Journal of Pregnancy and Child Health
Zinno F, et al. J Preg Child Health 7: 128.
www.doi.org/10.29011/JPCH-124.100028
www.gavinpublishers.com

OPEN ACCESS
GAVIN PUBLISHERS

Case Report

Integrated Clinical-Laboratory Pathway in Rapid Differential Diagnosis of Thrombotic Microangiopathies: A Case Report

Francesco Zinno[1#], Livia Bernardi[2#], Dario Terzi[1], Elvira Stamile[2], Francesca Sinopoli[2-5], Luigi Carpino[3], Francesca Greco[4], Domenico Sperlì[3], Stefania Catalano[2-5]*

[1]Department of Immunohematology and Transfusion Medicine, Annunziata Hospital, Italy

[2]Department of Laboratory Medicine, Annunziata Hospital, Italy

[3]Department of Pediatrics, Annunziata Hospital, Italy

[4]Department of Microbiology and Virology, Annunziata Hospital, Italy

[5]Department of Pharmacy, Health and Nutritional Science, University of Calabria, Italy

[#]These authors contributed equally to this work.

***Corresponding author:** Stefania Catalano, Department of Laboratory Medicine, Annunziata Hospital, Via Migliori, 87100 Cosenza, (CS), Italy

Citation: Zinno F, Bernardi L, Terzi D, Stamile E, Sinopoli F, et al. (2026) Integrated Clinical-Laboratory Pathway in Rapid Differential Diagnosis of Thrombotic Microangiopathies: A Case Report. J Preg Child Health 7: 128. https://doi.org/10.29011/2998-2405.100028.

Received Date: March 13, 2026; **Accepted Date:** March 23, 2026; **Published Date:** March 26, 2026

Background

Thrombotic microangiopathies (TMAs) are a rare heterogeneous group of diseases, affecting both children and adults, characterized by microangiopathic hemolysis, thrombocytopenia, and thrombus formation leading to tissue damage. The incidence in children is estimated to be ~3.0 cases/106 population per year [1]. Endothelial disorders are present, with thrombi formation enriched by platelets and fibrin in small blood vessels [2]. When thrombi form, microangiopathy leads to secondary consumption of platelets and mechanical hemolysis, due to erythrocyte disruption, causing the typical manifestations of TMA, thrombocytopenia and microangiopathic hemolytic anemia (MAHA), marked by reticulocytosis, negative Coombs test, schistocytes in blood smear, low haptoglobin, unconjugated hyperbilirubinemia and increased lactate dehydrogenase (LDH) [3]. Primary TMA forms are classified as thrombotic thrombocytopenic purpura (TTP, or Moscowitz's disease), more common in adults, and hemolytic uremic syndrome (HUS), more common in children. TTP often presents with neurologic symptoms, abdominal pain (35%-39%), proteinuria, hematuria, but rarely severe acute kidney injury (AKI) [4]. TTP is caused by deficiency of plasma ADAMTS-13, a specific von Willebrand factor (VWF)-cleavage protease, which leads to accumulation of large VWF multimers, resulting in occlusive microvascular thrombi [4]. TTP occurs either congenitally (cTTP, autosomal recessive), or as an acquired event (aTTP), due to development of anti-ADAMTS13 antibodies [5]. When the predominant feature at presentation is AKI, the disorder can be classified as HUS. The most common form is typical-HUS (T-HUS) associated with bloody diarrhea, due to a Shiga toxin-producing enteropathogenic bacterial infection (especially Escherichia coli, STEC-HUS). Approximately 50% these cases present AKI requiring kidney replacement therapy [6], which may evolve into chronic kidney disease in 20%-30% [7]. Atypical HUS (aHUS) occurs less frequently, and it is caused by dysregulation of the alternative complement pathway, of either acquired or genetic origin [8]. Rapid differential diagnosis of TMAs is pivotal to allow prompt lifesaving therapy and often distinguishes between TTP and HUS. Therapeutic plasma exchange (TPE) remains highly

effective treatment in aTTP (in conjunction with corticosteroids, caplacizumab, and rituximab), whereas STEC-HUS may require supportive care, including hydration and dialysis, to preserve renal function. Delays in diagnosis and treatment can lead to irreversible organ damage or death. Differential diagnosis is difficult, due to the significant overlap in the clinical presentation of TTP and HUS [2]. Diagnosis is performed by integrating clinical data and time-consuming, costly laboratory tests. ADAMTS13 enzyme activity levels ≤10% are considered diagnostic for TTP and the activity test is preceded by a rapid and inexpensive clinical assessment tool for predicting severe ADAMTS13 deficiency (plasmic score). The plasmic score helps clinicians distinguish between TTP and other conditions with similar symptoms, even without the ADAMTS13 test results. aHUS is a diagnosis "per exclusion" and STEC-HUS is the first diagnosis to exclude [2].

