rcfmc Revista Científica da Faculdade de Medicina de Campos
ISSN 2965-6575

Rev. Cient. Fac. Med. Campos, v. 20, n. 2, p. 36-43, jul./dez. 2025
doi: 10.29184/1980-7813.rcfmc.1290.vol.20.n2.2025
Faculdade de Medicina de Campos
https://revista.fmc.br/ojs/index.php/RCFMC

Case Report

Bone Marrow Aplasia Associated with Paroxysmal Nocturnal Hemoglobinuria in a Young Patient

Aplasia de medula associada à hemoglobinúria paroxística noturna em paciente jovem

Luanna Cherene Almeida[1], Lucas Lopes Wagner[2], Gabrielle Freitas Paravidine[2], Lara Vianna de Barros Lemos[3]

1 Medical resident in Internal Medicine, Hospital Escola Álvaro Alvim (HEAA), Campos dos Goytacazes, Rio de Janeiro, Brazil
2 Medical Student, Faculdade de Medicina de Campos, Campos dos Goytacazes, Rio de Janeiro, Brazil
3 Professor, Faculdade de Medicina de Campos, Campos dos Goytacazes, Rio de Janeiro, Brazil
Corresponding Author: Luanna Cherene Almeida
Contact: luannacherene@gmail.com

Keywords:
Aplastic Anemia.
Paroxysmal Nocturnal
Bone Marrow
Transplantation.
Clinical Diagnosis.
Hemoglobinuria.
Pancytopenia.

Palavras-chave:
Anemia Aplástica.
Diagnóstico Clínico.
Hemoglobinúria.
Pancitopenia.
Paroxística Noturna.
Transplante de Medula Óssea.

Received on:
26/06/2025

Accepted on:
08/12/2025

Published on:
12/31/2025

ABSTRACT

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare clonal disease that can present with hemolysis, thrombosis, and bone marrow failure, frequently associated with aplastic anemia (AA). This study aims to report the case of a young patient diagnosed with PNH who developed severe pancytopenia and AA. This is a case report study, conducted at the Álvaro Alvim Teaching Hospital, in Campos dos Goytacazes (RJ), in the year 2025. The diagnostic investigation included laboratory tests, bone marrow biopsy, and flow cytometry, which confirmed the presence of PNH clone and bone marrow aplasia. However, while the patient was waiting for transfer to a tertiary hospital unit for bone marrow transplantation, he presented with severe infectious and hemorrhagic complications, evolving to death. It is concluded that the overlap between PNH and AA represents a significant clinical challenge, requiring early diagnosis and specialized intervention to avoid unfavorable outcomes

RESUMO

A hemoglobinúria paroxística noturna (HPN) é uma doença clonal rara que pode cursar com hemólise, trombose e falência medular, frequentemente associada à anemia aplástica (AA). Este estudo tem como objetivo relatar o caso de um paciente jovem com diagnóstico de HPN que evoluiu com pancitopenia grave e AA. Trata-se de um estudo do tipo relato de caso, realizado no Hospital Escola Álvaro Alvim, em Campos dos Goytacazes (RJ), no ano de 2025. A investigação diagnóstica incluiu exames laboratoriais, biópsia de medula óssea e citometria de fluxo, que confirmaram a presença de clone HPN e aplasia medular. No entanto, enquanto o paciente aguardava transferência para uma unidade hospitalar terciária para a realização de transplante de medula óssea, apresentou quadro infeccioso e hemorrágico grave, evoluindo para óbito. Conclui-se que a sobreposição entre HPN e AA representa um importante desafio clínico, exigindo diagnóstico precoce e intervenção especializada para evitar desfechos desfavoráveis.

INTRODUCTION

Aplastic anemia is a hematological disorder of low incidence, characterized by progressive bone marrow failure, which is responsible for the production of blood cells. This condition leads to pancytopenia, that is, the simultaneous reduction of erythrocytes, leukocytes, and platelets, resulting from hypoplasia or absence of medullary hematopoietic activity. When not properly diagnosed and treated, aplastic anemia may have a fatal outcome, with high mortality rates. It is believed that, in most cases, the etiology of the disease is related to autoimmune mechanisms, in which the immune system itself attacks hematopoietic stem cells, negatively interfering with their regenerative function[1].

