

**QUESTION**  
 A 65-year-old male patient with a long history of hypertension and hyperlipidemia presents to the clinic with a 2-week history of increasing fatigue, weight loss, and a low-grade fever. He reports that he has been unable to complete his usual activities of daily living. He has no chest pain, shortness of breath, or changes in bowel habits. His medical history is significant for hypertension, hyperlipidemia, and a recent diagnosis of type 2 diabetes mellitus. He is currently on lisinopril, atorvastatin, and metformin. He has no known drug allergies. His family history is notable for coronary artery disease and type 2 diabetes mellitus. He is a former smoker (quit 10 years ago) and drinks alcohol socially. He is currently taking his medications as prescribed.

**ANSWER**  
 The patient's symptoms are concerning for a systemic illness, such as a malignancy or an autoimmune condition. The most likely diagnosis is a hematologic malignancy, such as multiple myeloma or a lymphoproliferative disorder. The patient's symptoms of fatigue, weight loss, and low-grade fever are consistent with a systemic illness. The absence of chest pain, shortness of breath, or changes in bowel habits makes a primary pulmonary or gastrointestinal process less likely. The patient's medical history and current medications do not suggest a drug-induced illness. Further diagnostic workup, including a complete blood count, serum protein electrophoresis, and imaging studies, is warranted to confirm the diagnosis.

## CLINICAL PEARLS



**KEY POINTS**  
 Systemic illness should be considered in the differential diagnosis of a patient with unexplained fatigue, weight loss, and low-grade fever. Hematologic malignancies, such as multiple myeloma and lymphoproliferative disorders, are common causes of these symptoms. Autoimmune conditions, such as rheumatoid arthritis and systemic lupus erythematosus, are also potential causes. A thorough history and physical examination, along with appropriate laboratory and imaging studies, are essential for identifying the underlying cause.