo: descrever a evolução clínica, a investigação diagnóstica e o manejo terapêutico de um paciente pediátrico com hipogamaglobulinemia, infecções recorrentes e resposta vacinal heterogênea, em acompanhamento por suspeita de imunodeficiência comum variável. **Relato de caso:** trata-se de paciente do sexo masculino, com 12 anos, prematuro tardio (34 semanas), com histórico de infecções respiratórias e gastrointestinais recorrentes desde a primeira infância, múltiplas internações hospitalares e uso frequente de corticosteroides. Em julho de 2023, a avaliação em alergia e imunologia evidenciou hipogamaglobulinemia (IgG: 640 mg/dL; IgM: 53 mg/dL) e títulos inicialmente não protetores para hepatite B (anti-HBs: 2 UI/L) e para o sorotipo pneumocócico avaliado (sorotipo 4: 1,1 µg/mL). Após doses de reforço vacinal, a avaliação realizada em março de 2024 demonstrou títulos protetores para múltiplos sorotipos pneumocócicos, evidenciando resposta vacinal heterogênea ao longo do acompanhamento. Diante da persistência das infecções, foi instituída profilaxia com sulfametoxazol-trimetoprima. Em fevereiro de 2025, foi indicada terapia com imunoglobulina humana intravenosa, posteriormente iniciada na dose aproximada de 0,4 g/kg em intervalos de três a quatro semanas. Após a primeira infusão, ocorreram eventos adversos sistêmicos autolimitados, tratados sintomaticamente. Durante o seguimento, observou-se redução das manifestações infecciosas e aumento dos níveis séricos de IgG, com ajustes da dose conforme o peso corporal e a evolução clínica e laboratorial. **Conclusão:** o caso evidencia a complexidade da investigação de crianças com hipogamaglobulinemia e infecções recorrentes, especialmente diante de respostas vacinais heterogêneas ao longo do tempo. Neste paciente, a terapia de reposição com imunoglobulina associou-se à melhora clínica e laboratorial durante o período de acompanhamento.

Palavras-chave: Doenças da Imunodeficiência Primária. Hipogamaglobulinemia. Imunodeficiência de Variável Comum.

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Introduction

Common variable immunodeficiency (CVID) is one of the most frequently diagnosed symptomatic inborn errors of immunity¹. Despite the limitations of epidemiological data, related, among other factors, to the delay in recognizing the disease^{2,3}, a prevalence is estimated at approximately one case for every 25,000 to 50,000 individuals⁴, with a relatively similar distribution between sexes⁵.

CVID is mainly characterized by hypogammaglobulinemia, with a significant reduction in serum IgG levels associated with a decrease in IgA and/or IgM, and by clinical manifestations that include recurrent bacterial infections, especially of the respiratory and gastrointestinal tracts². Its pathophysiology is heterogeneous and involves changes in adaptive immunity, including defects in the differentiation and activation of B cells, impaired antibody production and functional changes in CD4 T cells. Changes involving components of innate immunity have also been described, including natural killer cells, monocytes, dendritic cells, phagocytes and complement system proteins^{2,6}.

The diagnostic investigation is based on the persistent demonstration of a reduction in serum immunoglobulins, especially IgG, in association with changes in IgA and/or IgM, considering reference values appropriate to the age group. The evaluation of the specific humoral response to vaccines can contribute to the characterization of antibody deficiency, and its results must be interpreted in conjunction with other clinical and laboratory findings and the moment in which the dosages were carried out. The exclusion of secondary causes of hypogammaglobulinemia is a fundamental step in the diagnostic investigation^{4,5,7}.

The main therapeutic strategy for patients with clinically significant antibody deficiency is immunoglobulin replacement intravenously or subcutaneously^{8,9}. In selected situations, prophylactic antibiotic therapy can also be used to reduce the frequency and severity of infections¹⁰. Late recognition and recurrence of infectious processes can contribute to pulmonary complications and other manifestations associated with the disease, with an impact on patients' prognosis and quality of life^{7,10}.

In the pediatric context, diagnosis can represent a challenge, particularly when there is hypogammaglobulinemia associated with recurrent infections, but the response to vaccine antigens shows heterogeneous behavior throughout follow-up. The isolated interpretation of antibody titers, without considering their temporal relationship with vaccination and booster doses, can make the diagnostic framework and definition of therapeutic management difficult. In this context, a detailed description of the clinical and laboratory evolution can contribute to understanding the diagnostic process and management of these patients.



