

When COVID-19 Coagulopathy Masks Thrombotic Thrombocytopenic Purpura: An Atypical Presentation with Multifocal Cerebral Infarction - A Case Report

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Case Report

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Abstract

This case demonstrates that when COVID-19 coagulopathy, septic shock, and thrombotic microangiopathy overlap, the classic signs of thrombotic thrombocytopenic purpura (TTP) may be obscured-yet timely recognition and treatment are lifesaving. Despite the patient's active COVID-19 infection, multifocal cerebral infarctions, thrombocytopenia, microangiopathic hemolytic anemia (elevated LDH, low haptoglobin, reticulocytosis), and near-normal coagulation studies (PT/INR) pointed away from disseminated intravascular coagulation and toward TTP. Notably, the peripheral smear showed only slight schistocytosis, a potential pitfall that should not delay suspicion. The critical "cure" was confirming severe ADAMTS13 deficiency (0.013%) and promptly initiating therapeutic plasma exchange, corticosteroids, and supportive care. Even after five days of plasma exchange, hemoglobin and platelets improved and LDH declined, allowing recovery from respiratory failure and renal failure requiring dialysis. The key lessons are: (1) Do not rely solely on schistocyte count to exclude TTP in critically ill COVID-19 patients; (2) near-normal PT/INR with unexplained hemolysis and thrombocytopenia should raise TTP suspicion; (3) while awaiting ADAMTS13 results, early plasma exchange can be life-saving; and (4) COVID-19-associated hypercoagulability and TTP can coexist, and the former does not rule out the latter. Delayed access to ADAMTS13 testing is a common barrier, but high clinical suspicion and prompt empiric plasma exchange remain the definitive "cure" for preventing irreversible neurologic injury and death.

Introduction

Thrombotic thrombocytopenic purpura (TTP) is a rare, life threatening thrombotic microangiopathy caused by severe ADAMTS13 deficiency, leading to platelet-rich microthrombi, microangiopathic hemolytic anemia (MAHA), and thrombocytopenia [1]. Early diagnosis is critical because delay in initiating therapeutic plasma exchange (TPE) carries high mortality [2]. However, the classic pentad of fever, renal impairment, neurologic changes, thrombocytopenia, and MAHA is often incomplete at presentation, and overlapping conditions can obscure the diagnosis. The COVID-19 pandemic introduced a new diagnostic challenge: SARS-CoV-2 infection itself induces endothelial dysfunction, elevated von Willebrand factor, and a hypercoagulable state that can clinically mimic TTP sometimes termed "COVID-19 TTP-like syndrome [3]." Differentiating true immune-mediated TTP from COVID-19-associated coagulopathy is essential, as the latter does not respond to plasma exchange [4]. Here, we present a case of a 65-year-old woman with active COVID-19 infection who developed multifocal cerebral and cerebellar infarctions [5], thrombocytopenia, and MAHA with only slight schistocytosis on peripheral smear [6]. The presence of near-normal coagulation studies and progressive multiorgan failure raised suspicion for superimposed TTP, which was confirmed by severely reduced ADAMTS13 activity [7]. This case highlights the diagnostic pitfalls of relying on peripheral smear alone, the importance of maintaining a high index of suspicion for TTP in critically ill COVID-19 patients, and the potential consequences of delayed confirmatory testing [8].

Case Presentation

A 65-year-old woman with chronic kidney disease stage 3B, type 2 diabetes mellitus, hypertension, hyperlipidemia, and gout presented with anemia identified on outpatient laboratory testing and progressive generalized weakness associated with recurrent falls. She lived alone and had become largely bedridden prior to admission.

On presentation, she was hypertensive and tested positive for COVID-19 infection. Initial laboratory evaluation revealed acute kidney injury (creatinine 5.1 mg/dL; baseline approximately 2 mg/dL), leukocytosis, anemia, and thrombocytopenia. Troponin was markedly elevated at 14,155 ng/L with a subsequent downtrending pattern, while lactate dehydrogenase (LDH) was elevated. Electrocardiography demonstrated ischemic changes, and chest radiography showed cardiomegaly with mild pulmonary vascular congestion. Serial laboratory trends before, during, and after plasma exchange therapy are summarized in Table 1.