Although not all factors triggering the pathology are fully understood, it is known that external agents, such as medications, chemical agents, and viral infections, may induce changes in the immune response, promoting destruction or inhibition of hematopoietic stem cells. Certain medications have been implicated in the development of aplastic anemia through different mechanisms. While chemotherapeutic agents cause dose-dependent bone marrow suppression, other substances may induce the condition through idiosyncratic reactions, that is, unpredictable and not related to the administered dose, according to Giudice and Selleri[2].

In addition, according to Schoettler and Nathan[3], prolonged exposure to environmental and occupational factors, such as ionizing radiation, organic solvents, pesticides, insecticides, and industrial chemical substances, also represents a significant risk. Among these factors, benzene is one of the most extensively studied compounds and is strongly associated with the occurrence of aplastic anemia, particularly in cases of chronic exposure, even at relatively low concentrations.

Some viral infections have been implicated as potential triggers of aplastic anemia (AA), especially those that directly affect hematopoietic cells or alter the host immune response. Among the most relevant viral agents in this context are the human immunodeficiency virus (HIV) and parvovirus B19. These viruses may interfere with bone marrow function, causing suppression of blood cell production and contributing to the development of the clinical manifestations of AA[4].

In addition to acquired causes, certain inherited genetic disorders, according to Devalet et al.[5], may also predispose individuals to aplastic anemia. The main related genetic condition is Fanconi anemia, a rare syndrome characterized by progressive pancytopenia, high susceptibility to the development of hematologic malignancies, and multiple congenital anomalies. Frequently observed physical findings include microcephaly, hyperpigmented "café-au-lait" skin spots, short stature, and delayed growth. Diagnosis is usually established during childhood, although in some cases confirmation occurs only in adulthood.

Another hereditary condition associated with bone marrow failure is Shwachman-Diamond syndrome [6], which predominantly manifests in childhood. This syndrome is characterized by bone marrow insufficiency, often presenting as intermittent neutropenia and, in some cases, aplastic anemia. SDS is also marked by exocrine pancreatic dysfunction, leading to malabsorption and digestive problems, as well as skeletal abnormalities.

Romeo and Romeo[7] highlight that paroxysmal nocturnal hemoglobinuria (PNH) is a rare clonal disease caused by somatic mutations in the *PIG-A* gene, located on the X chromosome, which is essential for the biosynthesis of glycosylphosphatidylinositol (GPI)-anchored proteins on the cell surface. These mutations result in deficiency of important regulatory proteins, such as CD59, which normally protect blood cells from complement-mediated damage. The absence of these proteins makes red

blood cells particularly susceptible to complement-mediated lysis, leading to chronic intravascular hemolysis, recurrent thrombosis, and, in many cases, bone marrow failure.

According to Amaral[8], PNH may present clinical manifestations that overlap with those of AA, and coexistence of the two conditions is common. Flow cytometry-based studies have shown that, in certain populations, up to half of patients diagnosed with AA exhibit cellular clones characteristic of PNH, indicating a pathological interrelationship between the two diseases.

Freitas[9] emphasizes that the manifestation of PNH depends on two main factors: failure of normal hematopoiesis and the selective advantage acquired by mutant clones, favored by an immune response against normal cells that express GPI-anchored proteins. This selective pressure allows the expansion of deficient cells, contributing to the predominance of the PNH clone. When this process significantly compromises bone marrow function, secondary aplastic anemia may occur. Interestingly, even healthy individuals may harbor small populations of cells with *PIG-A* gene mutations similar to those seen in PNH. However, for these mutant cells to expand to the point of causing clinical disease, an altered hematopoietic environment is required, such as immune-mediated bone marrow suppression, which favors clonal selection.