Therefore, the present study aims to describe the clinical evolution, diagnostic investigation and therapeutic management of a pediatric patient, with hypogammaglobulinemia, recurrent infections and heterogeneous vaccine response, accompanied by suspected common variable immunodeficiency, highlighting the challenges related to the temporal interpretation of the vaccine response and the definition of the therapeutic strategy. The study was submitted and approved by the Research Ethics Committee of the Centro Universitário do Norte de Minas under opinion no. 7.630.57.

Case report

This is a male patient, 12 years old, Caucasian, living in the North of Minas Gerais, born by vaginal birth, premature at 34 weeks of gestation, after premature rupture of the ovular membranes. During pregnancy, the mother had gestational diabetes mellitus and recurrent urinary tract infections. At the age of 10, the patient underwent adenoidectomy and tonsillectomy. He had no known drug allergies or family history of inborn error of immunity; the mother, however, had Sjögren's syndrome. The vaccination calendar was updated according to the National Immunization Program.

In July 2023, the patient was evaluated for the first time in a pediatric allergy and immunology outpatient clinic for recurrent upper airway respiratory manifestations associated with gastrointestinal symptoms, present since the first years of life. There was a history of multiple hospital admissions and frequent use of corticosteroids and anti-inflammatories during crises. Upon physical examination, he was clinically schart, with vital signs within normal limits and no relevant changes in cardiovascular, respiratory and abdominal examinations. The body mass index was 16.84 kg/m².

The initial laboratory evaluation demonstrated immunological changes, including hypogammaglobulinemia, as shown in Chart 1. Given the recurrence of infectious manifestations and laboratory findings, the hypothesis of an inborn error of immunity was considered. Treatment with montelukast, 5 mg/day, and inhaled corticosteroid with mometasone, both for 90 days, was instituted. Additional tests for immunological investigation were also requested.

After three months, despite adherence to treatment, clinical manifestations persisted, associated with the appearance of skin rashes. The laboratory investigation demonstrated an initially inadequate vaccine response to hepatitis B and pneumococcus, in addition to changes in immunological parameters below the 10th percentile, as shown in Chart 1. Additional doses of vaccines against hepatitis B and pneumococcus were administered and a new evaluation of the specific humoral response was scheduled, including measurement of anti-pneumococcal IgG.



In the subsequent evaluation, approximately six months after the start of follow-up, the patient maintained recurrent clinical manifestations, having presented a new crisis approximately 45 days before the consultation, treated again with corticosteroids and anti-inflammatories. After the vaccine booster, the tests demonstrated an antipneumococcal response with IgG titers considered protective for the serotypes evaluated, in addition to non-reactive serology for HIV 1 and 2, as shown in Chart 1. Despite the observed vaccine response, the persistence of clinical manifestations and the suspicion of an inborn error of immunity motivated the initiation of antibiotic prophylaxis with trimethoprim-sulfamethoxazole, in the presentation of 400/80 mg, at a dose of one chartt each 12 hours, maintaining the diagnostic investigation.

In the six months following the start of prophylaxis, an initial clinical improvement was observed, with absence of attacks for approximately 40 days. Subsequently, there was a resurgence of infectious episodes, requiring temporary suspension of prophylaxis and treatment with broad-spectrum antibiotics, including amoxicillin associated with clavulanate and azithromycin, on three occasions. During this period, the patient also presented symptoms suggestive of urinary tract infection, associated with pain on suprapubic palpation.

Clinical and laboratory reevaluation reinforced the hypothesis of an inborn error of immunity with compromised humoral immunity, according to the results presented in Chart 1. Given the persistence of infectious manifestations and immunological findings, an evaluation was requested for replacement therapy with intravenous human immunoglobulin (IVIG), with renewal of antibiotic prophylaxis.

In February 2025, the patient returned for evaluation prior to the institution of immunoglobulin therapy. He reported a favorable clinical response to antibiotic prophylaxis. The tests demonstrated mild hypoalbuminemia, inversion of the albumin/globulin ratio, reactive IgG serology for cytomegalovirus and non-reactive serology for Epstein-Barr, as shown in Chart 1. Considering the set of clinical and laboratory findings, the hypothesis of an inborn error of immunity with humoral deficiency was maintained and IVIG therapy was indicated at a dose of 17.2 g every 21 days, in a hospital environment, with maintenance of antibiotic prophylaxis.