Table 1
Serial Laboratory Findings Before, During, and After Plasma Exchange TherapyLDH, lactate dehydrogenase; CRP, C-reactive protein. Reference ranges: hemoglobin 12–16 g/dL; platelet count 150–450 ×10³/μL; creatinine 0.6–1.2 mg/dL; LDH 100–220 U/L; haptoglobin 30–200 mg/dL; reticulocyte 0.5–2.5%; D-dimer < 500 ng/mL; troponin < 14 ng/L; CRP < 5 mg/L.

Laboratory	Value On admission	Before plasmaphoresis	Day 3 of plasmaphoresis	After 4 days of plasmaphoresis	Before Discharge
Hemoglobin	6.8	7.2	8.5	8.5	7.7
Platelet count	203	66	114	129	156
Creatinine	5.10	4.8	4.3	2.7	4.2
LDH	841	906	297	250	199

Neuroimaging revealed multifocal infarctions involving the bilateral frontal, parietal, and occipital lobes, as well as the left cerebellum. Magnetic resonance imaging confirmed multiple acute and subacute infarcts involving both cerebral and cerebellar hemispheres without evidence of intracranial hemorrhage [Figure1,2].

FIGURE 2

Axial T2-weighted magnetic resonance imaging (MRI) of the brain showing a hyperintense cortical-subcortical lesion in the occipital lobe (arrow), consistent with cerebral infarction.

Further evaluation demonstrated reticulocytosis (9.1%), uptrending LDH (peak 906 U/L), low haptoglobin (< 30 mg/dL), and few schistocytes on peripheral smear. D-dimer was elevated at 2,500 ng/mL. Coagulation studies on admission showed a PT of 14 seconds and INR of 1.3, findings that were not

suggestive of overt disseminated intravascular coagulation (DIC). Additional laboratory findings supporting microangiopathic hemolysis and systemic inflammation are summarized in Table 2.

Table 2
Additional Laboratory Findings
CRP, C-reactive protein. Troponin was markedly elevated at 14,155 ng/L on admission, with a subsequent downtrending pattern to > 12,000 ng/L (value reported as exceeding the upper limit of detection). Reference ranges: haptoglobin 30–200 mg/dL; reticulocyte 0.5–2.5%; D-dimer < 500 ng/mL; troponin < 14 ng/L; CRP < 5 mg/L.

Laboratory	Value
Heptoglobin	< 30
Reticulocyte%	9.1
D-Dimer	2500
Troponin	14155 > 12000
CRP	9.5

In the setting of active COVID-19 infection with associated inflammatory and hypercoagulable features, the initial differential diagnosis remained broad and included COVID-19-associated coagulopathy, septic shock-related multiorgan dysfunction, and thrombotic microangiopathy. Initial management included dexamethasone, antiviral therapy, and empiric antibiotics. However, the combination of thrombocytopenia, microangiopathic hemolytic anemia, elevated LDH, neurologic infarctions, and slight schistocytes on peripheral smear [Figure3] raised concern for superimposed thrombotic thrombocytopenic purpura (TTP). ADAMTS13 testing was therefore obtained.

Her clinical course rapidly deteriorated with hypotension concerning septic shock, requiring transfer to the intensive care unit, intravenous fluid resuscitation, and vasopressor support. On the same day, she developed acute hypoxic respiratory failure necessitating intubation and mechanical ventilation.

Echocardiography demonstrated a left ventricular ejection fraction of 55% with hypokinesis of the distal anterolateral wall and apex. Progressive renal failure required initiation of hemodialysis.

Because ADAMTS13 testing was performed at an outside reference laboratory rather than on-site, confirmatory results were delayed compared with availability at tertiary care centers. ADAMTS13 activity subsequently returned markedly reduced at 0.013, confirming severe acquired TTP. Plasma exchange therapy was initiated and continued for five days, resulting in improvement in hemoglobin and platelet counts with a corresponding decline in LDH levels.

Esophagogastroduodenoscopy performed for evaluation of anemia demonstrated gastritis, and the patient was treated with proton pump inhibitor therapy and sucralfate.

After a two-week hospitalization, the patient was successfully weaned from mechanical ventilation, transitioned to tracheostomy care, and discharged to an acute rehabilitation facility.

Discussion

Thrombotic thrombocytopenic purpura (TTP) is a rare but life-threatening thrombotic microangiopathy characterized by severe ADAMTS13 deficiency, resulting in platelet-rich microvascular thrombosis, thrombocytopenia, and microangiopathic hemolytic anemia. Although neurologic manifestations are common in TTP, extensive bilateral cerebral and cerebellar infarctions involving multiple vascular territories are rare and reflect severe systemic microvascular involvement [5]. In this patient, neuroimaging demonstrated multifocal infarctions without an identifiable cardiac embolic source, supporting diffuse microvascular thrombosis as the most likely mechanism rather than isolated embolic disease or COVID-19-associated hypercoagulability alone.