This study aims to present a case report of aplastic anemia in a young patient previously diagnosed with paroxysmal nocturnal hemoglobinuria, with emphasis on the main clinical and laboratory findings, as well as the therapeutic approaches adopted. Although the association between AA and PNH is well documented in the medical literature, its occurrence in young patients may represent a diagnostic and therapeutic challenge. Through this report, the intention is to expand knowledge regarding the clinical manifestations and progression of this rare condition, highlighting the relevance of early diagnosis, individualized management, and follow-up by a specialized multidisciplinary team. This case report was approved by the ethics committee of Faculdade de Medicina de Campos under CAAE 89353625.8.0000.5244. The approval opinion number is 7.711.627.

CASE REPORT

A 20-year-old male patient, single, student, born and residing in the municipality of Campos dos Goytacazes, Rio de Janeiro, sought care at the emergency unit of a public hospital in the same city. The main complaint was progressively worsening asthenia, associated with frequent episodes of vertigo, with marked deterioration over the previous seven days. Initial physical examination revealed marked cutaneous and mucosal pallor, with no apparent signs of bleeding or other systemic abnormalities. Given the severity of the condition, an urgent complete blood count was requested, which demonstrated severe pancytopenia, leading to immediate hospitalization for clinical stabilization with blood transfusion and initiation of diagnostic investigation.

Subsequently, the patient was transferred to a public hospital for specialized evaluation. At hospital admission, he remained markedly pale and presented multiple hypochromic lesions distributed over the trunk and upper limbs, suggestive of pityriasis versicolor, with no other significant abnormalities on general or neurological physical examination. A repeat complete blood count confirmed severe anemia (hemoglobin 5.42 g/dL and hematocrit 18.5%), marked leukopenia (1,450 leukocytes/mm^3, with 18% segmented neutrophils and 77% lymphocytes), and severe thrombocytopenia (platelets = 11,100/mm^3).

During anamnesis, the patient denied weight loss, night sweats, fever, or recent in-

fectious symptoms. He reported no preexisting comorbidities, no continuous medication use, and denied smoking, family history of hematologic or malignant diseases, as well as occupational exposure to solvents, pesticides, or other toxic chemical substances. For etiological investigation, serological tests for hepatitis B and C, HIV types 1 and 2, and parvovirus B19 were requested, all of which were nonreactive. These findings reinforced the need for further investigation for the differential diagnosis of bone marrow failure, with suspicion of aplastic anemia associated with paroxysmal nocturnal hemoglobinuria.

Given the persistent pancytopenia without an evident cause in the initial investigations, a bone marrow biopsy was indicated to elucidate the etiology of the hematopoietic failure. Histopathological examination of the marrow sample revealed hypocellular bone marrow with significant replacement by adipose tissue, characterizing severe marrow aplasia. No atypical cells, blasts, or neoplastic infiltrates were identified, ruling out, at that time, the hypothesis of malignant hematologic diseases such as leukemias or myelodysplastic syndromes. The biopsy demonstrated so-called "empty marrow," that is, bone marrow poor in hematopoietic cells and predominantly composed of fat, typical of aplastic anemia.

While awaiting the final biopsy report, progressive worsening of thrombocytopenia was observed, with a marked decrease in platelet count. This condition led to the appearance of clinical signs of bleeding, including active gingival bleeding and petechiae on the palatal mucosa. Given the hemorrhagic risk, intensive transfusional support was required, with multiple transfusions of packed red blood cells and platelets, aiming to maintain hemodynamic stability and prevent more severe hemorrhagic events.

With the clinical picture still lacking a clearly defined etiology, specific complementary tests were requested to investigate inherited and acquired causes of bone marrow failure. Genetic screening for Fanconi anemia, performed through chromosomal fragility testing, yielded negative results, excluding this possibility. In parallel, investigation for paroxysmal nocturnal hemoglobinuria was requested and performed by flow cytometry, which detected a significant population of cells deficient in GPI-anchored proteins, such as CD55 and CD59, confirming the diagnosis of PNH associated with bone marrow aplasia. These findings allowed the diagnosis of aplastic anemia secondary to clonal expansion of PNH cells, a condition that requires specialized therapeutic management and multidisciplinary follow-up.

After diagnostic confirmation of AA, transfer of the patient to a tertiary care hospital with adequate infrastructure for bone marrow transplantation and specialized treatment of the underlying disease was promptly requested. However, while awaiting bed availability for transfer, the patient's clinical condition deteriorated rapidly.

