

Therapeutic plasma exchange: rescue for severe hemolytic anemia associated with Pylera®

Recambio plasmático terapéutico: rescate para la anemia hemolítica grave asociada a Pylera®

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Abstract

We report the case of a 32-year-old male who presented to the emergency department with abdominal pain, weight loss, dark urine and fever, ten days after starting Pylera® for *Helicobacter pylori* eradication. Initial laboratory findings showed hemolytic anemia with a direct antiglobulin test positive for IgG, elevated lactate dehydrogenase, indirect hyperbilirubinemia and undetectable haptoglobin, suggesting drug-induced autoimmune hemolytic anemia. Despite early corticosteroid therapy, the patient rapidly deteriorated, developing severe intravascular hemolysis with marked hemoglobinemia that interfered with immunohematological testing. Urgent plasmapheresis was therefore initiated to remove circulating antibodies and free plasma hemoglobin, allowing completion of the immunohematological study. After two plasma exchanges, a significant clinical and analytical improvement was observed, with progressive normalization of hemolysis parameters. Stool culture later identified *Campylobacter jejuni* infection, which may have contributed to intravascular hemolysis in the context of tetracycline therapy, possibly through a neoantigen-mediated mechanism. Therapeutic plasma exchange played a crucial role in the patient's recovery. To our knowledge, this is the first reported case of hemolytic anemia associated with Pylera® therapy, and it was reported to pharmacovigilance authorities.

Keywords: Autoimmune hemolytic anemia. Drug-induced hemolytic anemia. Tetracycline. Plasma exchange. Intravascular hemolysis. *Campylobacter jejuni*.

Resumen

Se presenta el caso de un varón de 32 años que acude a urgencias por dolor abdominal, coluria y fiebre diez días después de iniciar tratamiento con Pylera® para la erradicación de *Helicobacter pylori*. En la evaluación inicial se objetivó anemia hemolítica con test de Coombs directo positivo para IgG, aumento de lactato deshidrogenasa, hiperbilirrubinemia indirecta y haptoglobina indetectable, orientando hacia una anemia hemolítica autoinmune inducida por fármacos. A pesar del inicio precoz de corticoterapia, el paciente presentó rápido deterioro clínico y analítico, desarrollando hemólisis intravascular grave con hemoglobinemia que interfería en el estudio inmunohematológico. Ante esta situación, se decidió realizar un recambio plasmático urgente para la eliminación del anticuerpo circulante y de la hemoglobina libre en plasma, lo que permitió completar el estudio inmunohematológico. Tras dos recambios plasmáticos se observó mejoría analítica, con normalización progresiva de los parámetros de hemólisis. El coprocultivo resultó positivo para *Campylobacter jejuni*, infección que probablemente contribuyó a la hemólisis intravascular en el contexto de tratamiento con tetraciclina, mediante mecanismo de neoantígeno.

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La realización del recambio plasmático fue determinante para la recuperación del paciente. Se trata del primer caso descrito de anemia hemolítica asociada al tratamiento con Pylera®, que fue notificado al sistema de farmacovigilancia.

Palabras clave: Anemia hemolítica autoinmune. Anemia hemolítica inducida por fármacos. Tetraciclina. Recambio plasmático. Hemólisis intravascular. *Campylobacter jejuni*.

Introduction

Autoimmune hemolytic anemia (AIHA) is a rare condition characterized by autoantibody-mediated destruction of red blood cells.¹⁻³ Among its secondary forms, drug-induced hemolytic anemia is a rare but potentially serious cause, with an estimated incidence of 1 case per 100,000 patients.^{4,5}

The mechanisms involved include the formation of drug-dependent antibodies, through hapten-type or neoantigen mechanisms, and drug-independent mechanisms, which may trigger both intra- and extravascular hemolysis.^{5,6}

Helicobacter pylori infection causes chronic inflammation of the gastric mucosa and is associated with multiple GI diseases.¹ Pylera® is a combination therapy used for the eradication of *H. pylori* that contains bismuth subcitrate potassium, metronidazole, and tetracycline hydrochloride. Although it has a favorable safety profile, severe hematologic reactions associated with some of its components have been reported exceptionally.⁷⁻¹⁰

We report a case of severe hemolytic anemia in this setting, highlighting the role of therapeutic plasma exchange.

Case report

Reason for consultation: general malaise and abdominal pain.

