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A Depressing Diagnostic Error

To the Editor:

A 52-year-old woman with diabetes presented to the hospital with acute onset of right flank pain, in the setting of profound lower extremity weakness and cachexia with a 30-lb unintentional weight loss over the past 6 months. She was diagnosed with ascending pyelonephritis and treated with empiric antibiotics. On hospital day 2, she was transferred to the intensive care unit (ICU) because of septic shock.

During her ICU stay, a thorough investigation of her weakness and cachexia was undertaken, including testing for malignant, neuromuscular, autoimmune, metabolic, and nutritional etiologies. A computed tomography scan incidentally noted multiple subcentimeter, well-defined, hypodense liver lesions. Computed tomography and magnetic resonance imaging of the brain showed a stable tuberculoma. Owing to concomitant normocytic anemia, upper endoscopy and colonoscopy were performed, which were unrevealing. Results from paraneoplastic and myositis antibody panels were negative. Nerve conduction studies and electromyography were unrevealing. Human immunodeficiency virus testing and fungal culture were negative. Vitamins B12 and E, cortisol, thyroid-stimulating hormone, creatine kinase, and aldolase levels were normal. She was subsequently transferred to the medicine wards service with a working diagnosis of metastatic cancer to the liver of unknown primary origin.

On further review of the patient's history, she reported a 6-month history of severely depressed mood, anhedonia, immobility to the point of being bed bound, severe anorexia, and feelings of worthlessness. She was formerly prescribed venlafaxine but discontinued this medication because of xerostomia. She was diagnosed with severe recurrent major depression. She was prescribed mirtazapine, which led to a dramatic improvement in her mood, appetite, and strength. One-year follow-up confirmed no evidence of metastatic disease.

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This case illustrates how biased clinical reasoning resulted in unnecessary testing, prolonged hospitalization, and ultimately a diagnostic error. Diagnostic errors are common, occurring in 7% to 17% of hospitalized patients.¹ Diagnostic errors stem from faulty knowledge, faulty data gathering, and faulty synthesis, all 3 of which contributed to this patient's misdiagnosis.

Faulty knowledge was evident in the over-interpretation of the nondescript hypodense liver lesions as probable metastatic disease. However, incidental imaging findings are common: 23.6% of diagnostic imaging studies and 31.1% of computed tomography studies reveal incidental findings.² Alternative causes of her weakness were dismissed because of premature closure and anchoring bias, and a workup to identify the primary malignancy could have been avoided. Furthermore, understanding that severe depression is one of the top 3 causes of unexplained weight loss, accounting for up to 25% of cases, would have raised the pretest probability for depression, leading to better data gathering and synthesis.³

Additionally, cognitive biases complicated clinical reasoning, which subsequently resulted in faulty data gathering. Because our patient was transferred to the ICU, concern for life-threatening causes of weakness and weight loss, such as neoplastic and neurologic etiologies, was heightened, an example of ascertainment bias and framing effect. Although these other etiologies should be initially considered, the patient's history makes depression far more likely. However, symptoms related to depression, such as feelings of worthlessness and anhedonia, were never elucidated in the data-gathering process.

Finally, faulty synthesis led to an incomplete and inaccurate problem representation.⁴ Failure to articulate the problem representation results in the generation of hypotheses that account for only a specific symptom but do not explain the case as a whole.⁴ An accurate problem representation for this case would have been, "a 52-year-old woman with a history of depression off of medical therapy who presented with progressively worsening cachexia and sarcopenia over the past 6 months with feelings of anhedonia, worthlessness, and depressed mood."

In summary, this case exemplifies the importance of clinical reasoning in preventing diagnostic errors and subsequent unnecessary testing. Sound clinical reasoning requires being aware of potential biases and being skilled in cognitive debiasing techniques.⁵ In our patient, despite an extensive workup, the "diagnostic test performed" was returning to the basics of gathering a relevant history and

using clinical reasoning to recreate a more accurate problem representation.

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