Case Presentation

A 1-year-old girl, presenting with previous fever (3 days), diarrhea (20 days), vomiting (5 days), associated with asthenia, in absence of critical kidney injury, was admitted to the Pediatric Emergency Department of "Annunziata" Hospital, Cosenza, (CS), Italy. Her medical and family history was unremarkable, and all vaccinations were up to date. Physical examination revealed no fever, skin pallor, periorbital edema, clear chest, tender abdomen, negative neurological examination, blood pressure 112/60 mmHg, pulse 130 beats/min, saturation 99%, weight 9.6 kg. A stool culture from three days earlier was negative. Laboratory tests showed normal white blood cell count, severe anemia, thrombocytopenia, and high reticulocyte, indirect bilirubin, LDH, reduced haptoglobin levels, creatinine <2 mg/dL; coagulation parameters were normal. Proteinuria, hematuria and glycosuria were present. Peripheral blood smear demonstrated a high number of schistocytes (13%) (Table 1). Coombs tests were negative. TTP diagnosis was suspected and the plasmic score for TTP risk prediction was calculated as 6 (high risk) (Table 2). ADAMTS13 activity was measured within 25 minutes as >10% using the Technofluor ADAMTS13 Activity assay (Technoclone), excluding the TTP diagnosis. Therefore, further investigations were requested. The following day, polymerase chain reaction analysis of a stool sample collected upon admission detected virulence genes encoding Shiga toxins 1 and 2. Consequently, a presumptive diagnosis of STEC-HUS was made. C3 and C4 plasma levels were normal. Blood culture was negative. Diuretic therapy was administered, along with red blood cell (RBC) transfusions and eculizumab (300 mg, days 1 and 8). Dialysis was not required. Successively, the patient received diuretic and antibiotic therapy, and two more RBC transfusions, until normalization of platelet count, hemoglobin, creatinine and LDH values (Table 1).

	Laboratory testing	At admission (day 0)	At discharge (day 15)	Follow-up (day 22)	Normal value or range
Hematological	Hb (g/dL)	5.2	8.8	8.9	12–16 (g/dL)
	PLT count (*10^6/mL)	47	274	351	150-450 (*10^6/mL)
	WBC (*10^6/mL)	9.9	7.4	6.7	4-11 (*10^6/mL)
	Schistocytes (%)	13%	<0.5%	<0.5%	<0.5%
	Haptoglobin (mg/dL)	0.6	20	30	30-200 (mg/dL)
	LDH (U/L)	1207	469	424	50-248 (U/L)
Kidney	Creatinine (mg/dL)	1.67	0.34	0.34	0.55-1.18 (mg/dL)
	Urine test	Proteinuria, hematuria, glycosuria	Mild hematuria	Mild hematuria	/
Liver	AST (U/L)	63	40	53	5-50 (U/L)
	ALT (U/L)	24	33	27	5-50 (U/L)
	GGT (U/L)	5	12	11	7-55 (U/L)
	Total bilirubin (mg/dL)	1.57	0.41	0.52	0.1-1.2 (mg/dL)

Abbreviations: Hb, hemoglobin; PLT, platelets; WBC, white blood cells; LDH, lactate dehydrogenase; ALT, alanine transaminase; AST, aspartate transaminase; GGT, gamma-glutamyl transferase.

Table 1: Biochemical parameters at admission, during hospitalization and follow up. Laboratory reference ranges are shown for comparison.

Clinical features and laboratory results	Patient	Points
Platelet count <30 × 10^6/mL	47 *10^6/mL	0
Hemolysis (indirect bilirubin > 2 mg/dL, reticulocyte count > 2.5%, or undetectable haptoglobin)	Reticulocyte count 4.6%	1
No active cancer in the previous year	No	1
No history of solid organ or stem cell transplant	No	1
MCV < 90 fL	57.7 fL	1
INR < 1.5	1	1
Creatinine < 2 mg/dL	1.93 mg/dL	1
Total score: 6 (High risk of severe ADAMTS13 deficiency)		

Abbreviations: MCV, mean corpuscular volume; INR, international normalized ratio.

Table 2: Plasmic score calculation for TTP risk prediction in our patient.

Discussion

We report the case of a 1-year-old girl presenting with persisting fever, abdominal pain, gastrointestinal symptoms associated with asthenia, severe anemia, and thrombocytopenia. STEC-HUS was diagnosed. Therapy comprised diuretic treatment, RBC transfusions, and eculizumab. Dialysis was not required. The outcome was favorable, with no relapse, critical AKI or death. In our case, establishment of the correct diagnosis was fundamental for administering correct and life-saving therapy. In fact, differential diagnosis among TMA syndromes reported in children (HUS, aHUS, and TTP) is challenging, due to overlapping of clinical and biological features.