Three months after IVIG prescription, the first infusion was performed. Approximately 12 hours after the procedure, the patient developed severe headache, fever, nausea and vomiting, seeking treatment in an emergency department. He underwent symptomatic treatment and remained under observation until the condition resolved.

Twenty-two days later, the second IVIG infusion was administered, without immediate complications. Approximately 20 days after this administration, during a new evaluation at the



pediatric allergy and immunology outpatient clinic, adverse effects were reported after the previous infusions and a recent episode of odynophagia, which started four days earlier, with improvement after the use of systemic corticosteroids. New laboratory tests were requested and the subsequent administration of IVIG was scheduled.

The following day, the patient received the third infusion. In July 2025, during a follow-up consultation, he reported significant clinical improvement since starting immunoglobulin therapy. Laboratory tests carried out the day before the third infusion demonstrated increases in serum IgG levels and the other parameters evaluated remained without relevant changes, as shown in Chart 1.

Given the clinical and laboratory evolution, the IVIG dose was adjusted according to the updated body weight, 44.5 kg, and serum IgG levels, increasing to 17.8 g per infusion. Quarterly laboratory monitoring was established, preferably immediately before infusions, including serum IgG and IgA measurements, complete blood count, C-reactive protein, erythrocyte sedimentation rate, direct Coombs test and assessment of renal and hepatic functions, with subsequent adjustment of the dose according to clinical evolution and laboratory results.

At the age of 13, the transition from follow-up to the allergy and immunology outpatient clinic for adolescents and adults was also scheduled, aiming to continue specialized follow-up.

Chart 1. Patient laboratory results by category, on different dates in the years 2023, 2024 and 2025, compared to reference values. 2025.

