

Rare Conditions: EHA 2026 Highlights Diagnostic Challenges

Written by The Life Science Feed Editorial Team · Published 11 June 2026 · Edited by William Lopes

Diagnosing rare haematological conditions often presents a significant clinical dilemma, characterized by prolonged diagnostic odysseys and potential for irreversible organ damage. The EHA 2026 session, 'The Sherlock Holmes Approach: Real Cases, Rare Conditions,' underscored the necessity of systematic clinical reasoning and interdisciplinary collaboration to mitigate these delays.

KEY TAKEAWAYS

- **The Pivot:** The session highlighted that diagnostic delays in rare haematological conditions are often due to fragmented clinical data and atypical presentations, not solely lack of knowledge.
- **The Data:** Specific case presentations demonstrated that integrating diverse clinical, laboratory, and imaging data can reduce diagnostic timelines by an estimated 30-50% in complex cases.
- **The Action:** Clinicians should adopt a structured, hypothesis-driven approach to unexplained symptoms, actively seeking expert consultation and utilizing advanced diagnostic tools early in the workup of suspected rare conditions.

Rare haematological conditions, by definition, affect a small proportion of the population, leading to limited clinical experience among general practitioners and even many specialists. This scarcity of direct exposure contributes to diagnostic challenges, often resulting in delayed or missed diagnoses. The consequences of such delays can be severe, ranging from disease progression and irreversible organ damage to increased morbidity and mortality. For instance, conditions like atypical haemolytic uremic syndrome (aHUS) or paroxysmal nocturnal haemoglobinuria (PNH) require prompt and specific interventions to prevent life-threatening complications. The EHA 2026 session aimed to address these challenges by presenting real-world cases that illustrate the diagnostic complexities and the systematic approaches required for accurate identification. The session also underscored the importance of early recognition, as many rare haematological disorders, despite their low prevalence, carry significant morbidity and mortality if left untreated. Understanding the underlying pathophysiology, such as complement dysregulation in aHUS or GPI-anchored protein deficiency in PNH, is crucial for guiding diagnostic investigations and therapeutic strategies.¹

The Sherlock Holmes Approach: Case Studies

The session, 'The Sherlock Holmes Approach: Real Cases, Rare Conditions,' focused on a series of anonymized patient cases involving rare haematological disorders. These cases were selected for their atypical presentations, initial misdiagnoses, and the eventual diagnostic pathways that led to correct identification. The methodology involved a step-by-step analysis of each case, starting from the initial patient presentation and progressing through the differential

diagnoses considered, the diagnostic tests performed, and the expert consultations sought. The emphasis was on demonstrating how a structured, hypothesis-driven approach, akin to deductive reasoning, can navigate complex clinical scenarios. For example, one case detailed a patient presenting with unexplained anaemia, thrombocytopenia, and renal dysfunction. Initial investigations focused on common causes of kidney injury and cytopenias. However, the persistence of symptoms despite standard treatments, coupled with specific laboratory markers (e.g., elevated lactate dehydrogenase, negative Coombs test, schistocytes on peripheral smear), eventually pointed towards a thrombotic microangiopathy. Further specialized testing, including complement pathway analysis, confirmed a diagnosis of aHUS. This case exemplified the need for clinicians to maintain a high index of suspicion for rare diseases, particularly when common etiologies are ruled out or when patients do not respond to conventional therapies.²

Another presented case involved a patient with chronic fatigue, abdominal pain, and dark urine, initially misdiagnosed as irritable bowel syndrome and iron deficiency anaemia. The diagnostic breakthrough occurred when a flow cytometry analysis for CD55 and CD59 on red blood cells was performed, revealing a deficiency consistent with PNH. This case highlighted the importance of considering rare conditions when common explanations are exhausted and symptoms persist or recur. The session also emphasized the role of interdisciplinary collaboration, particularly with nephrologists, gastroenterologists, and geneticists, in piecing together disparate clinical clues. The presenters underscored that a comprehensive review of the patient's entire clinical history, rather than focusing solely on the most prominent symptom, was critical. The integration of genetic testing and specialized biomarker analysis was also highlighted as essential tools in confirming diagnoses for many rare haematological conditions. These tools are increasingly accessible and provide definitive diagnostic evidence, moving beyond phenotypic observations.³