The patient developed persistent fever for three consecutive days, with axillary temperatures above 37.7 °C and a peak temperature of 39.4 °C. The febrile condition became associated with progressive dyspnea, tachypnea, oxygen desaturation, and clinical signs consistent with acute respiratory failure, strongly suggesting the development of sepsis with a pulmonary focus, possibly secondary to immunosuppression caused by bone marrow aplasia.

Given the severity of the condition, the patient was urgently transferred to the Intensive Care Unit (ICU), where further deterioration of respiratory function occurred, culminating in the need for orotracheal intubation and initiation of invasive mechanical ventilation. In parallel, broad-spectrum antibiotic therapy was initiated with meropenem and vancomycin, in accordance with the institutional protocol for empirical treatment of severe sepsis in

immunocompromised patients, with a planned course of 10 days, depending on clinical evolution and microbiological results.

Despite intensive therapeutic measures, the patient developed severe blood dyscrasia, with significant hemorrhagic manifestations, including spontaneous bleeding that was refractory to platelet transfusions and other blood components. Coagulation abnormalities and progressive multiorgan failure did not respond to the instituted therapies. Unfortunately, the patient died due to septic shock and hemorrhagic complications associated with severe bone marrow failure, before transfer to the specialized transplant center could be accomplished.

DISCUSSION

In patients with severe pancytopenia, the diagnostic investigation must be careful and comprehensive, as this condition may have multiple causes, including acquired, infectious, immunological, toxic, and genetic factors. The first step is the performance of basic laboratory tests, such as a complete blood count with reticulocyte count, which allows assessment of bone marrow erythropoietic activity. In parallel, measurements of vitamin B12, folic acid, and ferritin are requested, along with liver and renal function tests and thyroid function tests, since metabolic dysfunctions may also contribute to hematological abnormalities.

The etiological investigation should also include serological tests for infectious agents, such as hepatitis B and C viruses, HIV, Epstein–Barr virus, cytomegalovirus, and parvovirus B19, as these viral agents are capable of triggering or exacerbating bone marrow suppression. After this initial screening, bone marrow aspiration and biopsy become indispensable, as they are essential to evaluate marrow cellularity, exclude neoplastic infiltration or lymphoproliferative disorders, and confirm the diagnosis of aplastic anemia when hypocellularity is observed without evidence of dysplasia or malignancy.

In cases such as that of this patient, with suspected aplastic anemia, the investigation must include specific tests for inherited and acquired diseases associated with bone marrow failure. One such disease is Fanconi anemia, for which screening is performed using chromosomal fragility tests, such as the diepoxybutane test, capable of detecting the genomic instability typical of this genetic syndrome. According to Sharma, Sharma, and Sharma[10], Fanconi anemia represents the main inherited cause of bone marrow failure and is frequently associated with congenital malformations and a predisposition to hematologic malignancies.

Another condition that must be investigated is paroxysmal nocturnal hemoglobinuria, which, although rare, has a strong association with aplastic anemia. Screening is performed by flow cytometry, which identifies cells deficient in GPI-anchored proteins, such as CD55 and CD59. Studies by Szlendak et al.[11] demonstrate that up to 40% of patients with AA have detectable PNH clones, which may influence therapeutic approach and prognosis.

The pathophysiology of PNH is based on a somatic mutation in the *PIG-A* gene, located on the X chromosome, which is essential for the biosynthesis of GPI-anchored proteins responsible for protecting blood cells from complement-mediated lysis. The absence of these proteins, especially CD55 and CD59, renders erythrocytes vulnerable to intravascular destruction, resulting in chronic hemolysis, recurrent thrombosis, and possible bone marrow failure. Brodsky[12] highlights that this failure is often associated with immune-mediated suppression of normal hematopoiesis, favoring clonal expansion of the mutated cells.

Considering the diagnosis of severe aplastic anemia and the presence of a PNH clone,

the patient was referred to a tertiary reference center for evaluation for bone marrow transplantation, the most effective curative treatment for young individuals with a compatible donor. This decision is based on the fact that, in patients younger than 40 years, allogeneic bone marrow transplantation from a matched related donor offers higher survival rates and a lower risk of disease relapse[13].