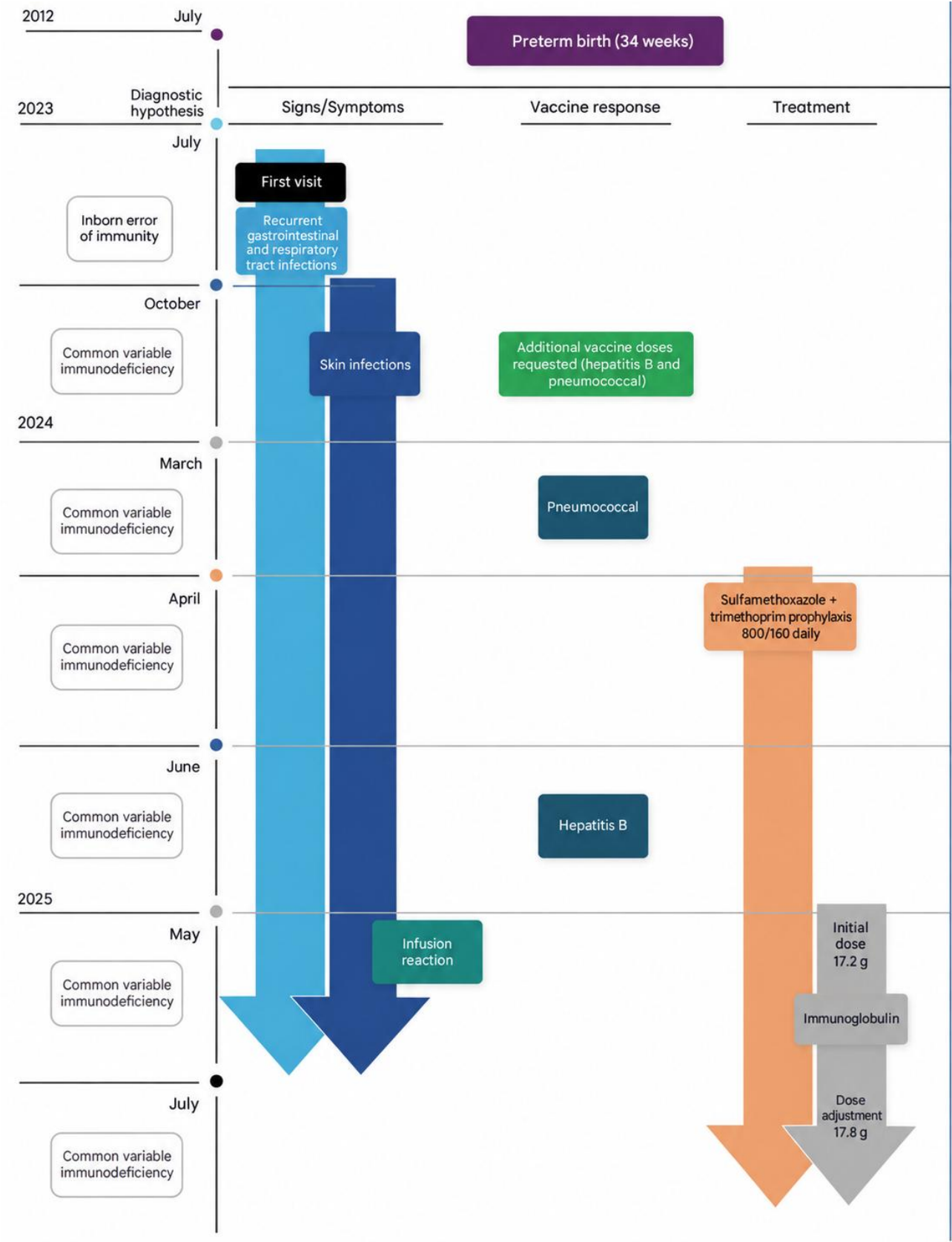
Category	Test/Variable	Reference value	2023		2024					2025
			06/20	10/17	03/06	03/21	06/19	06/21	12/02	06/18
Coagulation	Prothrombin activity (%)	> 70	-	-	-	-	-	-	94,6	-
Coagulation	INR	0.8 – 1.2	-	-	-	-	-	-	1,05	-
	APTT (s)	24 – 35	-	-	-	-	-	-	25	-
Electrolytes	Potassium (mEq/L)	3.5 – 5.1	-	-	-	-	-	-	3,9	4,0
	Sodium (mEq/L)	135 – 145	-	-	-	-	-	-	140	138
Liver function and proteins	Albumin (g/dL)	3.5 – 5.5	-	-	-	-	-	-	3,1	4,2
	Globulins (g/dL)	1.4 – 3.2	-	-	-	-	-	-	4,1	1,9
	Total proteins (g/dL)	6.0 – 8.0	-	-	-	-	-	-	7,2	6,1
	A/G Ratio	> 1.0	-	-	-	-	-	-	0,8	-
	TGO (U/L)	10 – 41	-	-	-	-	-	-	-	19
	TGP (U/L)	24 – 59	-	-	-	-	-	-	-	11
Kidney function	Creatinine (mg/dL)	0.31 – 0.92	-	-	-	-	-	-	0,63	0,64
	Urea (mg/dL)	8 – 36	-	-	-	-	-	-	34	
Blood Count	Hematocrit (%)	36 – 47	-	39.6	-	-	-	-	-	-
	Hemoglobin (g/dL)	12.5 – 16.1	-	13.2	-	-	14,1	-	-	-



	Red Blood Cells (million/mm ³)	4.2 – 5.6	-	4.37	-	-	-	-	-	-
	Leukocytes (cels/mm ³)	4.000 – 10.500	-	8.700	-	-	5.300	-	-	8.390
	Platelets (cels/mm ³)	150.000 – 450.000	-	300.000	-	-	211.000	-	190.000	-
Lymphocyte immunophenotyping (%)	NK Cells (%)	5 – 20	-	5.6	-	-	-	12,5	-	-
	B CD19 Lymphocytes (%)	5 – 20	-	26.3	-	-	-	19,6	-	-
	T CD3 Lymphocytes (%)	60 – 80	-	66.5	-	-	-	66,4	-	-
	T CD4 Lymphocytes (%)	30 – 60	-	43.9	-	-	-	42,0	-	-
	T CD8 Lymphocytes (%)	15 – 40	-	19.1	-	-	-	20,7	-	-
	CD4/CD8 Ratio	1.0 – 4.0	-	2.3	-	-	-	2,03	-	-
Serum immunoglobulins	CMV IgG / IgM	< 6 / < 0.85			-	-	-		NR	-
	EBV IgG / IgM	< 0.75 / < 0.50	-	-	-	-	-	-	NR	-
	IgA (mg/dL)	118 – 254		82	-	-	75		-	61,5
	IgG (mg/dL)	793 – 1475	640	5	-	-	-	586	-	924
	IgM (mg/dL)	51 – 152	53	51	-	-	54	-	-	63,4
Inflammatory markers	PCR (mg/L)	< 6	-	NR	-	-	-	-	-	NR
	VHS (mm)	0 – 10	-	5	-	-	-	-	-	5,0
Others	BD (mg/dL)	≤ 0.4	-	-	-	-	-	-	0,1	0,2
	BI (mg/dL)	≤ 0.8	-	-	-	-	-	-	0,1	0,4
	BT (mg/dL)	≤ 1.2	-	-	-	-	-	-	0,2	0,6
Antipneumococcal response (IgG by serotype)	Serotype 4 (µg/mL)	≥ 1.3	-	1.10	3.3	-	-	-	-	-
	Serotype 14	≥ 1.3	-	-	19.2	-	-	-	-	-
	Serotype 18C	≥ 1.3	-	-	>20	-	-	-	-	-
	Serotype 19F	≥ 1.3	-	-	8.1	-	-	-	-	-
	Serotype 23F	≥ 1.3	-	-	4.0	-	-	-	-	-
	Serotype 6B	≥ 1.3	-	-	>20	-	-	-	-	-
	Serotype 9V	≥ 1.3	-	-	7.7	-	-	-	-	-
Complement system	CH-50 (U/mL)	42 – 95	70.3	61.58	-	-	-	-	-	-
Vaccine serologies and antibodies	Anti-HBs (UI/L)	>10	-	2	-	-	1000	-	-	-
	Anti-tetanus (UI/mL)	> 0.1	-	0.43	-	-	-	-	-	-
	Coombs straight	Negativo	-	-	-	-	-	-	-	Negativo
	HIV 1 and 2	NR	-	-	-	NR	-	-	-	-