For patients presenting with MAHA and thrombocytopenia, the predictive plasmic score for TTP, using laboratory data, can guide empirical treatment initiation for TTP before ADAMTS13 results are accessible. When ADAMTS13 test results are unavailable, therapy should be initiated based on a high plasmic score (e.g., 6–7). This score indicates a high probability of severe ADAMTS13 deficiency and justifies starting immediate treatment with TPE and steroids, to avoid detrimental outcomes, as failure to treat promptly can be fatal [9]. The time required to obtain the results of the biological investigations (usually 48 h) should not delay plasma therapy. In our case, the negative Coombs tests and the calculation of the plasmic score (6, high-risk), in a context of severe hemolysis and lack of critical renal dysfunction, pointed toward a probable diagnosis of TTP, with TPE to be started as soon as possible. ADAMTS13 is the unique biological marker able to differentiate TTP from other TMA syndromes. Unfortunately, ADAMTS13 testing is not available in all centers, and establishment of the correct diagnosis is challenging in children and is of primary importance, given that treatments for these disorders are different and not all benefit from TPE. In our case, TPE would have been inadequate. Instead, diuretic therapy, along with RBC transfusions and eculizumab, proved effective.

The administration of eculizumab, a monoclonal antibody, which targets complement protein C5, used in aHUS therapy, despite the absence of established clinical guidelines, may be considered appropriate in STEC-HUS cases as rescue therapy [10]. In the presence of life-threatening conditions, eculizumab represents a plausible therapeutic approach at the onset of HUS, given the current absence of other treatments [10]. The early use of eculizumab may have played an important role in the disease remission of our patient, avoiding dialysis and severe AKI.

Conclusions

This case highlights the importance of rapid ADAMTS13 activity testing: 1) to shorten diagnosis time, differentiating TTP from other TMAs; 2) to optimize therapeutic outcomes with administration of the lifesaving therapy in potentially fatal pathologies; and 3) to avoid ineffective and expensive TPE sessions, given the limited availability of blood products in clinical practice. It is hoped that this laboratory test will become increasingly available for use in authorized centers, accompanied by the potential update of all international and local TTP guidelines indicating TPE only in presence of a positive ADAMTS13 activity.

Author Contributions

LB, DT, ES, FS, and LC collected the data. FZ and LB drafted the manuscript. FZ, SC, DS, and FG revised the manuscript and provide critical feedback. All authors have read and agreed to the published version of the manuscript.

Acknowledgments

We thank all blood donors for their invaluable help in saving

numerous lives. We would like to thank Anna G. Recchia (www.agreedbiomedica.com) for language editing.

Ethic statements

This study was performed in accordance with the Declaration of Helsinki.

References

1. Joly BS, Zheng XL, Veyradier A (2018) Understanding thrombotic microangiopathies in children. Intensive Care Med 44(9): 1536-1538.
2. Sheerin NS, Glover E (2019) Haemolytic uremic syndrome: diagnosis and management. F1000Res 8:F1000 Faculty Rev-1690.
3. Brocklebank V, Wood KM, Kavanagh D (2018) Thrombotic microangiopathy and the kidney. Clin J Am Soc Nephrol 13(2): 300-317.
4. George JN, Nester CM (2014) Syndromes of thrombotic microangiopathy. N Engl J Med 371(7): 654-66.
5. Zheng X, Chung D, Takayama TK, Majerus EM, Sadler JE, et al. (2001) Structure of von Willebrand factor-cleaving protease (ADAMTS13), a metalloprotease involved in thrombotic thrombocytopenic purpura. J Biol Chem 276(44): 41059410-63.
6. Mody RK, Gu W, Griffin PM, Jones TF, Rounds J, et al. (2015) Postdiarrheal hemolytic uremic syndrome in United States children: clinical spectrum and predictors of in-hospital death. J Pediatr 166(4): 1022-1029.
7. Spinale JM, Ruebner RL, Copelovitch L, Kaplan BS (2013) Long-term outcomes of Shiga toxin hemolytic uremic syndrome. Pediatr Nephrol 28(11): 2097-2105.
8. Arnold DM, Patriquin CJ, Nazy I (2017) Thrombotic microangiopathies: a general approach to diagnosis and management. CMAJ 189(4): E153-159.
9. Linee Guida (2021) Società Italiana di Ematologia per la Porpora Trombotica Trombocitopenica, March 2021.
10. Mortari G, Bigatti C, Gaffi GP, Lionetti B, Angeletti A, et al. (2025) Shiga toxin-producing Escherichia coli infection as a precipitating factor for atypical hemolytic-uremic syndrome. Pediatr Nephrol 40(2): 449-461.