The diagnostic process in this case was particularly challenging because the initial presentation substantially overlapped with COVID-19-associated coagulopathy and critical illness. The patient developed shock requiring ICU-level care, and septic shock with multiorgan dysfunction remained an important competing diagnosis during the early course of hospitalization. COVID-19 infection itself has been increasingly recognized to produce endothelial dysfunction, inflammatory cytokine activation, elevated von Willebrand factor levels, and dysregulation of the ADAMTS13-von Willebrand factor axis [9]. These overlapping features complicated the distinction between severe COVID-related coagulopathy and superimposed TTP.

Patients with COVID-19-associated coagulopathy may clinically mimic TTP but typically demonstrate markedly elevated fibrinogen and D-dimer levels, mild thrombocytopenia, and mildly prolonged PT/aPTT. In many cases, the underlying mechanism reflects endothelial injury with disproportionate elevation of von Willebrand factor relative to mildly reduced ADAMTS13 activity, sometimes referred to as a “COVID-19 TTP-like syndrome” [3]. Unlike true immune-mediated TTP, these cases generally do not demonstrate severe ADAMTS13 deficiency and are less likely to respond to therapeutic plasma exchange. Neurologic manifestations are also less common in these patients.

Although thrombocytopenia, elevated LDH, neurologic infarctions, and multiorgan dysfunction raised concern for thrombotic microangiopathy, the peripheral smear initially demonstrated only limited schistocytosis, adding diagnostic uncertainty [6]. Coagulation studies were not consistent with overt disseminated intravascular coagulation, with PT and INR near normal on admission. Given competing considerations of COVID-19 coagulopathy and septic shock, initial management emphasized corticosteroids and supportive critical care while awaiting confirmatory ADAMTS13 testing.

A further challenge was delayed access to confirmatory testing: ADAMTS13 activity was sent to an outside reference laboratory rather than processed on-site, prolonging turnaround time compared with centers with on-site rapid ADAMTS13 testing capability [7]. This delay contributed to later initiation of plasma exchange until severe ADAMTS13 deficiency was confirmed.

Recent literature increasingly recognizes COVID-19-associated TTP and dysregulation of the ADAMTS13-von Willebrand factor pathway [3, 4]. Reports suggest endothelial injury and inflammatory activation from SARS-CoV-2 may precipitate thrombotic microangiopathy in susceptible individuals [8]. However, true TTP overlapping with COVID-19 remains extremely rare, with only a limited number of reported cases demonstrating severe ADAMTS13 deficiency (< 10%) together with clear evidence of microangiopathic hemolytic anemia. Cases with extensive multifocal cerebral infarctions and simultaneous multiorgan failure remain particularly uncommon. Patients with confirmed severe ADAMTS13 deficiency should receive standard TTP-directed therapy, including therapeutic plasma exchange, corticosteroids, caplacizumab [2], rituximab [10], and adjunctive immunosuppressive therapy when indicated, as was done in our patient.

This case highlights that absence of marked schistocytosis early does not exclude TTP in critically ill patients with COVID-19. The classic pentad of fever, renal dysfunction, neurologic abnormalities, thrombocytopenia, and microangiopathic hemolytic anemia is often incomplete at presentation [1]. Reliance on peripheral smear findings alone may therefore contribute to delayed diagnosis and treatment initiation.

Early recognition of TTP remains essential because delayed treatment is associated with rapid progression and high mortality [1]. Current evidence supports prompt initiation of plasma exchange and corticosteroids when clinical suspicion for TTP is high, even before confirmatory ADAMTS13 results become available [1]. In this patient, the overlap between COVID-19 coagulopathy, septic shock, and TTP created substantial diagnostic uncertainty, ultimately prolonging diagnostic confirmation and definitive therapy.

Conclusions

This case underscores the importance of maintaining a high index of suspicion for thrombotic thrombocytopenic purpura in patients with COVID-19 who present with thrombocytopenia, hemolytic anemia, elevated LDH, and unexplained multifocal ischemic infarctions, even when the presentation initially appears more consistent with COVID-19-associated coagulopathy or septic shock. Near-normal coagulation studies and evidence of microangiopathic hemolysis should prompt consideration of TTP despite limited schistocytosis on peripheral smear. Early recognition and timely initiation of plasma exchange remain critical to improving outcomes, particularly in settings where confirmatory ADAMTS13 testing may be delayed due to limited institutional availability.

