

## Portal vein thrombosis in a patient with protein S deficiency and PAI-1 4G/5G polymorphism

*Trombose da veia porta em paciente com deficiência de proteína S e polimorfismo PAI-1 4g/5g*

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### ABSTRACT

**Introduction:** Portal vein thrombosis (PVT), characterized by clot formation in the portal venous system, can cause complications such as portal hypertension, gastrointestinal bleeding, and liver dysfunction. Its primary mechanism is a hypercoagulable state, common in cirrhosis, malignancies, and inherited thrombophilias, including prothrombin mutations, factor V Leiden, and protein C, S, and antithrombin deficiencies. The PAI-1 4G/5G polymorphism has been associated with changes in plasminogen activator inhibitor levels, although its relationship with venous thrombosis remains controversial. We report a case of PVT associated with protein S deficiency and PAI-1 polymorphism in a 45-year-old patient, highlighting diagnostic and therapeutic challenges.

**Methods:** Case report and literature review of a 45-year-old patient treated at Hospital Federal Cardoso Fontes. Clinical data, exams, and history were analyzed, with a review of bibliographic databases. **Clinical and Diagnostic Findings:** In March 2021, the patient presented with weakness, vomiting, weight loss, and recurrent urinary infections. CT scan revealed ureteropelvic junction stenosis and thrombosis in the right portal vein branch. Laboratory tests showed protein S deficiency (56%) and PAI-1 4G/5G polymorphism. No mutations were detected in prothrombin, JAK2V617E, or factor V Leiden genes, and serology tests were negative. **Therapeutic Interventions and Results:** Rivaroxaban was initiated, with no new thrombotic events during follow-up, with imaging monitoring. **Conclusion:** This case demonstrates the complex management of PVT associated with inherited thrombophilias. Rivaroxaban proved effective, despite limited data. Further research is needed to guide treatment in patients with multiple risk factors.

**Keywords:** Venous thrombosis; Protein S deficiency; Plasminogen activator inhibitor-1.

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## RESUMO

**Introdução:** A trombose da veia porta (TVP), caracterizada pela formação de coágulos no sistema venoso portal, pode causar complicações graves, como hipertensão portal, sangramento gastrointestinal e disfunção hepática. Seu principal mecanismo é um estado de hipercoagulabilidade, comum em condições como cirrose, malignidades e trombofilias hereditárias, incluindo mutações da protrombina, fator V Leiden e deficiências de proteínas C, S e antitrombina. O polimorfismo PAI-1 4G/5G tem sido associado a alterações nos níveis plasmáticos do inibidor do ativador do plasminogênio, ainda que sua relação com risco aumentado de trombose venosa permaneça controversa. Relata-se caso de TVP associada à deficiência de proteína S e polimorfismo PAI-1 em paciente de 45 anos, destacando desafios diagnósticos e terapêuticos.

**Métodos:** Relato de caso e revisão de literatura sobre paciente de 45 anos atendida no Hospital Federal Cardoso Fontes. Dados clínicos, exames e anamnese foram analisados, com revisão de bases bibliográficas virtuais.

**Achados Clínicos e Diagnósticos:** Em março de 2021, a paciente apresentou fraqueza, vômitos, perda de peso e infecções urinárias recorrentes. Tomografia revelou estenose da junção ureteropielica e trombose no ramo direito da veia porta. Exames laboratoriais indicaram deficiência de proteína S (56%) e polimorfismo PAI-1 4G/5G. Não foram detectadas mutações nos genes da protrombina, JAK2V617F ou fator V Leiden, e sorologias foram negativas. Intervenções Terapêuticas e Resultados: Iniciou-se rivaroxabana, sem novos eventos trombóticos no seguimento ambulatorial, com monitoramento por imagem.

**Conclusão:** O caso demonstra o complexo manejo de TVP associada a trombofilias hereditárias. A rivaroxabana mostrou-se eficaz, apesar de dados limitados. Pesquisas adicionais são necessárias para guiar o tratamento em pacientes com múltiplos fatores de risco.