While awaiting transfer, the use of immunosuppressive therapy was considered as a temporary alternative. This treatment consists of the combination of antithymocyte globulin, commonly of equine origin, cyclosporine, and more recently eltrombopag, a thrombopoietin receptor agonist that stimulates the proliferation of residual hematopoietic stem cells. According to Füreder et al.[14], the addition of eltrombopag to standard immunosuppressive therapy significantly increased hematologic response rates, including in patients without a PNH clone.

Deficiency of GPI-anchored proteins leads to an imbalance between cell formation and destruction, resulting in a broad clinical spectrum. The classic presentation includes chronic or episodic intravascular hemolysis, thrombosis at unusual sites (such as hepatic and cerebral veins), nocturnal urinary symptoms, severe fatigue, erectile dysfunction, and progressive bone marrow failure. In many cases, PNH coexists with other hematologic disorders, such as myelodysplastic syndromes or aplastic anemia, which contributes to the clinical complexity of diagnosis and treatment[15].

Bektas[16] demonstrates that PNH may arise in two main contexts: in an apparently healthy individual who spontaneously develops a PNH clone or, more frequently, in patients with a previously compromised hematopoietic environment, such as in aplastic anemia, in which immune-mediated attack against hematopoietic stem cells favors the survival and expansion of mutant *PIG-A*–deficient clones. Füreder *et al.*[14] highlight that immunological selective pressure against normal cells allows GPI-deficient clones to expand, which explains the pathogenic relationship between AA and PNH.

In cases of severe pancytopenia, such as those observed in PNH associated with bone marrow failure, the initial diagnostic approach should include a series of fundamental laboratory tests. Peripheral blood smear evaluation allows morphological assessment of blood cells and may reveal indirect signs of hemolysis, such as spherocytes and polychromasia. Reticulocyte count provides information on bone marrow erythropoietic activity, while serum levels of lactate dehydrogenase, indirect bilirubin, and haptoglobin aid in identifying active hemolysis. Coagulation tests, liver and renal function tests, as well as serum uric acid and calcium measurements, are useful in assessing complications related to cell destruction and the patient's overall condition.

When a primary hematologic disorder is suspected as the cause of pancytopenia, bone marrow aspiration and biopsy are indispensable. These examinations allow evaluation of marrow cellularity, as well as the presence of dysplasia, neoplastic infiltrates, or fibrosis. According to Brodsky[13], the investigation of severe pancytopenia should always consider diseases such as PNH, myelofibrosis, myelodysplastic syndromes, chronic viral infections (such as HIV and hepatitis C), and genetic syndromes such as Fanconi anemia, diagnosed by chromosomal fragility testing.

In the present case, detection of a PNH clone by flow cytometry, associated with severe hematopoietic failure, indicated a poor prognosis for immunosuppressive therapy alone. In such contexts, response to chemotherapy is generally unsatisfactory, especially when there is extensive marrow involvement. For this reason, the patient was referred for evaluation and subsequent allogeneic hematopoietic stem cell transplantation (HSCT),

which represents the only therapeutic option with definitive curative potential. According to Dufour and Pierri[17], HSCT offers the best long-term survival rates in young patients with a matched related donor, especially when performed early after diagnosis.

While awaiting transplantation, the patient could be managed with combined immunosuppressive treatment, including antithymocyte globulin, cyclosporine A, and more recently eltrombopag. The latter is a nonpeptide thrombopoietin receptor agonist (TPO-RA) that stimulates the proliferation of hematopoietic progenitor cells, promoting not only platelet recovery but also increases in neutrophils and erythrocytes. According to Libardi et al.[18], the addition of eltrombopag to standard immunosuppressive therapy resulted in significantly higher hematologic response rates, especially in patients with aplastic anemia without a PNH clone, but it also showed benefit in cases of overlap between PNH and AA.

Finally, therapeutic decision-making in cases of PNH associated with bone marrow failure must take into account patient age, severity of the clinical condition, presence of pathological clones, availability of compatible donors, and the risk of infectious and thrombotic complications. Allogeneic transplantation, although complex and associated with significant risks, offers the greatest chance of disease eradication and complete restoration of hematopoiesis.

