Case Report

Pulmonary Complications in Wiskott-Aldrich Syndrome

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ABSTRACT: Wiskott-Aldrich Syndrome (WAS) is a rare primary immunodeficiency that presents with thrombocytopenia, eczema, and recurrent respiratory infections, leading to severe pulmonary complications. This report describes the case of a 32-year-old man with the classic form of WAS who opted not to undergo hematopoietic stem cell transplantation. The patient developed bilateral bronchiectasis and subsequently an aspergilloma, presenting with recurrent, difficult-to-control hemoptysis. Due to severe thrombocytopenia and borderline pulmonary function, surgical resection was contraindicated. Following a multidisciplinary discussion, bronchial artery embolization was used as the primary measure for hemorrhage control, combined with antimicrobial and antifungal therapy. The case illustrates the complex therapeutic dilemma in managing the pulmonary sequelae of WAS in the context of advanced lung disease, highlighting the importance of a multidisciplinary approach for high-risk patients, as well as exposing the socioeconomic challenges faced by individuals with rare diseases.

KEYWORDS: *Wiskott-Aldrich Syndrome, hemoptysis, bronchiectasis, aspergillosis.*

Introduction

Wiskott-Aldrich Syndrome (WAS) is a rare genetic syndrome characterized by a mutation in the WAS gene (Wiskott-Aldrich Syndrome), located on the short arm of the X chromosome.

The WAS gene, expressed in hematopoietic cells of the myeloid lineage, codes for the WASp protein, a cytoskeletal regulator that coordinates actin filament assembly, which is essential for immunological synapses, signaling, and cell migration events [1,2].

Mutation of this gene predisposes individuals to the classic clinical triad of thrombocytopenia, immunodeficiency, and eczema, in addition to an increased incidence of neoplasms and autoimmune diseases [2,3].

The clinical phenotype is variable depending on the type of mutation, presenting in the following forms: classic (severe), X-linked thrombocytopenia and X-linked congenital neutropenia.

The disease has an estimated incidence of 1 to 10 in 1 million individuals, with a predominant manifestation in males [4].

Diagnostic confirmation of Wiskott-Aldrich Syndrome can be achieved by sequencing the *WAS* gene to identify a pathogenic variant, and by flow cytometry using an anti-WASP antibody [5,6].

Currently, the only curative therapy for the disease is allogeneic hematopoietic stem cell transplantation.

Supportive treatments may include platelet transfusion, prophylactic antibiotic therapy, oral glucocorticoids, immunosuppressants, and intravenous immunoglobulin [7].

In this report, we will address the pulmonary complications of an adult patient diagnosed with Wiskott-Aldrich Syndrome, who presents numerous treatment challenges due to bronchiectasis, difficult-to-control hemoptysis, and aspergilloma.

Case Report

A 32-year-old white man was referred to a tertiary care university hospital in 2023 due to recurrent episodes of hemoptysis.

At 5 years old, he was diagnosed with the classic form of Wiskott-Aldrich Syndrome, manifested by thrombocytopenia, immunosuppression, and eczema.

Due to immunosuppression, he presented with recurrent infections during childhood, mainly of the skin and lungs, which led to the formation of bilateral cylindrical bronchiectasis, in addition to a case of osteomyelitis in the right lower limb at 8 years old, which resolved after surgical treatment.

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Regarding family history, the patient has two first-degree cousins, already deceased, also diagnosed with Wiskott-Aldrich Syndrome.

Although informed about the curative possibility of allogeneic hematopoietic stem cell transplantation, he opted not to undergo it.

Thus, he maintains treatment with intravenous human immunoglobulin infusion (40 grams every 3 weeks), azithromycin (500mg 3 times a week), cyclosporine (75mg-twice daily) for the management of severe eczema, and budesonide/formoterol (12/400mcg-twice daily).

He receives elective platelet transfusion before invasive medical procedures and resorts to the use of tranexamic acid during episodes of hemoptysis.

Complementary exams were requested to investigate the cause of the hemoptysis.

A chest computed tomography (CT) scan evidenced mosaic attenuation of the bilateral pulmonary parenchyma, cylindrical and cystic bronchiectasis containing secretions and distributed predominantly in the right upper lobe, lingula, and left lower lobe, where they are associated with fibroatelectatic opacities and volumetric reduction of these regions.