**Palavras-chave:** Trombose venosa; Deficiência de proteína S; Inibidor 1 de ativador de plasminogênio.

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None.

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## INTRODUCTION

Portal vein thrombosis (PVT) is a rare but potentially serious condition characterized by the formation of blood clots within the portal vein or its branches<sup>1</sup>. This complication can trigger a series of adverse events, notably portal hypertension and gastrointestinal bleeding. Although most commonly associated with liver cirrhosis, PVT can also occur in non-cirrhotic individuals, albeit at a lower incidence<sup>2</sup>.

The main mechanism underlying the development of PVT is a hypercoagulable state, frequently observed in patients with liver cirrhosis, malignancies, acquired prothrombotic disorders, and hereditary inflammatory conditions. In some cases, PVT may be associated with inherited thrombophilic disorders, with increased procoagulant activity, such as prothrombin and factor V Leiden mutations, or hereditary

deficiencies of natural anticoagulants, such as proteins C and S and antithrombin<sup>3</sup>. Recently, studies have focused on plasminogen activator inhibitor-1 (PAI-1), the main inhibitor of tissue-type plasminogen activator, crucial in the regulation of fibrinolysis. A functional deletion/insertion polymorphism (4G/5G) in the PAI-1 gene promoter may be associated with increased plasma levels of the protein, and its direct contribution to thrombotic events has been the subject of debate in recent literature<sup>4</sup>.

A less common but clinically significant development is portal vein thrombosis associated with protein S deficiency, an inherited thrombophilic disorder. Protein S deficiency is a genetic condition that affects the blood coagulation system, predisposing affected individuals to an increased risk of venous thromboembolism. Protein S, produced by the liver, plays a crucial role in modulating the coagulation

process by inhibiting the activation of coagulation factors V and VIII. Protein S deficiency can precipitate an increased tendency to clot formation, thus increasing the risk of venous thrombosis, including portal vein thrombosis<sup>5</sup>.

Furthermore, the clinical presentation of PVT can vary widely among individuals, depending on the acute or chronic nature of the event, as well as the presence of collateral circulation. Symptoms can encompass a wide range of clinical manifestations, from diffuse abdominal discomfort to more severe complications, such as gastrointestinal bleeding and intestinal ischemia<sup>6</sup>.

In summary, portal vein thrombosis associated with protein S deficiency presents a unique diagnostic and therapeutic challenge, requiring a multidisciplinary approach for appropriate management and prevention of serious complications. In this context, a deeper understanding of the underlying pathophysiological mechanisms, as well as diagnostic and treatment strategies, emerges as a key element in optimizing clinical outcomes and improving the quality of life of patients affected by this condition.

## METHODS

This study is a case report, based on a literature review, conducted in accordance with the CARE (CAse REport) guidelines, aiming to provide a detailed description of a rare clinical case of portal vein thrombosis associated with protein S deficiency and the PAI-1 4G/5G polymorphism. The patient, a young woman, was treated at Cardoso Fontes Federal Hospital, where information was collected through history taking, physical examination, and medical record review, including clinical, laboratory, and imaging data. The methodology also included a systematic literature review conducted in the PubMed database using the descriptors "Protein S deficiency," "Portal vein thrombosis," and "PAI-1 4G/5G polymorphism." Opinion articles or those lacking relevant information were excluded.

Given the descriptive nature of the study, no statistical analyses were performed; the methodological approach was based on a critical reading of the selected literature and its correlation with the reported case. In compliance with ethical principles, patient confidentiality and anonymity were guaranteed, ensuring the protection of sensitive data and eliminating any possibility of identification.

The relevance of this study lies in the potential to expand knowledge about portal vein thrombosis in patients with inherited coagulation disorders. Further exploration of this topic can contribute to the development of more robust guidelines, aiding clinical decision-making and improving management strategies for this complex condition.