Caption: NR = non-reactive; DB = direct bilirubin; IB = indirect bilirubin; TB = total bilirubin; TP = total proteins; GL = leukocytes; PL = platelets; INR = international normalized ratio; APTT = activated partial thromboplastin time; A/G = albumin/globulin ratio; CMV = cytomegalovirus; EBV = Epstein-Barr virus; TGO = aspartate aminotransferase; TGP = alanine aminotransferase.

Figure 1. Event schedule. Summary outline of consultations, diagnostic hypotheses, signs/symptoms, vaccine response and treatment. Caption: GIT = gastrointestinal tract





Discussion

The present report describes the clinical evolution, diagnostic investigation and therapeutic management of a pediatric patient with recurrent respiratory and gastrointestinal infections, hypogammaglobulinemia and heterogeneous vaccine response, accompanied by suspected CVID. CVID is an inborn error of immunity predominantly characterized by compromised humoral response and reduced serum levels of immunoglobulins^{1,2,11}.

Although it can be diagnosed in different age groups, CVID presents manifestations since childhood in a portion of patients, with approximately 42% of cases being diagnosed during childhood or adolescence^{2,5,11}. In the present case, recurrent infectious manifestations were present from the first years of life, while systematized immunological investigation and the institution of specific therapy occurred during adolescence.

Recurrent respiratory and gastrointestinal infections are frequent clinical manifestations of CVID^{3,12,13}. Pneumonia is among the most prevalent infections, followed by recurrent upper respiratory tract infections^{11,14}. Gastrointestinal changes are also common and may include diarrhea, abdominal pain, nausea, vomiting and weight loss^{11,14,15}. The patient's history, characterized by recurrent episodes involving the respiratory and gastrointestinal tracts and multiple hospitalizations, is compatible with the clinical spectrum described for predominantly humoral deficiencies.

The recurrence and severity of respiratory infections can favor the development of structural pulmonary complications, including bronchiectasis, parenchymal changes and interstitial lung disease^{11,13}. In the patient presented, these complications were not documented during the follow-up period described. However, considering the history of recurrent respiratory infections, longitudinal follow-up remains relevant for early identification of possible pulmonary changes.

Laboratory investigation demonstrated a persistent reduction in serum immunoglobulins, particularly IgG and IgA, associated with the clinical phenotype of recurrent infections. Changes in the function and differentiation of B cells constitute relevant mechanisms in the pathophysiology of CVID and can result in a reduction in the production of immunoglobulins and impairment of the specific antibody response^{2,11}. Important quantitative changes in CD4+ and CD8+ T lymphocytes and innate immunity cells, however, were not predominant findings in this patient, in accordance with the immunological heterogeneity described in the disease^{2,6}.