Bronchial arteriography was also performed, identifying two arterial malformations in the descending aorta, one on the left and one on the right.

Spirometry showed characteristics of marked restrictive ventilatory disorder with no significant response to the bronchodilator (Table 1).

Table 1. Diffusion and Spirometry Test. The table shows the results of the diffusion and spirometry tests performed on the patient in September 2023. Abbreviations: TLC-Total Lung Capacity;FVC-Forced Vital Capacity; FEV1-Expiratory Volume in 1 Second; FEF 25-75-Forced Expiratory Flow; L-Litres.

	Predicted	Lower Limit of Normal	Pre-bronchodilator	Post-bronchodilator
TLC	5,56 L	4,51	3,20 (58%)	-
FVC	4,57 L	3,67	1,85 (40%)	1,91 (42%)
FEV_1	3,93 L	3,17	1,5 (38%)	1,61 (41%)
FEV_1/FVC	0,86	0,78	0,81 (94%)	0,84 (98%)
FEF_{25-75}	1,05L	0,67	0,77 (73%)	0,89 (85%)

Among the laboratory tests performed, all were normal, with the exception of a platelet count of 22,000/mm³, alkaline phosphatase of 204 U/l, and C-reactive protein of 2.21mg/dl (Table 2).

Table 2. Laboratory Tests.
The table shows the results of the laboratory tests performed on the patient in 2025.

	RESULTS	REFERENCE	UNITS
Complete Blood Count			
Hemoglobin (Hb)	15,1	13,9-17,7	g/dl
Hemat**o**crit (H**c**t)	45,3	39,6-51,8	%
White Blood Cells	5.000	3.790-10.330	/mm³
Total Neutrophils	3.965		/mm³
Segmented Neutrophils	3.890	1.700-7.200	/mm³
Blasts	75		/mm³
Eosinophils	60	30-470	/mm³
Basophils	10	20-110	/mm³
Lymphocytes	520	1.070-3.120	/mm³
Monocytes	450	240-730	/mm³
Platelets	22.000	166.000-389.000	/mm³
Glucose	83	70-100	mg/dl
Creatinine	0,98	0,7-1,3	mg/dl
Urea	35	19 -49	mg/dl
Sodium	138	136-145	mEq/l
Potassium	3,8	3,5-5,1	mEq/l
Aspartate Aminotransferase (AST)	25	< 38	U/l
Alanine Aminotransferase (ALT)	26	10-49	U/l
Gamma-Glutamyl Transferase (GGT)	54	< 73	U/l
Alkaline Phosphatase (ALP)	204	46-116	U/l
C-Reactive Protein (CRP)	2,21	< 1	mg/dl

Serologies for human immunodeficiency virus (HIV), Hepatitis B, and Hepatitis C were also performed, all negative.

Direct smear and culture for acid-fast bacilli (AFB), fungi, and bacteria were negative. Rheumatoid factor (RF) and the Anti-Nuclear Factor (ANF) test were negative.

Considering the exams described above, bronchiectasis was defined as the most likely cause for the hemoptysis, and surgical resection of the affected segments was proposed in a multidisciplinary meeting.

However, this procedure was contraindicated due to the high risk of intraoperative bleeding and high morbidity and mortality.

Therefore, the team opted to perform embolization via arteriography in July 2023, which improved the patient's clinical condition, with a reduction in the frequency of hemoptysis episodes.

In January 2025, the patient returned to the service complaining again of large-volume hemoptysis.

On physical examination, diminished vesicular breath sounds were observed in the right hemithorax, with the presence of crackles in the inferior base of the left lung and the apex of the right lung, and reduced chest expansion.

Xerosis and hyperpigmentation were noted in the lower limbs.

Associated with the hemoptysis, the patient reported dyspnea requiring him to stop to breathe when walking (MMRC 2) and a productive cough with yellowish sputum.

He denied fever and weight loss.

An arteriography examination showed vascular blush in the topography of the right pulmonary apex and the left pulmonary base, with the presence of arterio-arterial fistulas between the bronchial and pulmonary arteries.