## RESULTS

A 45-year-old female patient presented in March 2021 with weakness, vomiting, weight loss, and recurrent urinary tract infections. Despite multiple emergency room visits, her symptoms were treated symptomatically

without a definitive diagnosis. Recognizing the importance of further investigation, the patient, who happened to be a healthcare professional, underwent a contrast-enhanced abdominal CT scan, which revealed UPJ stenosis and portal vein thrombosis. Recent clinical findings, combined with radiological imaging, were consistent with acute portal vein thrombosis. Based on these findings, the patient was referred to the hematology and vascular surgery department for a comprehensive evaluation.

Further investigations were performed to determine the underlying cause of the portal vein thrombosis. Her past medical history revealed no abdominal surgeries, episodes of sepsis, or significant childhood medical conditions. Laboratory findings on October 20, 2021, revealed low protein S levels (56%) and normal protein C levels (92%). Protein S levels were measured using an immunological method with free antigen assessment, a technique currently considered the most appropriate due to its lower analytical variability. Immunophenotyping for paroxysmal nocturnal hemoglobinuria (PNH) was within normal limits, and no mutations were detected in the prothrombin (factor II) gene. Furthermore, no mutations were found in the JAK2V617F gene. Viral serologies were negative, and the anti-HBs level was above 1000. No mutation was detected in the factor V Leiden gene. The antinuclear antibody (ANA) test was nonreactive, while antithrombin levels were normal. Other serological tests, including haptoglobin, anticardiolipin IgM and IgG, and anti-beta 2 glycoprotein 1 IgM and IgG, were all within normal ranges.

The patient underwent subsequent imaging studies to assess the progression of thrombosis and evaluate any associated complications. A contrast-enhanced computed tomography scan of the abdomen and pelvis on September 7, 2021, revealed a significant reduction in the caliber of the right branch of the portal vein, suggestive of thrombosis. Additionally, there was a mild reduction in the volume of segments VI and VII and ectasia of the intrahepatic bile ducts within these segments. A bilateral extrarenal pelvic prominence, more prominent on the right side, along with mild calyx dilation and a normal-sized ureter, indicated possible UPJ stenosis. Further evaluation using color Doppler ultrasound of the portal system on September 24, 2021, showed a slight reduction in the volume of the right lobe, likely associated with reduced volumes of segments VI and VII. No dilation of the intrahepatic bile ducts was observed. The patient was initiated on anticoagulant therapy with rivaroxaban, a direct oral anticoagulant, for the management of portal vein thrombosis associated with protein S deficiency. It is important to note that there is limited scientific literature available on the use of rivaroxaban specifically in this context, highlighting the need for further research to evaluate its efficacy and safety in similar cases.

Further investigations during the patient's outpatient follow-up revealed the presence of the PAI-1 4G/5G polymorphism. She continued anticoagulation and follow-up, with no new thrombotic events observed.

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## DISCUSSION

Portal vein thrombosis (PVT) poses a significant clinical challenge, especially when associated with inherited thrombophilias, such as protein S deficiency. The genetic predisposition to thrombotic events can be potentiated by other risk factors, such as the PAI-1 4G/5G polymorphism, which compromises the regulation of fibrinolysis by increasing plasma levels of plasminogen activator inhibitor-1. Although some case-control studies have explored the association between the PAI-1 4G/5G polymorphism and thrombotic events, the findings remain inconclusive, demonstrating the need for further studies in this area<sup>7</sup>.

The diagnosis of PVT in patients without obvious risk factors requires a thorough evaluation, as symptoms are often nonspecific. In this case, the definitive diagnosis was established by contrast-enhanced CT, highlighting the importance of imaging in detecting PVT and differentiating it from other abdominal conditions. Early recognition of this condition is essential to reduce complications such as portal hypertension and liver failure<sup>8</sup>.

