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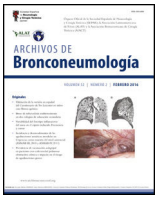

Clinical Letter

Fulminant Thromboembolism and Cold Agglutinin Hemolysis Secondary to *Mycoplasma pneumoniae* Infection

To the Director,

Although *Mycoplasma pneumoniae* commonly presents as a self-limited respiratory illness, it can infrequently provoke severe extrapulmonary complications, including thrombotic and hematologic crises. These manifestations are attributed to the organism's capacity to trigger immune-mediated hypercoagulability and hemolysis. We report a case of extensive thromboembolic disease and coagulopathy secondary to *M. pneumoniae* infection, managed successfully with a multimodal approach including plasmapheresis.

A 59-year-old previously healthy man presented with dyspnea, tachycardia, and hypoxia following a recent return from Europe. He initially developed a productive cough and right leg pain. Imaging demonstrated multiple bilateral pulmonary emboli with right heart strain. He underwent emergent thrombolysis and mechanical thrombectomy. A gross thrombus was retrieved, confirming the large clot burden responsible for the hemodynamic compromise. He was started on anticoagulation and empiric antimicrobials with Ceftriaxone and Azithromycin. Respiratory PCR later detected *M. pneumoniae*. As macrolide resistance testing was unavailable, resistance was inferred from the high prevalence in Northern Europe and the lack of clinical response rather than confirmed, prompting a switch from Azithromycin to Doxycycline. Unexpectedly, the patient developed new bilateral lower extremity deep vein thromboses, worsening thrombocytopenia, and hemolytic anemia with features suggestive of cold agglutinin disease. Laboratory findings indicated disseminated intravascular coagulation (DIC). A peripheral blood smear revealed marked red blood cell agglutination and polychromasia, supportive of cold agglutinin hemolysis (Fig. 1). The cold agglutinin titer was markedly elevated at >1:512, significantly above the reference threshold (<1:64), supporting the diagnosis of cold agglutinin disease in the setting of hemolytic anemia and red cell agglutination. Alternative causes of hemolysis include warm AIHA, microangiopathy from DIC, and drug-induced hemolysis. In our case, the absence of IgG-mediated positivity, lack of schistocytes, and no temporal drug trigger favored cold agglutinin disease as the dominant mechanism. Given the constellation of immune-mediated pathology, therapeutic plasmapheresis was initiated, alongside supportive transfusions and ongoing anticoagulation. The patient responded remarkably, with resolution of hemolysis, normalization of coagulation parameters, and full recovery of respiratory function.

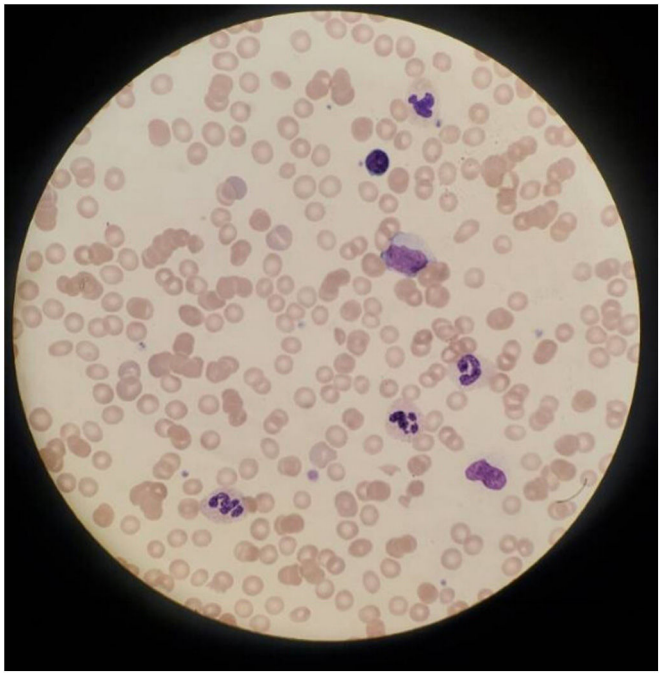

Fig. 1. The smear demonstrates significant red blood cell (RBC) agglutination, with clumping of RBCs evident throughout the field, characteristic of cold agglutinin disease (CAD). Neutrophils with toxic granulation are also observed, reflecting an ongoing systemic inflammatory response.

This case underscores the potential of *M. pneumoniae* to act as a systemic pathogen capable of triggering thrombotic microangiopathy and disseminated coagulopathy. While cold agglutinin disease is seen in about 2–3% of *M. pneumoniae* infections, thrombotic events are rarely reported beyond isolated case descriptions. In our patient, antiphospholipid antibodies were not evaluated, though prior studies note that transient positivity can accompany acute *M. pneumoniae* infection and may amplify thrombotic risk. Although transient, such immunologic shifts could contribute to overlapping hematologic syndromes, warranting close monitoring for evolving coagulopathies. In a 2020 case series, severe coagulopathy was noted in a minority of *Mycoplasma*-infected patients, often requiring advanced therapies. Although not standard therapy, plasmapheresis has prior precedent in severe *M. pneumoniae*-induced cold agglutinin disease and coagulopathy, where antibody removal has been reported to stabilize otherwise refractory cases. Our case contributes to growing awareness of

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this unusual but serious complication of a common respiratory pathogen and emphasizes the value of a high index of suspicion and interdisciplinary management.

Author contributions

Ayman Salih conceptualized the case, collected clinical data, and drafted the manuscript.

Amna Al-Tkrit contributed to the literature review, diagnostic reasoning, and manuscript revision.

Ragheb Assaly provided case supervision, contributed to imaging interpretation, and critically revised the manuscript for intellectual content.

All authors reviewed and approved the final version of the manuscript.

Artificial intelligence involvement

Artificial intelligence tools were used to assist with language enhancement and readability improvements. No content was generated or interpreted by AI.

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Conflicts of interest

The authors declare no conflicts of interest.

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