Bronchoscopy revealed only a diffusely hyperemic bronchial tree with small, diffuse streaks of blood (Figure 1).

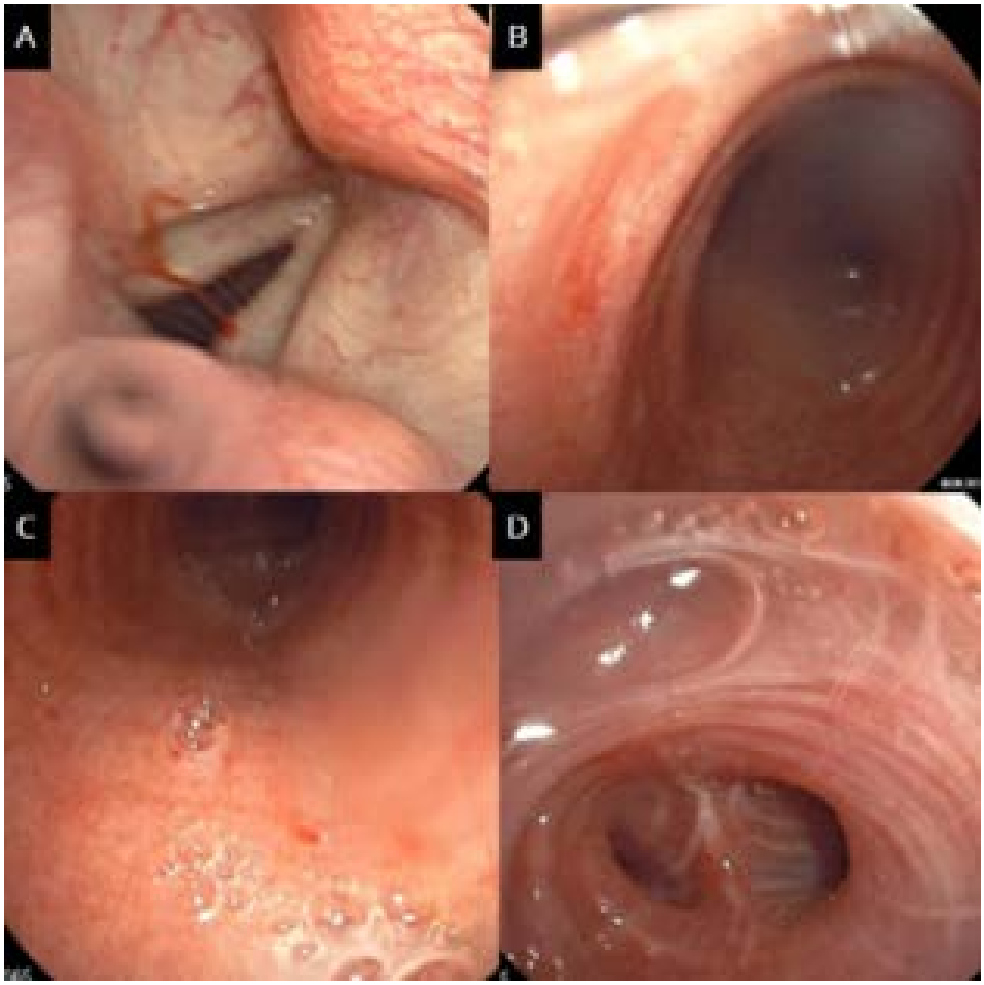


Figure 1. Bronchoscopy. Visualization of the bronchoscopic examination. Caption (A) Visualization of the larynx with a streak of blood on the vocal cord. (B) and (C) Visualization of the trachea and main carina with petechiae and slight diffuse hyperemia. (D) Visualization of a subsegment of the right upper lobe bronchus (subsegment I, II+III) with no active bleeding.

10.12865/CHSJ.52.03.16

A new CT scan was also performed which, in addition to the bronchiectasis, revealed a cavity in the right upper lobe with an image compatible with a fungal ball (Figure 2).