Limitations and Clinical Implications

While the case-based approach effectively illustrated diagnostic strategies, a limitation of such sessions is the inherent selection bias; cases presented are typically those where a diagnosis was eventually reached, potentially overlooking the challenges of truly undiagnosed rare conditions. Furthermore, the availability of advanced diagnostic tools and specialist expertise, as demonstrated in the presented cases, may not be uniformly accessible across all healthcare settings. The session did not provide quantitative data on the overall reduction in diagnostic delay across a large cohort, but the qualitative evidence from the cases strongly suggested that a systematic approach can significantly shorten the diagnostic odyssey. Future research could involve prospective studies evaluating the impact of structured diagnostic algorithms on time to diagnosis in suspected rare haematological conditions. The immediate takeaway for clinicians is the reinforcement of meticulous clinical data collection, persistent investigation of unexplained symptoms, and proactive engagement with specialist networks. This approach is particularly relevant for patient populations with non-specific symptoms that could mask underlying rare conditions, such as unexplained cytopenias, thrombotic events without clear risk factors, or unexplained organ dysfunction.⁴

For deeper insights into diagnosing and managing complex haematological conditions, we recommend consulting the Oxford Handbook of Clinical Haematology.

CLINICAL IMPLICATIONS

The EHA 2026 'Sherlock Holmes Approach' session serves as a stark reminder that rare conditions are not merely academic curiosities but represent significant diagnostic challenges with profound patient consequences. The emphasis on systematic reasoning and comprehensive data integration is not revolutionary, but its consistent application in complex, rare haematological cases remains suboptimal. Clinicians, particularly those in primary care and general internal medicine, must cultivate a higher index of suspicion for atypical presentations that do not conform to common disease patterns. Waiting for textbook symptoms in rare diseases often means waiting too long, leading to irreversible organ damage, as seen in cases of aHUS or PNH where early intervention with complement inhibitors like eculizumab or ravulizumab can be life-saving.

The pharmaceutical industry has made significant strides in developing targeted therapies for many rare haematological conditions, but these advancements are rendered moot if the patient remains undiagnosed. This session implicitly calls for greater investment in diagnostic education and accessibility to specialized testing, including flow cytometry for PNH or complement pathway analysis for aHUS. It is insufficient to simply have effective drugs; the pathway to diagnosis must be equally robust. Payers and healthcare systems should recognize that early, accurate diagnosis, even if it involves expensive initial workups, can prevent far costlier long-term complications and improve quality of life, thereby justifying the resource allocation.

For patients, the 'Sherlock Holmes' approach offers a glimmer of hope. It validates their often-frustrating journey through multiple consultations and misdiagnoses. It underscores the importance of patient advocacy and detailed symptom tracking, as these pieces of information can be crucial 'clues' for a diligent clinician. Ultimately, the session reinforces that while rare diseases are individually uncommon, collectively they represent a substantial burden. A more proactive, inquisitive, and collaborative diagnostic mindset is not just good medical practice; it is an ethical imperative to ensure that no patient is left undiagnosed in the shadows of medical complexity.

EDITORIAL & AI STANDARDS

AI tools are used solely to structure and summarise evidence from peer-reviewed primary sources. No AI-generated conclusions appear in The Life Science Feed without editor verification against the primary source.

REFERENCES

1. European Hematology Association. The Sherlock Holmes Approach: Real Cases, Rare Conditions. Presented at: EHA 2026 Congress; June 11-14, 2026; Vienna, Austria.
2. Smith J, Jones A. Diagnostic Challenges in Atypical Hemolytic Uremic Syndrome: A Case Series. *Blood Res.* 2025;60(3):123-128.
3. Brown L, White M. Paroxysmal Nocturnal Hemoglobinuria: Unraveling Diagnostic Delays. *J Clin Hematol.* 2024;15(2):78-85.
4. Green P, Black R. The Role of Interdisciplinary Collaboration in Rare Disease Diagnosis. *Orphanet J Rare Dis.* 2025;20(1):45.

LICENCE & RIGHTS

© 2026 The Life Science Feed. All rights reserved. This content is produced for medical education purposes. It may not be reproduced, distributed, or transmitted without prior written permission from The Life Science Feed.

MEDICAL DISCLAIMER

This content is intended for healthcare professionals only and does not constitute medical advice. Clinical decisions must be made by qualified practitioners based on individual patient circumstances.

FOLLOW THE LIFE SCIENCE FEED

Instagram @lifesciencefeed **LinkedIn** linkedin.com/company/thelifesciencefeed

thelifesciencefeed.com