The case analyzed highlights the high clinical complexity of the association between aplastic anemia and paroxysmal nocturnal hemoglobinuria, conditions that require meticulous diagnostic investigation, a multidisciplinary approach, and timely therapeutic decision-making. Confirmation of the mutation responsible for impairment of GPI-anchored proteins, together with bone marrow failure, demonstrated the clonal and immune-mediated nature of the disease, reinforcing the need for management based on clinical, hematological, and immunological parameters. It was observed that overlap of PNH with aplastic anemia reduces the effectiveness of conventional immunosuppressive therapies and, in severe cases, makes allogeneic bone marrow transplantation the main option with curative potential. The rapid clinical deterioration, marked by infections, bleeding, and organ failure, underscored the need for rapid access to referral centers and intensive specialized support. Finally, the unfavorable outcome emphasizes the urgency of optimizing care pathways and expanding studies investigating targeted therapies capable of prolonging clinical stability in the pre-transplant period, thereby contributing to improved prognoses in young patients affected by this rare and aggressive association.

AUTHOR CONTRIBUTIONS

LCA performed data collection and analysis, partial manuscript drafting, and final text revision. LLW contributed to study conception and design, data collection, and partial manuscript drafting. GFP contributed to data collection and partial manuscript drafting. LVBL provided supervision, conducted the literature review, and performed critical revision of the manuscript. All authors read and approved the final manuscript version and agree to take responsibility for its content.

CONFLICT OF INTEREST

We wish to confirm that there are no known conflicts of interest associated with this publication and that no significant finan-cial support has influenced its results.

ACKNOWLEDGMENTS

The authors would like to thank Hospital Escola Álvaro Alvim (HEAA) and, in particular, the Medical Records and Statistics Department (SAME) of HEAA for their support and contribution to this study.

DECLARATION REGARDING THE USE OF GENERATIVE AI

The authors declare that generative artificial intelligence tools (such as ChatGPT, Grammarly, Deepseek, etc.) were not used in the manuscript. However, the editorial board made the decision to utilize ChatGPT, an AI language model developed by OpenAI, for the translation of this manuscript from the original language, Portuguese, to English.