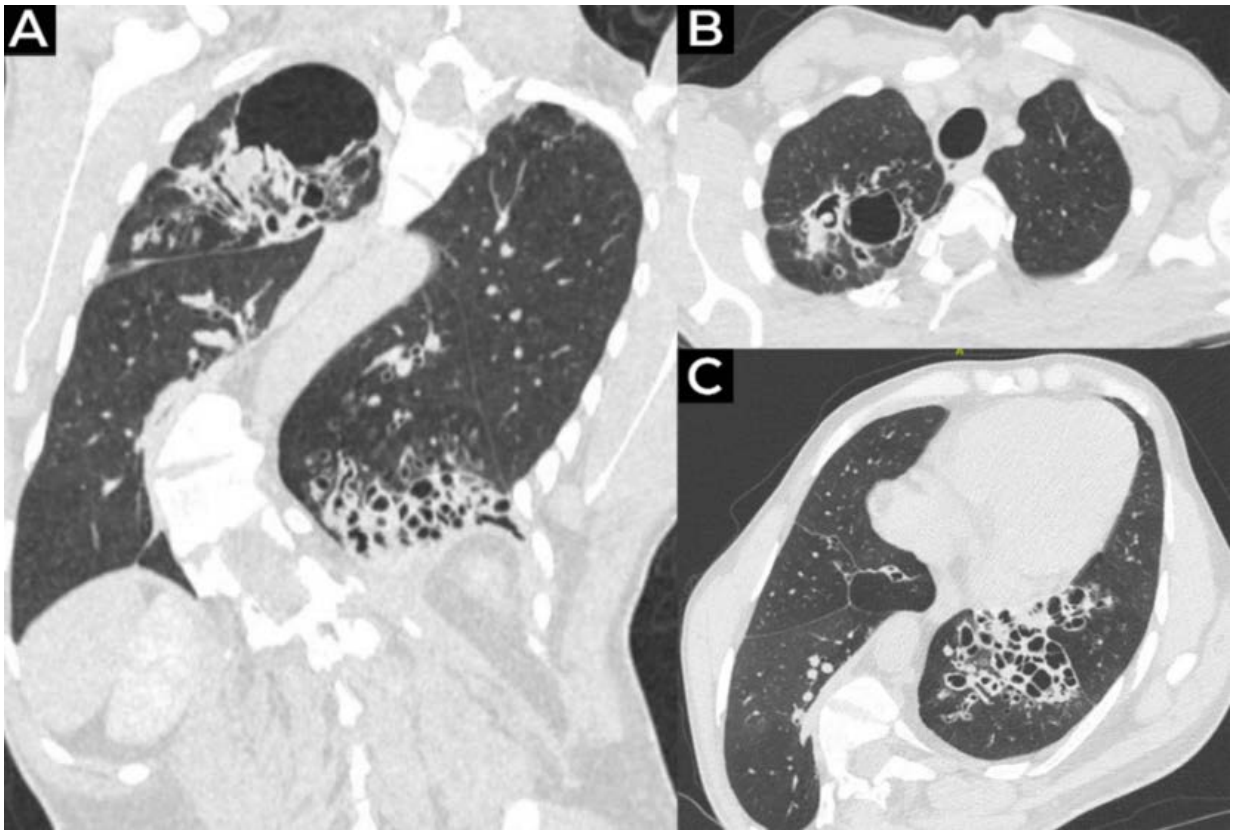


Figure 2. Chest Computed Tomography Scan.
Caption: (A) Visualization of a cavity in the right upper lobe, bronchiectasis in the left lower lobe, and evident thoracic asymmetry. (B) Visualization of a cavity in the right upper lobe with the presence of a fungal ball (aspergilloma). (C) Visualization of bronchiectasis in the left lower lobe and evident thoracic asymmetry.

In light of these findings, cultures for fungi from the bronchoalveolar lavage and sputum were requested, in addition to acid-fast bacilli smear and a rapid molecular test for tuberculosis.

All tests for Mycobacterium tuberculosis were negative; however, there was growth of Aspergillus niger in one of three sputum culture tubes.

Finally, the Galactomannan test by ELISA was performed, which resulted positive, supporting the diagnosis of aspergilloma.

Considering the diagnosis of aspergilloma with hemoptysis, new therapeutic possibilities were discussed in a multidisciplinary meeting.