Declarations

Ethics and consent to participate

Not applicable. This manuscript describes a single clinical case and did not constitute human-subjects research requiring institutional ethics committee approval according to institutional policy.

Consent to publish

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data and materials

All data relevant to this case are included in the manuscript. Additional deidentified information may be available from the corresponding author upon reasonable request and subject to institutional and patient-privacy requirements.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Michael Botros and Ebram Said contributed to the conception and design of the manuscript, review and interpretation of the clinical data, literature review, and drafting of the manuscript. Amel Saad, Azka Ali, Isra Nour, Sandara Gadalla, Dominick Gordon, and Pam Khosla contributed to the interpretation of the clinical data, literature review, and critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript.

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Not applicable.

Authors' information

Not applicable.

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Figures

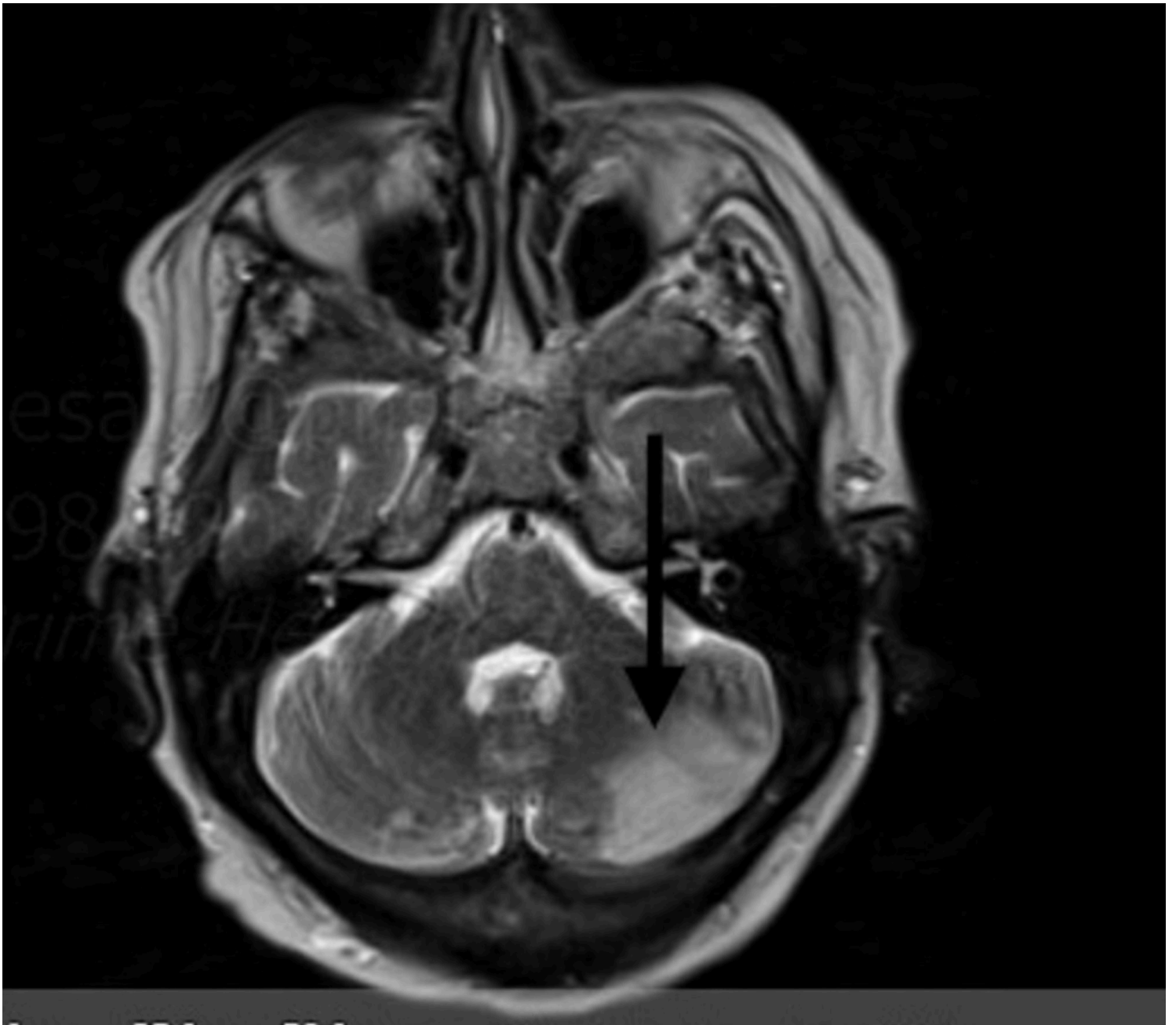


Figure 1

Axial T2-weighted magnetic resonance image demonstrating a hyperintense area of infarction involving the left cerebellar hemisphere (arrow).

