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Hickam's Dictum Vs. Occam's Razor in Diagnosing Subacute Bacterial Infective Endocarditis

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Introduction

Infective endocarditis (IE) is a fatal time-dependent diagnosis that clinicians should suspect in patients with prosthetic heart valves, implanted intracardiac devices, and those with a history of intravenous (IV) drug use, immunosuppression, or recent dental or surgical procedures. Subtleties in the presentation of IE pose a challenge to clinicians in the diagnostic process. IE can present as an acute, rapidly progressive infection or in an insidious, subacute, and chronic nature with non-specific symptoms. Common signs and symptoms include fever and cardiac murmur in the vast majority of cases. However, splenomegaly, splinter hemorrhages, and petechial hemorrhages are found less frequently. Immediate workup of symptoms in a high-risk patient plays a significant role in the morbidity and mortality of patients with IE. Critical complications that arise from delayed identification and management include systemic septic embolization of valvular vegetations and their sequelae, including infarction and infection of the kidneys, spleen, lungs, brain and other organ systems. IE can ultimately result in non-reversible complications such as congestive heart failure (CHF) with valvular insufficiency. Early detection and treatment can improve survival in two-thirds of patients.[1] This case report outlines the subtleties found in a patient presenting with subacute bacterial IE and how a thorough investigation of clinical signs, symptoms, and history plays a vital role in the clinical course.

Case Report

- A 56-year-old male presented to the Emergency Department (ED) with gait disturbance
- **PMH:** Alcohol abuse, chronic kidney disease (CKD) stage II, and vitamin B12 deficiency
- **Initial imaging:**
  - CT: ischemic stroke in the left Sylvian fissure
  - MRI: confirmed acute infarction from embolic stroke of the right middle cerebral artery (MCA) region
- **Physical exam:** No other focal neurological deficits & all motor and sensory functions were intact
- **Significant labs:**
  - Borderline low vitamin B12 level: 252 ng/mL
  - Low erythrocyte count: 3.8 5 x 10e6/µL
  - Low platelets: 67,000 x 10e3/µL
  - Low leukocyte count: 2 x 10e3/µL
  - Low hemoglobin: 9.4 gm/dL,
- Antiplatelet therapy was held; Hematology consulted for pancytopenia
- **Further diagnostics:**
  - Anemia work-up was non-diagnostic
  - Transthoracic echocardiogram (TTE): mild aortic valve sclerosis & mild bilateral atrial enlargement
  - Abdominal ultrasound: hypoechoic lesions in the liver, consistent with hemangiomas
- **Discharge diagnosis:** ischemic stroke, B12 deficiency, and pancytopenia from chronic alcohol abuse
- **Readmission two weeks later:** dysphagia for endoscopic evaluation
  - Worsening thrombocytopenia: platelets down to 33 x10e3/µL → deferral of endoscopy
  - CT imaging: mild bilateral atelectasis, mild pericardial effusion, and splenomegaly
  - Barium swallow: no obstruction
  - Bone marrow aspiration and biopsy: concerning for myelodysplastic syndrome with left-shift and mildly atypical myeloid maturation pattern
  - AKI, hematuria, and hypocomplementemia → concerning for IgA glomerulonephritis or amyloidosis
  - Thrombocytopenia → deferral of kidney biopsy
  - Urine cultures remained negative
- **Readmission one week later:** respiratory symptoms
  - Low leukocyte count: 1.3 x 10e3/µL
  - Low hemoglobin: 6.3 gm/dL
  - Low platelets: 30 x 10e3/µL
  - High serum creatinine: 4.2 mg/dL
  - High procalcitonin: 0.59 ng/mL
  - High lactic acid: 1.2 mmol/L
  - Viral PCR was positive for influenza A
  - Sepsis criteria met → blood cultures drawn → positive for *Enterococcus faecalis*
  - Physical exam: new diastolic murmur, widened pulse pressure, Janeway lesions, splinter hemorrhages
  - Repeat TTE: unchanged
  - Transesophageal echocardiogram (TEE): aortic valve perforation → infective endocarditis