Taking into account the surgical risks of bilateral lobectomy, borderline pulmonary function, and severe, clinically uncorrectable thrombocytopenia, surgery was contraindicated.

Therefore, the team opted for angioembolization of the arteries of the right upper lobe and left lower lobe, associated with the administration of the systemic antifungal drug, voriconazole 200mg, twice daily, which resulted in the stabilization of the patient's condition.

Discussion

This case report describes the complex management of pulmonary complications in an adult individual with the classic form of Wiskott-Aldrich Syndrome (WAS), who opted against undergoing hematopoietic stem cell transplantation, the only curative therapy currently available [8].

WAS is a primary immunodeficiency that, due to the WAS gene mutation, results in dysfunction of myeloid lineage hematopoietic cells.

As described in the literature, this immunodeficiency predisposes patients to recurrent infections, which are the main cause of long-term pulmonary complications [9,10].

The presented case clearly illustrates this progression: recurrent pulmonary infections during childhood led to the development of bilateral cylindrical and cystic bronchiectasis.

These structural changes in the lung are not primary manifestations of WAS but rather a direct consequence of the immune system's

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inability to control infections, leading to a vicious cycle of inflammation, tissue damage, and further infections [11].

Hemoptysis is a known and potentially fatal complication of bronchiectasis, usually caused by the rupture of hypertrophied and extremely fragile bronchial arteries in the wall of inflamed airways [12,13].

Management in a WAS patient, however, is particularly challenging for two conflicting reasons: severe thrombocytopenia, a central feature of the syndrome, which drastically increases the bleeding risk; and the hemoptysis itself, which requires intervention to be controlled [14].

In selected cases, the definitive treatment for localized bronchiectasis is surgical resection of the most affected pulmonary lobes.

However, this was contraindicated due to the marked restrictive ventilatory disorder, severe thrombocytopenia, prohibitive risk of intraoperative bleeding, and high morbidity and mortality [15].

In this scenario, embolization via arteriography of the bronchial arteries emerges as the main therapeutic alternative, as it is a safer procedure for acute bleeding control in high-risk patients [16].

The development of fungal disease can be explained by the risk triad: primary immunodeficiency, pre-existing pulmonary structural changes (bronchiectasis and cavitation), and the use of immunosuppressants (cyclosporine) [17,18].

Therefore, the aspergilloma added a layer of complexity to the clinical picture as it is a frequent cause of massive hemoptysis [19].

This patient's case represents a complex therapeutic dilemma.

The patient's refusal to undergo curative transplantation in childhood placed him on a trajectory of continuous management of complications.

The confluence of severe structural lung disease (bronchiectasis and aspergilloma), severe coagulopathy (thrombocytopenia), and immunodeficiency created a scenario where standard therapies for each isolated problem were contraindicated.

The strategy of surveillance and palliative intervention associated with prophylactic polypharmacy represents the safest and most appropriate conduct for a patient with such elevated risks.

Conclusion

This case report highlights the challenges in the long-term management of pulmonary complications associated with Wiskott-Aldrich.

Syndrome, especially in patients who do not pursue the curative path of transplantation.

The recurrent hemoptysis, aggravated by thrombocytopenia and the development of aspergilloma, needs a careful and individualized approach.

Bronchial artery embolization proved to be a vital tool in the palliative control of bleeding, and the therapeutic decision, guided by a multidisciplinary team, was essential to optimize the quality of life and minimize risks in a patient with extreme clinical complexity.

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Author Contributions

GPF: Conceptualization, Supervision, Data Curation, Investigation, Writing-Original Draft; LCG: Data Curation, Investigation, Visualization, Writing-Original Draft; MADN: Investigation, Writing-Original Draft; TFT: Investigation, Writing-Original Draft; AAC: Investigation, Writing-Review & Editing.

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Conflicts of interest

The authors declare no competing interests.

Institutional Review Board

Ethical Approval

The study was conducted in accordance with the Declaration of Helsinki and approved by the Ethics Committee of Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto-USP (Approval number: 8.271.095; CAAE: 96013226.5.0000.5440; approved on March 10, 2026).

Consent Statement

Written informed consent was obtained from the patient his history and access his medical record, including any accompanying images.

Data availability

All data presented in the manuscript are available from authors upon request.

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