Getting Warmer: Barking up the Right Diagnosis

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Case

A previously healthy 22 year-old Pacific Islander female presented to the emergency department with fevers and rigors. Blood cultures quickly turned positive for Methicillin-resistant Staphylococcus aureus (MRSA).

At the initial evaluation, her physical exam was significant for ecchymosis of the right arm and labs demonstrated new leukopenia/anemia and acute renal failure. All of these findings were suggestive of sepsis secondary to MRSA bacteremia.

After an extensive evaluation, no source could be identified. Despite optimal antibiotic therapy, the patient continued to have fevers and worsening anemia and leukopenia. Further investigation of the anemia revealed that it was a warm autoimmune hemolytic anemia.

Type 1 vs Type 2 Clinical Reasoning

	Intuitive process	Analytical process
	System 1	System 2
Examples	Heuristics	Algorithm
	Pattern recognition	Hypothetical-deductive
Feature	Snapshot diagnosis	Comprehensive diagnosis
	Unconscientious	Conscientious
Advantages	Faster	Scientific
	Efficient	Analytical
Disadvantages	Biases	Slower

(https://www.researchgate.net/publication/323736243/figure/tbl1/AS:614297239576594@1523471283327/Comparison-of-System-1-and-System-2-Types-of-clinical-reasoning.png)

Evaluation of Suspected Hemolysis

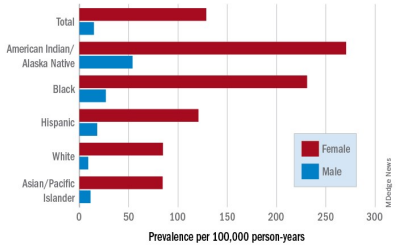
G6PD = glucose-6-phosphate dehydrogenase; HELLP = hemolysis, elevated liver enzymes, and low platelet count.
(American Academy of Family Physicians)

Results

Upon exploration of associated causes, ANA titer was with positive anti-Smith and anti-dsDNA antibodies. The constellation of findings met criteria for Systemic Lupus Erythematosus (SLE) per the American College of Rheumatology (2019).

The patient was initiated on methylprednisolone, hydroxychloroquine, and Rituximab infusions which lead to resolution of the patient's symptomatology and laboratory abnormalities. It was ultimately concluded that the SLE and its associated immunosuppression predisposed the patient to the bacteremia and its sequelae.

Estimated SLE Prevalence by Sex, Ethnicity (2018)



Note: Metaanalysis involved four state-specific registries and one in the Indian Health Service.
Source: Arthritis Rheumatol. 2021 Jan 20. doi: 10.1002/ART.41632

The results of this meta-analysis demonstrated that the prevalence of SLE may be lower compared to prior statistics. It was thought that the prevalence of SLE in the United States was ~1.5 million. The results of this meta-analysis were consistent with a suspected prevalence of 200,000.

Systemic Lupus Erythematosus Classification Criteria

Entry criterion
Antinuclear antibodies (ANA) at a titer of ≥1:80 on HEp-2 cells or an equivalent positive test (ever)

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If absent, do not classify as SLE
If present, apply additive criteria

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Additive criteria
Do not count a criterion if there is a more likely explanation than SLE.
Occurrence of a criterion on at least one occasion is sufficient.
SLE classification requires at least one clinical criterion and ≥10 points.
Criteria need not occur simultaneously.
Within each domain, only the highest weighted criterion is counted toward the total score§.

Clinical domains and criteria	Weight	Immunology domains and criteria	Weight
Constitutional		***Antiphospholipid antibodies***	
Fever	2	Anti-cardiolipin antibodies OR	
Hematologic		Anti-β2GP1 antibodies OR	
Leukopenia	3	Lupus anticoagulant	2
Thrombocytopenia	4	***Complement proteins***	
Autoimmune hemolysis	4	Low C3 OR low C4	3
Neuropsychiatric		Low C3 AND low C4	4
Delirium	2	***SLE-specific antibodies***	
Psychosis	3	Anti-dsDNA antibody* OR	
Seizure	5	Anti-Smith antibody	6
Mucocutaneous			
Non-scarring alopecia	2		
Oral ulcers	2		
Subacute cutaneous OR discoid lupus	4		
Acute cutaneous lupus	6		
Serosal			
Pleural or pericardial effusion	5		
Acute pericarditis	6		
Musculoskeletal			
Joint involvement	6		
Renal			
Proteinuria >0.5g/24h	4		
Renal biopsy Class II or V lupus nephritis	8		
Renal biopsy Class III or IV lupus nephritis	10		

Total score:

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Classify as Systemic Lupus Erythematosus with a score of 10 or more if entry criterion fulfilled.

§ = additional criteria within the same domain will not be counted; * = in an assay with 90% specificity against relevant disease controls. Anti-β_2GPI = anti–β_2-glycoprotein I; anti-dsDNA = anti–double-stranded DNA.
(https://onlinelibrary.wiley.com/doi/full/10.1002/art.40930)

Significance

Upon initial presentation, type 1 clinical reasoning was utilized due to the importance of proper recognition and treatment of sepsis. The disadvantage of this form of reasoning includes the propensity of bias. In this case, we anchored on sepsis given the patient's background and social history. It was not until we transitioned to type 2 clinical reasoning that we were able to broaden the diagnostic workup and determine the true etiology of the patient's presentation.

References

- American Academy of Family Physicians
- American College of Rheumatology
- Arthritis and Rheumatology
- European League Against Rheumatism

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