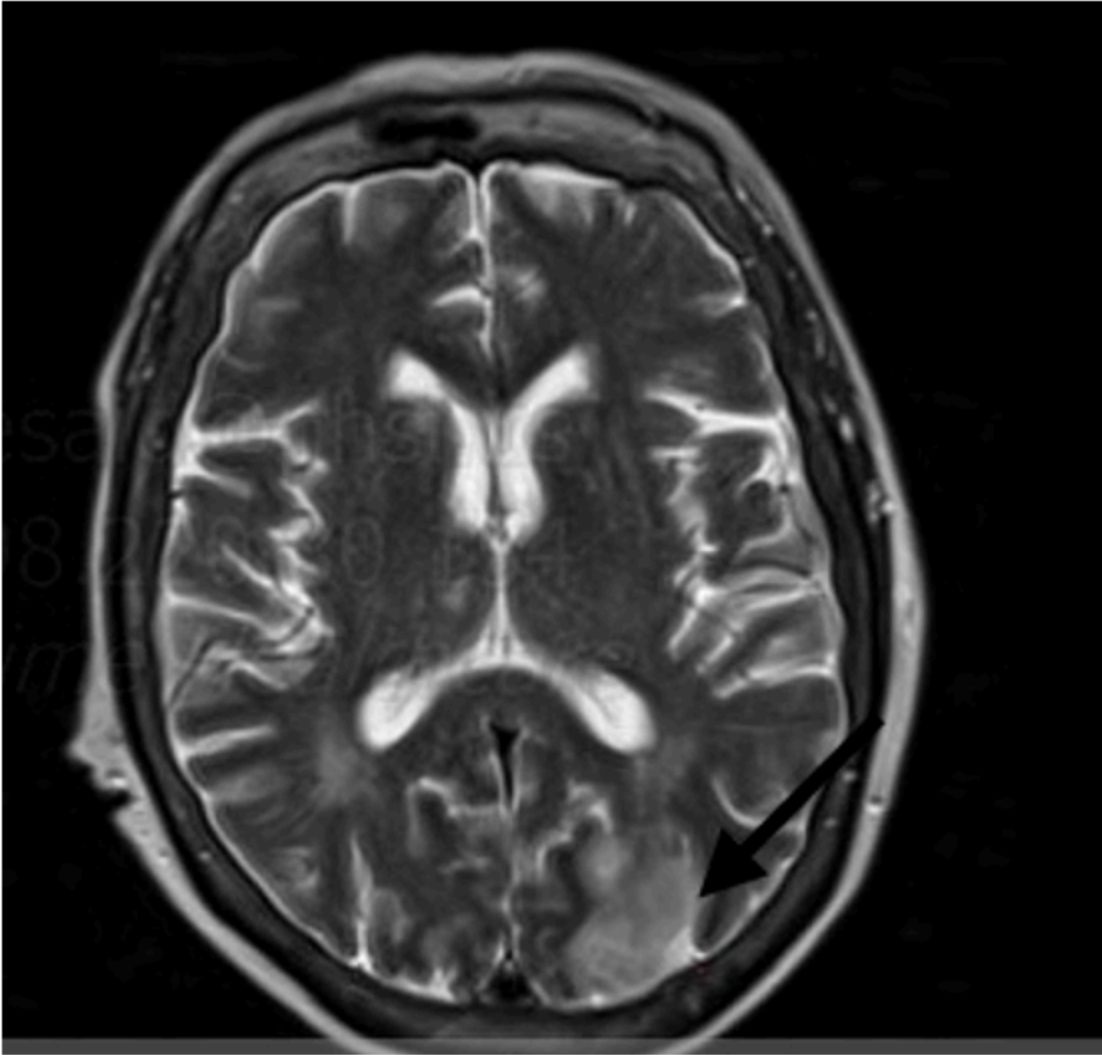


Figure 2

Axial T2-weighted magnetic resonance imaging (MRI) of the brain showing a hyperintense cortical-subcortical lesion in the occipital lobe (arrow), consistent with cerebral infarction.