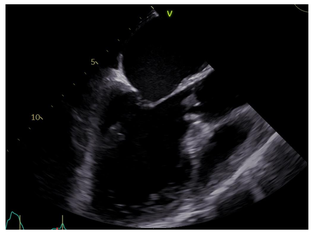

Figure 1: Valve vegetation as seen on TEE

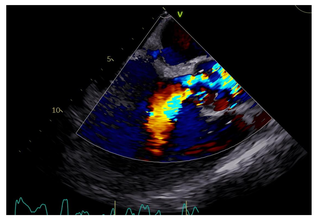

Figure 2: Valve vegetation as seen on TEE with doppler

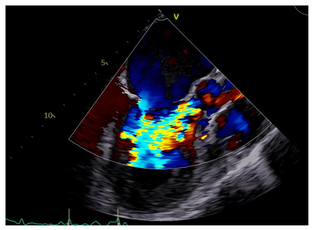

Figure 3: Valve vegetation as seen on TEE with doppler

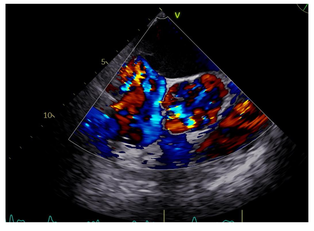

Figure 4: Valve perforation as seen on TEE with doppler

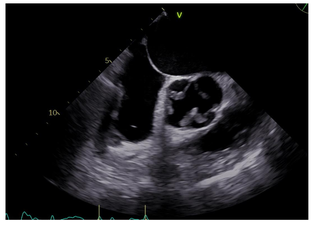

Figure 5: Valve destruction as seen on TEE

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Discussion

- Each organ pathology was considered to be the primary cause of our patient's symptoms, without considering infective endocarditis as a unifying cause
  - Using Hickam's dictum reasoning to separately explain this patient's presentation of CVA, pancytopenia, AKI, dysphagia, and B12 deficiency, rather than utilizing an Occam's razor approach to identify one encompassing diagnosis to link these findings, led to a delay in proper management.
- Patient's **first hospitalization** consisted of:
  - Gait disturbances and dysphagia → suggestive of CVA
    - CVA was appropriately investigated with a TTE and vascular imaging
      - Limitations of TTE: Operator dependent and less sensitive than TEE[2]
      - In the absence of an established cause of the stroke, a TEE would have been appropriate at this time and may have identified endocarditis
  - Pancytopenia, anemia, and B12 deficiency
    - Possibly alcohol related without the consideration of a unifying pathology
- Patient's **second hospitalization** concentrated on:
  - Pancytopenia and AKI
    - The patient's AKI was investigated for glomerulonephritis with non-diagnostic serology, but thrombocytopenia precluded kidney biopsy
    - AKI that was attributed to volume depletion could have been diagnostic since glomerulonephritis can point to endocarditis
    - Occult causes of pancytopenia are usually related to malignancy or bone marrow pathology, although bacteremia is an unusual cause of pancytopenia
    - While evaluating pancytopenia, underlying platelet destruction or reduced bone marrow production due to nutritional deficiencies or malignancy should be considered
      - A review of the literature revealed very few instances where pancytopenia was a presenting symptom of infective endocarditis and is not generally considered as a differential diagnosis for pancytopenia[3][4][5]
      - A negative work up should have alluded to possible chronic infection even though signs and symptoms did not suggest an infectious process
- Patient's **third hospitalization** showed that:
  - He met sepsis criteria-->blood cultures were drawn→ cultures showed enterococcus bacteremia
  - This diagnosis connected the full clinical picture: CVA, pancytopenia, AKI, and left-shifted myeloid proliferation in the bone marrow
- Prompt **diagnosis** and targeted therapy is required to reduce morbidity and mortality in infective endocarditis
  - Enterococcal infective endocarditis has a 20% in-hospital mortality rate[6]
  - Approximately 97% of these cases of IE are caused by *Enterococcus faecalis*, predominantly affecting the elderly with comorbidities[7]
  - In the setting of infective endocarditis, severe valvular insufficiency is seen in about 75% of cases due to mitral valve perforation while aortic valve perforation, which was seen in this patient, comprises about 23% of the remaining cases[10]
    - Valvular perforation due to infective endocarditis, seen in this patient's case, is associated with future hemodialysis, severe valvular insufficiency, and increased mortality[10]
- The **treatment** of *E. faecalis* infective endocarditis may involve both antibiotic therapy and valve replacement[7]
  - Preferred treatment of *E. faecalis* IE is 4-6 weeks of IV ampicillin or penicillin in combination with gentamicin[8][9]

Conclusion

Diagnosing infective endocarditis can be challenging in patients with subacute symptoms who are not meeting sepsis criteria. The delay is detrimental to the outcome. Blood cultures should be included in routine workup for pancytopenia if no other cause can be identified. TEE is more sensitive than TTE in visualizing heart valve pathology in CVA workup. Finally, a keen physical examination may help avoid premature closure bias. In diagnostic uncertainty, clinicians should attempt to connect all clinical manifestations under a single, encompassing diagnosis.

References:

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