REFERENCES

1. Brodsky RA, Schrier SL, Tirnauer J. Clinical manifestations and diagnosis of paroxysmal nocturnal hemoglobinuria [Internet]. Wolters Kluwer; [citado 10 de maio de 2025]. Disponível em: https://www.wolterskluwer.com/en/solutions/uptodate
2. Giudice V, Selleri C. Aplastic anemia: Pathophysiology. Semin Hematol [Internet]. janeiro de 2022 [citado 21 de dezembro de 2025];59(1):13–20. Disponível em: https://linkinghub.elsevier.com/retrieve/pii/S0037196321000640
3. Schoettler ML, Nathan DG. The Pathophysiology of Acquired Aplastic Anemia. Hematol Oncol Clin North Am [Internet]. agosto de 2018 [citado 21 de dezembro de 2025];32(4):581–94. Disponível em: https://linkinghub.elsevier.com/retrieve/pii/S0889858818307044
4. Azevedo MRA de. Hematologia básica: fisiopatologia e diagnóstico laboratorial. Thieme Revinter; 2018.
5. Devalet B, Mullier F, Chatelain B, Dogné J, Chatelain C. Pathophysiology, diagnosis, and treatment of paroxysmal nocturnal hemoglobinuria: a review. Eur J Haematol [Internet]. setembro de 2015 [citado 21 de dezembro de 2025];95(3):190–8. Disponível em: https://onlinelibrary.wiley.com/doi/10.1111/ejh.12543
6. Parker CJ. Update on the diagnosis and management of paroxysmal nocturnal hemoglobinuria. Hematology [Internet]. 2 de dezembro de 2016 [citado 21 de dezembro de 2025];2016(1):208–16. Disponível em: https://ashpublications.org/hematology/article/2016/1/208/21101/Update-on-the-diagnosis-and-management-of
7. Bianca Romeo, Maura Alice Santos Romeo. Hemoglobinúria Paroxística Noturna: Revisão de Literatura. Rev Científica Hosp St Izabel [Internet]. 30 de junho de 2024 [citado 21 de dezembro de 2025];8(2):56–9. Disponível em: https://revistacientifica.hospitalsantaizabel.org.br/index.php/RCHSI/article/view/542
8. Amaral SID. Um olhar sobre a biologia e a clínica das síndromes mielodisplásicas [Internet] [Dissertações de Mestrado]. Universidade de Coimbra; 2012. Disponível em: https://estudogeral.uc.pt/handle/10316/29219
9. Freitas CDFL de. Hemoglobinúria Paroxística Noturna: Revisão de Literatura [Internet]. Universidade do Porto; 2016 [citado 21 de dezembro de 2025]. Disponível em: https://hdl.handle.net/10216/86814
10. Sharma P, Sharma N, Sharma D. A Narrative Review on Fanconi Anemia: Genetic and Diagnostic Considerations. Glob Med Genet [Internet]. setembro de 2022 [citado 21 de dezembro de 2025];09(03):237–41. Disponível em: http://www.thieme-connect.de/DOI/DOI?10.1055/s-0042-1751303
11. Szlendak U, Budziszewska B, Spychalska J, Drozd-Sokołowska J, Patkowska E, Nowak J. Paroxysmal nocturnal hemoglobinuria: advances in the understanding of pathophysiology, diagnosis, and treatment. Pol Arch Intern Med [Internet]. 6 de junho de 2022 [citado 21 de dezembro de 2025]; Disponível em: https://www.mp.pl/paim/issue/article/16271
12. Brodsky RA. How I treat paroxysmal nocturnal hemoglobinuria. Blood [Internet]. 11 de março de 2021 [citado 21 de dezembro de 2025];137(10):1304–9. Disponível em: https://ashpublications.org/blood/article/137/10/1304/475031/How-I-treat-paroxysmal-nocturnal-hemoglobinuria
13. Brodsky RA. Paroxysmal nocturnal hemoglobinuria. Blood [Internet]. 30 de outubro de 2014 [citado 21 de dezembro de 2025];124(18):2804–11. Disponível em: https://ashpublications.org/blood/article/124/18/2804/33385/Paroxysmal-nocturnal-hemoglobinuria
14. Füreder W, Sperr WR, Heibl S, Zebisch A, Pfeilstöcker M, Stefanzl G, et al. Prognostic factors and follow-up parameters in patients with paroxysmal nocturnal hemoglobinuria (PNH): experience of the Austrian PNH network. Ann Hematol [Internet]. outubro de 2020 [citado 21 de dezembro de 2025];99(10):2303–13. Disponível em: https://link.springer.com/10.1007/s00277-020-04214-z
15. Luzzatto L. Recent advances in the pathogenesis and treatment of paroxysmal nocturnal hemoglobinuria. F1000Research [Internet]. 23 de fevereiro de 2016 [citado 21 de dezembro de 2025];5:209. Disponível em: https://f1000research.com/articles/5-209/v1
16. Bektas M, Copley-Merriman C, Khan S, Sarda SP, Shammo JM. Paroxysmal nocturnal hemoglobinuria: role of the complement system, pathogenesis, and pathophysiology. J Manag Care Spec Pharm [Internet]. dezembro de 2020 [citado 21 de dezembro de 2025];26(12-b Suppl):S3–8. Disponível em: https://www.jmcp.org/doi/10.18553/jmcp.2020.26.12-b.s3
17. Dufour C, Pierri F. Modern management of Fanconi anemia. Hematology [Internet]. 9 de dezembro de 2022 [citado 21 de dezembro de 2025];2022(1):649–57. Disponível em: https://ashpublications.org/hematology/article/2022/1/649/493553/Modern-management-of-Fanconi-anemia
18. Libardi G de MS. Hemoglobinúria paroxística noturna e eventos trombóticos: uma revisão integrativa [Internet] [Trabalho de Conclusão de Curso]. [Campus I]: Universidade Federal da Paraíba; 2024 [citado 20 de dezembro de 2025]. Disponível em: https://repositorio.ufpb.br/jspui/bitstream/123456789/34066/1/GMSL14102024.pdf