Past medical history

A 32-year-old man from Morocco who had been living in Spain for 3 years presented with a 1-month history of severe asthenia, abdominal pain, and anorexia. After initial laboratory testing showed no abnormalities other than a positive stool antigen test for *H. pylori*, treatment with Pylera® and omeprazole was initiated for 14 days because of epigastric pain. Ten days later, he presented to the emergency department because of worsening symptoms.

Personal history: no known drug allergies. He worked at a poultry slaughterhouse. There was no relevant medical, surgical, transfusion, or family history. He was

not on any regular treatment other than eradication therapy.

Current illness: epigastric pain, severe asthenia, weight loss of 9 kg, nausea, vomiting, diarrhea with melena, dark urine, and fever of up to 38 °C, without pruritus or skin lesions.

Physical examination: fair general condition, skin pallor, and conjunctival jaundice. Eupneic at rest. No lymphadenopathy. Cardiopulmonary auscultation revealed no pathologic findings. The abdomen was soft and depressible, with mild tenderness on palpation of the epigastrium and palpable splenomegaly of 1 cm. No edema was observed in the extremities.

Additional tests

At admission, laboratory tests showed normocytic normochromic anemia with evidence of hemolysis (Table 1). The peripheral blood smear showed poikilocytosis with a moderate number of stomatocytes and a small number of spherocytes, without schistocytes. Biochemical testing was normal except for elevated lactate dehydrogenase, indirect hyperbilirubinemia, and undetectable haptoglobin. Gastroscopy revealed chronic gastritis associated with *H. pylori*.

Clinical course and treatment

The patient was admitted to the Hematology Department with suspected drug-induced AIHA. Pylera® was discontinued, and treatment with corticosteroids at a dose of 1 mg/kg and folic acid supplementation was initiated. Twenty-four hours after admission, laboratory parameters worsened (Table 2), with overt intravascular hemolysis (Fig. 1) and hemoglobinemia that interfered with the immunohematologic workup. The Donath-Landsteiner test was negative.

Severe hemoglobinemia prevented the adequate performance of key immunohematologic tests, including ABO/Rh typing, irregular antibody screening, and compatibility testing, because of the optical and serologic interference caused by the markedly hemolyzed plasma.

Given the severity of the condition, emergency plasma exchange was performed (Fig. 2) in the

Table 1. Emergency complete blood count results

Parameter	Value
Hemoglobin (g/dL)	9.3
MCV (fL)	93.9
MCH (pg)	34.6
MCHC (g/dL)	36.8
Reticulocytes (%)	1.7
Leukocytes ($\times 10^3/\mu\text{L}$)	7.8
Platelets ($\times 10^3/\mu\text{L}$)	156
Haptoglobin (%)	Undetectable

MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin concentration.

Table 2. Complete blood count 24 hours after admission

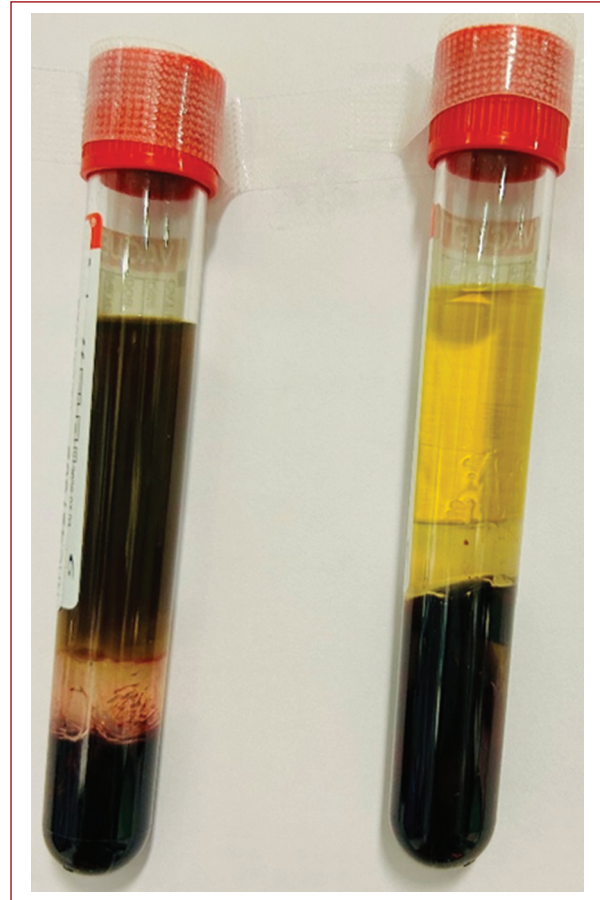
Parameter	Value
Hemoglobin (g/dL)	6.7
MCV (fL)	91.7
MCH (pg)	34.6
MCHC (g/dL)	36.8
Reticulocytes (%)	9.2
Leukocytes ($\times 10^3/\mu\text{L}$)	13.9
Platelets ($\times 10^3/\mu\text{L}$)	222
LDH (IU/L)	1,339
Total bilirubin (mg/dL)	4.12
Indirect bilirubin (mg/dL)	3.4

MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin concentration; LDH: lactate dehydrogenase.

Intensive Care Unit, exchanging approximately 1–1.5 plasma volumes per session and using 5% albumin as the replacement fluid. The indication was based on the need to rapidly remove circulating antibodies and free hemoglobin, which were responsible for both hemolysis and analytical interference.

After plasma exchange, these tests could be repeated under appropriate preanalytical conditions. The direct antiglobulin test was positive for IgG and negative for C3d, and the compatibility study was completed.

A second plasma exchange was performed, after which a clear clinical improvement and progressive normalization of hemolysis parameters were observed (Table 3).

**Figure 1.** Overt intravascular hemolysis observed in the tube.

Subsequently, stool culture tested positive for *Campylobacter jejuni*, and oral azithromycin was initiated for 7 days.

The patient received 3 units of packed red blood cells because of symptomatic anemia with a hemoglobin concentration of 6.7 g/dL. A restrictive transfusion strategy was followed, taking into consideration the theoretical risk of hyperhemolysis in the setting of AIHA.

Discussion

From a diagnostic perspective, this case illustrates the limitations of immunohematologic testing in the presence of massive intravascular hemolysis. Hemoglobinemia initially interfered with the performance of essential tests, which could only be completed after plasma exchange. This procedure enabled not only clinical stabilization but also the acquisition of reliable results, highlighting its dual diagnostic and therapeutic role.

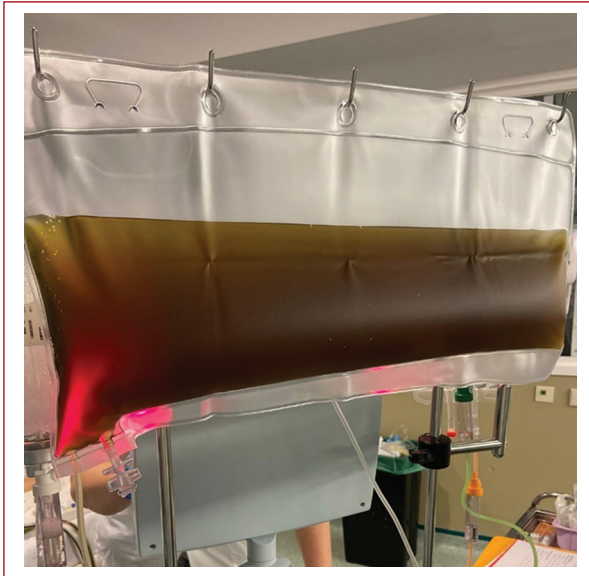


Figura 2. Patient plasma during the first plasma exchange.

Table 3. Hemolysis parameters normalized after two plasma exchanges

Parameters	Value
Hemoglobin (g/dL)	8.8
LDH (IU/L)	373
Total bilirubin (mg/dL)	2.6
Indirect bilirubin (mg/dL)	1.2
Haptoglobin (%)	20

LDH: lactate dehydrogenase.

Drug-induced hemolytic anemia is a rare and probably underdiagnosed form of this condition.⁵ Antibody generation may occur through drug-dependent or drug-independent mechanisms.⁵ In the former, the antibody may act through a hapten mechanism or through the formation of a neoantigen, triggering intravascular hemolysis.

Specific testing for drug-dependent antibodies was not performed because of its technical complexity and limited availability in routine clinical practice. Therefore, although the temporal relationship with Pylera[®] suggests a possible drug-induced origin, it is not possible to establish with certainty which component of the combination therapy was responsible. Tetracycline has previously been associated with hemolytic anemia, generally through drug-dependent mechanisms.⁷⁻¹⁰

Concomitantly, the patient had *C. jejuni* infection, a pathogen capable of inducing immune activation phenomena that may have contributed to worsening the hemolytic episode.¹¹ However, a direct causal relationship cannot be established.