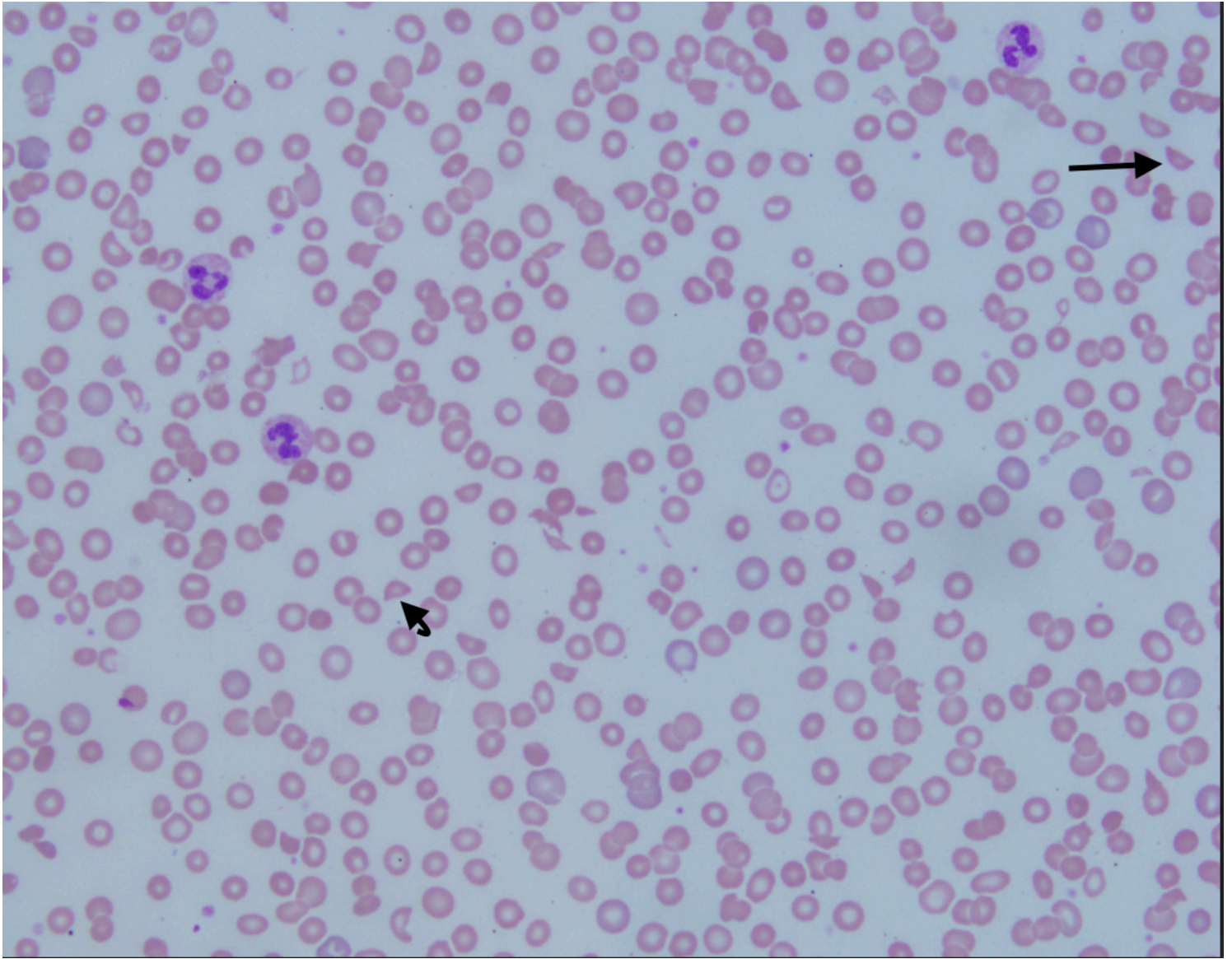


Figure 3

Peripheral blood smear demonstrating schistocytes (arrows).

Peripheral blood smear showing schistocytes (arrows), consistent with the reported slight schistocytosis. Additional smear findings included few (+2) polychromasia, few (+2) anisocytosis, slight stomatocytosis, normal platelet morphology, and rare giant platelets.

Supplementary Files

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