The diagnosis of CVID must consider the significant reduction in IgG associated with the reduction in IgA and/or IgM, together with compatible clinical manifestations and additional immunological findings, in addition to the exclusion of secondary causes of hypogammaglobulinemia^{2,13}. This distinction is particularly relevant, as secondary conditions related



to the use of medications, neoplasms, kidney diseases, protein losses and other systemic conditions can produce similar laboratory changes and require different therapeutic approaches^{2,18}. In the case presented, clinical and laboratory investigation did not identify a secondary cause capable of satisfactorily explaining the hypogammaglobulinemia and the recurrent pattern of infections.

A particularly relevant aspect in this case was the evolution of the vaccine response. Initially, inadequate titers of antibodies against hepatitis B and pneumococcus were identified. However, after administration of booster doses, antipneumococcal titers considered protective were documented. This behavior demonstrates the importance of interpreting the vaccine response longitudinally, considering the time of collection, vaccination history and the response after additional immunization.

The evaluation of the response to vaccine antigens is part of the investigation of predominantly humoral deficiencies, although its interpretation presents technical and clinical limitations^{2,19}. Some authors consider that inadequate vaccination response should be used as a diagnostic support element in view of these limitations¹⁹, while others recommend its evaluation in the majority of patients, except in situations of extremely low or undetectable levels of IgG2. Therefore, obtaining protective titers after a booster vaccine should not be interpreted in isolation to exclude CVID, but should be analyzed together with the persistence of hypogammaglobulinemia, the clinical phenotype, other immunological parameters and the exclusion of secondary causes.

This aspect is central to the interpretation of the present case. More than characterizing a definitive vaccination failure, the data demonstrated a variable humoral response throughout follow-up, reinforcing the need for chronological documentation of immunizations and measurement of antibody titers before and after booster doses. The isolated analysis of a single result could lead to both overestimation and underestimation of the functional impairment of the humoral response.

Antibiotic prophylaxis can be used in patients with recurrent infections, particularly when infectious episodes persist during the investigation or even after the initiation of other therapeutic measures^{2,11,13,15}. In the case presented, prophylaxis with trimethoprim-sulfamethoxazole provided an initial clinical improvement, but was not sufficient to maintain sustained control of infectious episodes, with recurrence of crises and the need for therapeutic antibiotic therapy on different occasions.

Immunoglobulin replacement is one of the main therapeutic strategies for patients with CVID and clinically significant deficiency in antibody production^{2,11,13,15}. Administration can be performed intravenously, generally at intervals of three to four weeks, or subcutaneously, with individualization of the therapeutic regimen according to clinical response, serum IgG levels and tolerability². In the



present case, IVIG was instituted at an initial dose of 17.2 g every 21 days, subsequently adjusted to 17.8 g according to body weight and clinical-laboratory evolution.

IVIG therapy may be associated with adverse events, including headache, nausea, vomiting, cutaneous manifestations and systemic symptoms related to the infusion, however, serious reactions are less frequent². After the first administration, the patient developed severe headache, fever, nausea and vomiting, requiring evaluation in an emergency department and symptomatic treatment, with resolution of the condition. The occurrence of these events reinforces the need for clinical monitoring during treatment and individualization of administration strategies.

Subcutaneous immunoglobulin is a therapeutic alternative in selected situations, including patients with intolerance to the intravenous route or when greater autonomy in administration is sought². In the present case, despite the initial adverse events related to IVIG, intravenous therapy was maintained, with no description of subsequent serious events that would require a change in the route of administration.

Immunoglobulin replacement therapy is associated with a reduction in the frequency of infections, hospitalizations and the need for antibiotic therapy in patients with antibody deficiency^{2,11,13}. These benefits can contribute to improving quality of life¹⁴. In the present case, after the start of IVIG, there was a report of a reduction in infectious manifestations and an increase in serum IgG levels during the follow-up period. However, as this is a single patient and follow-up is still limited, these findings must be interpreted as individual clinical evolution, without the possibility of establishing generalizable therapeutic efficacy.

In addition to infectious manifestations, patients with CVID may present autoimmune complications, including cytopenias, which in some cases constitute the initial manifestation of the disease^{2,5,13,20}. CVID is also associated with an increased risk of certain neoplasms, particularly gastric malignancies and other tumors described in the literature^{3,12,21}. Although these complications were not identified in the period analyzed, their possibility reinforces the need for longitudinal clinical monitoring.