In the treatment of PVT, direct oral anticoagulants (DOACs), including rivaroxaban, have emerged as a promising alternative, despite the scarcity of specific studies on their efficacy in patients with inherited thrombophilias. In this case, the choice of rivaroxaban was based on its convenient dosage and favorable safety profile, with good clinical response and absence of thrombotic recurrence during follow-up<sup>9</sup>.

The scarcity of data in the literature on the association between inherited thrombophilias and PVT, as well as on the efficacy of DOACs in this context, reinforces the need for additional studies. A deeper understanding of these factors may allow for more accurate risk stratification and guide individualized therapeutic strategies for better clinical outcomes.

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## CONCLUSION

PVT is a potentially serious condition that requires a comprehensive diagnostic approach and careful therapeutic management, especially when associated with inherited thrombophilias. This case illustrates the complexity of diagnosing and treating PVT in patients with protein S deficiency and PAI-1 4G/5G polymorphism, highlighting the importance of detailed laboratory and imaging evaluations for accurate identification of the condition.

Rivaroxaban administration has been shown to be effective and safe in preventing thrombus progression and preventing thrombotic recurrences, although the literature on its use in this patient profile is still limited.

Therefore, this report emphasizes the need for further research to consolidate evidence-based therapeutic guidelines, improving the management of patients with

multiple thrombotic risk factors and ensuring a more precise and individualized approach.

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## AUTHORS' CONTRIBUTION

We describe contributions to the paper using the taxonomy (CRediT) provided above:

*Conceptualization, Investigation, Methodology, Visualization & Writing – review & editing:* LDR da Silva. *Methodology, Visualization & Writing – review & editing:* I Peryassu; H de C Canheo; VH Moraia; LM Pinto.

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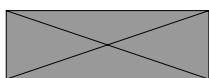
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## REFERENCES

1. Balta S, Altay S, Gurgey A. PAI-1 gene 4G/5G genotype. *J Thromb Haemost.* 2014;12(2):234–40.
2. Fisher NC, Wilde JT, Roper J, Elias E. Deficiency of natural anticoagulant proteins C, S, and antithrombin in portal vein thrombosis: a secondary phenomenon? *Gut.* 2000 Apr;46(4):534-9. doi: 10.1136/gut.46.4.534. Erratum in: *Gut* 2000 Jul;47(1):158.
3. Kocher T, Himmelmann A. Portal vein thrombosis (PVT). *J Hepatol.* 2012;45(3):123–30.
4. Middeldorp S, Nieuwlaat R, Baumann Kreuziger L, Coppens M, Houghton D, James AH, et al. American Society of Hematology 2023 guidelines for management of venous thromboembolism: thrombophilia testing. *Blood Adv.* 2023;7(22):7101–38.
5. Ponziani FR, Zocco MA, Campanale C, Rinninella E, Tortora A, Di Maurizio L, et al. Portal vein thrombosis: Insight into pathophysiology, diagnosis, and treatment. *World J Gastroenterol.* 2010;16(2):143–55.
6. Slavik L, Krcova V, Hlusi A, Prochazkova J, Prochazka M, Ulehlova J, Indrak K. Molecular pathophysiology of thrombotic states and their impact to laboratory diagnostics. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub.* 2009 Mar;153(1):19-25. doi: 10.5507/bp.2009.003. PMID: 19365521.
7. Kollabathula A, Sharma S, Kumar N, Ahluwalia J, Das R, Varma N, et al. Plasminogen activator inhibitor-1 4G/5G promoter polymorphism in adults with splanchnic vein thrombosis: A case-control study. *Indian J Hematol Blood Transfus.* 2022;38(1):169–72.

8. Huisman MV, Klok FA. Current challenges in diagnostic imaging of venous thromboembolism. *Hematol.* 2015;2015(1):202–9.
9. Ameku K, Higa M. Rivaroxaban treatment for warfarin-refractory thrombosis in a patient with hereditary protein S deficiency. *Case Rep Hematol.* 2018;2018:5217301.



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