Treatment of drug-induced hemolytic anemia is based on withdrawal of the suspected medication.^{1,3} Corticosteroids are commonly used, although their benefit has not been clearly established.^{1,3}

In severe cases, plasma exchange allows the rapid removal of circulating antibodies and free hemoglobin and may therefore constitute an effective therapeutic tool.⁶ In patients with progressive clinical deterioration, it should be considered early because of its immediate effect compared with the delayed therapeutic effect of corticosteroids.⁶

Interest of the case

To the best of the available knowledge in the literature, this is the first reported case of severe hemolytic anemia associated with Pylera[®] treatment. The case also highlights the role of plasma exchange as both a diagnostic and therapeutic tool in severe hemolysis, particularly when progressive clinical deterioration and limitations in the immunohematologic workup are present.

From a diagnostic perspective, the case illustrates the difficulties of immunohematologic testing in severe intravascular hemolysis with marked hemoglobinemia, which caused considerable analytical interference. The markedly hemolyzed plasma hindered interpretation of the immunohematologic tests. Plasma exchange enabled the removal of free hemoglobin and circulating antibodies, allowing the workup to be repeated under appropriate preanalytical conditions and enabling correct interpretation of the direct antiglobulin test and compatibility studies.

The case demonstrates the role of plasma exchange as a treatment strategy in patients with progressive clinical deterioration despite the treatment initially administered. The patient's clinical course supports the usefulness of therapeutic plasma exchange as a potentially life-saving intervention. Finally, the case provides a relevant educational message by emphasizing the importance of a thorough medical history and assessment of the epidemiologic context. In patients with persistent gastrointestinal symptoms and occupational exposure to poultry, prior complementary microbiologic testing, such as stool culture, may be essential for optimizing the diagnostic and therapeutic approach.

Conclusions

This case shows that Pylera® may exceptionally be associated with severe hemolytic anemia. Concomitant *Campylobacter jejuni* infection may act as an aggravating factor.

In cases of severe hemolysis with progressive clinical deterioration, plasma exchange should be considered early because of its immediate effect compared with the delayed therapeutic effect of corticosteroids.

Funding

None declared.

Conflicts of interest

None declared.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The study does not involve personal data,

medical records, or human biological samples and therefore does not require ethical approval. The SAGER guidelines do not apply.

Declaration on the use of artificial intelligence. The authors declare that no form of generative artificial intelligence was used in the writing or creation of content for this manuscript.

References

1. Sanz MA, editor. Hematología en pregrado. 5ª ed. Madrid: Sociedad Española de Hematología y Hemoterapia; 2024.
2. Hill QA, Stamps R, Massey E, Grainger JD, Provan D, Hill A. The diagnosis and management of primary autoimmune haemolytic anaemia. *Br J Haematol*. 2017;176(3):395-411.
3. Barcellini W, Fattizzo B. The changing landscape of autoimmune hemolytic anemia. *Front Immunol*. 2020;11:946.
4. Berentsen S. New insights in the pathogenesis and therapy of autoimmune hemolytic anemia. *Front Immunol*. 2021;12:748541.
5. Garratty G. Immune hemolytic anemia associated with drug therapy. *Blood Rev*. 2010;24(4-5):143-50.
6. Schwartz J, Padmanabhan A, Aqui N, Balogun RA, Connelly-Smith L, Delaney M, et al. Guidelines on the use of therapeutic apheresis in clinical practice-evidence-based approach from the Writing Committee of the American Society for Apheresis: the eighth special issue. *J Clin Apher*. 2019;34(3):171-354.
7. Simpson MB, Pryzbylik J, Innis B, Denham MA. Hemolytic anemia associated with tetracycline therapy. *N Engl J Med*. 1985;312:840-2.
8. Mazza JJ, Kryda MD. Tetracycline-induced hemolytic anemia. *J Am Acad Dermatol*. 1980;2:506-8.
9. Wenz B, Klein RL, Lalezari P. Tetracycline-induced immune hemolytic anemia. *Transfusion*. 1974;14:265-69.
10. Takahashi R, Tsukada T, Hasegawa M. Hemolytic anemia induced by tetracycline. *Keio J Med*. 1963;12:161-8.
11. Damani NN, Humphrey CA, Bell B. Hemolytic anemia in *Campylobacter* enteritis. *J Infect*. 1993;26:109-10.