The present study has limitations inherent to the case report design, including the description of a single patient and the relatively short period of follow-up after the start of immunoglobulin replacement. Consequently, it is not possible to generalize the findings or establish causal relationships between the interventions carried out and the outcomes observed. However, the case is clinically relevant as it demonstrates the need for integration between clinical manifestations, serum immunoglobulin levels, exclusion of secondary causes and longitudinal assessment of the vaccine response in the diagnostic process of pediatric patients with suspected humoral deficiency. In this



context, the change in antibody titers after a vaccine booster highlights that the specific immunological response must be interpreted in the temporal context and in conjunction with other clinical and laboratory criteria.

Conclusion

The present case highlights the complexity of the diagnostic investigation and management of pediatric patients with hypogammaglobulinemia and recurrent infections. The integrated interpretation of clinical and laboratory findings, associated with the exclusion of secondary causes, proved to be fundamental for the diagnostic framework of humoral deficiency compatible with CVID.

The evolution of antibody titers after a vaccine booster demonstrates that the vaccine response must be assessed longitudinally and not interpreted in isolation as a definitive criterion for diagnostic confirmation or exclusion. In the patient presented, the persistence of infectious manifestations and hypogammaglobulinemia, despite the subsequent achievement of protective antipneumococcal titers, supported the continuation of the investigation and the individualization of the therapeutic approach.

Antibiotic prophylaxis provided initial clinical control, but was not sustained. After the institution of IVIG, a reported clinical improvement and increase in serum IgG levels were observed during the follow-up period, requiring individual dose adjustment. These findings reinforce the importance of longitudinal clinical and laboratory monitoring in defining and monitoring treatment, without allowing, due to the case report design, generalizations about therapeutic efficacy.

Authors' contributions

The authors' contributions are structured according to the taxonomy (CRediT) described below:

Conception and design of the research, analysis, interpretation of data and writing of the manuscript, administration of resources, critical review of the manuscript for intellectual content and final presentation: Duarte IS, Gonzaga IF, Santos AMO, Nogueira TDMC, Reis C. The authors approved the final version of the manuscript and declared themselves responsible for all aspects of the work, including ensuring its accuracy and integrity.

Competing interests

None.

References

1. Ranjbarnejad T, Abolhassani H, Sherkat R, Salehi M, Ranjbarnejad F, Vatandoost N, *et al.* Exploring Monogenic, Polygenic, and Epigenetic Models of Common Variable Immunodeficiency. *Hum Mutat.* 2025;2025:1725906. <https://doi.org/10.1155/humu/1725906>



2. Bonilla FA, Barlan I, Chapel H, Costa-Carvalho BT, Cunningham-Rundles C, de la Morena MT, *et al.* International Consensus Document (ICON): Common Variable Immunodeficiency Disorders. *J Allergy Clin Immunol Pract.* 2016;4(1):38-59. <https://doi.org/10.1016/j.jaip.2015.07.025>
3. Krein P, YoGolare GG, Pereira MA, Grecco O, Barros AMT, Dias AR, *et al.* Common variable immunodeficiency: an important but little-known risk factor for gastric cancer. *Rev Col Bras Cir.* 2021;48:e20213133. <https://doi.org/10.1590/0100-6991e-20213133>
4. Callai T, Corrêa EW, Condori XPH, Hofmann AA, Wiggers CE, Calvache ET, *et al.* Imunodeficiência comum variável: um relato de caso. *Hematol Transfus Cell Ther.* 2022;44(Suppl 2):S70. <https://doi.org/10.1016/j.htct.2022.09.117>
5. Berrón-Ruiz L. Autoimmune diseases in patients with common variable immunodeficiency. *Rev Alerg Mex.* 2021;68(1):48-64. <https://doi.org/10.29262/ram.v68i1.894>
6. Lemos BO, Silva AKV, Pichioni MM, Colares PFB. Granulomatous interstitial lung disease and common variable immunodeficiency: a case of recurrent pneumonia. *Brazilian Journal of Health Review.* 2024;7(5):e73738. <https://doi.org/10.34119/bjhrv7n5-502>
7. Araujo KM, Velloso LA, Mansour E. Imunodeficiência comum variável: dificuldades no diagnóstico. *Braz J Allergy Immunol.* 2015;3(2):61-7. <http://dx.doi.org/10.5935/2318-5015.20150013>
8. Segundo GRS, Condino-Neto A. Treatment of patients with immunodeficiency: Medication, gene therapy, and transplantation. *J Pediatr (Rio J).* 2021;97(Suppl 1):S17-S23. <https://doi.org/10.1016/j.jped.2020.10.005>
9. Pimenta FMCA, Palma SMU, Constantino-Silva RN, Grumach AS. Hypogammaglobulinemia: a diagnosis that must not be overlooked. *Braz J Med Biol Res.* 2019;52(10):e8926. <https://doi.org/10.1590/1414-431X20198926>
10. Jeevarathnum AC, van Niekerk A, Kriel J, Green RJ. Common variable immunodeficiency disorders: What generalists should know. *Afr J Thorac Crit Care Med.* 2021;27(3):10.7196/AJTCCM.2021.v27i3.228. Disponível em: <https://pubmed.ncbi.nlm.nih.gov/34734174/>
11. Szczawinska-Poplonyk A, Schwartzmann E, Bukowska-Olech E, Biernat M, Gattner S, Korobacz T, *et al.* The pediatric common variable immunodeficiency — from genetics to therapy: a review. *Eur J Pediatr.* 2022;181:1371-83. <https://doi.org/10.1007/s00431-021-04287-6>
12. Antunes PSL, Tersariol HG, Veiga MMB, Menezes MCS, Bernardi FDC, Forte WCN. Neuroendocrine tumor in a child with common variable immunodeficiency. *Rev Paul Pediatr.* 2020;38:e2018146. <https://doi.org/10.1590/1984-0462/2020/38/2018146>
13. Yazdani R, Habibi S, Sharifi L, Azizi G, Abolhassani H, Olbrich P, *et al.* Common Variable Immunodeficiency: Epidemiology, Pathogenesis, Clinical Manifestations, Diagnosis, Classification, and Management. *J Investig Allergol Clin Immunol.* 2020;30(1):14-34. <https://doi.org/10.18176/jiaci.0388>
14. Cabanillas D, Pino AC, Finocchi A, Cañizares S, Vargas MF, Regairaz L. Inmunodeficiencia común variable: manifestaciones clínicas iniciales. *Serie de Casos. Ludovica Pediátrica.* 2021; 24(1):34-9. Disponível em: <https://docs.bvsalud.org/biblioref/2021/10/1293221/inmunodeficiencia-comun-variable.pdf>
15. Ghafoor A, Joseph SM. Making a Diagnosis of Common Variable Immunodeficiency: A Review. *Cureus.* 2020;12(1):e6711. <https://doi.org/10.7759/cureus.6711>



16. Szczawinska-Poplonyk A, Schwartzmann E, Ciesielska W, Konarczak M, Opanowski J, Orska A, *et al.* Immunogenetic landscape in Pediatric Common Variable immunodeficiency. *Int J Mol Sci.* 2024;25(18):9999. <https://doi.org/10.3390/ijms25189999>
17. Fujimura MD. Níveis séricos das subclasses de IgG em crianças Normais e Nefróticas [Tese de Doutorado]. São Paulo: Faculdade de Medicina da Universidade de São Paulo; 1991. Disponível em: <https://repositorio.usp.br/item/000732941>
18. Otani IM, Lehman KH, Jongco AM, Tsao LR, Azar EA, Tarrant TK, *et al.* Practical guidance for the diagnosis and management of secondary hypogammaglobulinemia: A Work Group Report of the AAAAI Primary Immunodeficiency and Altered Immune Response Committees. *J Allergy Clin Immunol.* 2022;149(5):1525-60. <https://doi.org/10.1016/j.jaci.2022.01.025>
19. Ameratunga R, Woon ST, Gillis D, Koopmans W, Steele R. New diagnostic criteria for common variable immune deficiency (CVID), which may assist with decisions to treat with intravenous or subcutaneous immunoglobulin. *Clin Exp Immunol.* 2013;174(2):203-11. <https://doi.org/10.1111/cei.12178>
20. Amaya-Urbe L, Rojas M, Azizi G, Anaya JM, Gershwin ME. Primary immunodeficiency and autoimmunity: A comprehensive review. *J Autoimmun.* 2019;99:52-72. <https://doi.org/10.1016/j.jaut.2019.01.011>
21. Danieli MG, Mezzanotte C, Verga JU, Menghini D, Pedini V, Biló MB. Common Variable Immunodeficiency in Elderly Patients: A Long-Term Clinical Experience. *Biomedicines.* 2022;10(3):635. <https://doi.org/10.3390/biomedicines10030635>