An 80-year-old woman has a 3-month history of increasing dysphagia (with both solids and liquids), fatigue, and dyspnea on exertion. She has also involuntarily lost 50 lb during the same period. She reports no abdominal pain or change in bowel function.

**Physical Examination**
This elderly woman appears frail. Heart rate is 92 beats per minute; respiration rate, 16 breaths per minute; and blood pressure, 100/80 mm Hg. Temporal wasting and patchy alopecia are evident. Parotid glands are enlarged bilaterally; the tongue is also enlarged, and indentations made by the teeth are visible. Results of a chest examination are normal. The liver and spleen are not enlarged. Her shoulders appear muscular and are out of proportion to the rest of her frame. The remainder of the examination is unremarkable.

**Laboratory Results**
Hemoglobin level is 9.9 g/dL. Mean corpuscular volume (MCV) is 96 fL. White blood cell count and platelet count are normal. Results of a chemistry panel and liver function tests are within normal limits.

Which of the following is the most appropriate next step?
A. Esophagogastroduodenoscopy (EGD).
B. Serum protein electrophoresis and immunofixation.
C. Radionucleotide bone scan.
D. Iron studies.

**Correct Answer:** B

The clinical findings in this patient are consistent with a diagnosis of amyloidosis, a rare monoclonal plasma cell disorder. The classification of amyloidosis is based on which precursor plasma proteins form amyloid deposits. In primary amyloidosis, fragments of immunoglobulin light chains deposit in a variety of organs and cause dysfunction. The most common symptoms associated with primary amyloidosis are fatigue, weight loss, and peri-orbital purpura. Common physical findings include palpable liver, enlarged tongue, and edema. An enlarged liver is seen in only about 15% of patients but may be associated with concomitant congestive heart failure. Enlargement of the tongue is seen in only about 10% of patients. Soft tissue infiltration may also occur in a variety of other areas, which can result in alopecia, the "shoulder-pad sign," and submandibular swelling. All of these were present in this patient. Because the signs and symptoms of the disease are relatively nondescript, it may be parenchymal organ involvement that brings amyloidosis to the clinician's attention. The kidneys, heart, liver, and peripheral nerves are most commonly involved. Consider amyloidosis in a patient with nephrotic syndrome with no alternative explanation, such as long-standing diabetes. Consider cardiac amyloid involvement in any patient with unexplained cardiomyopathy and no history of ischemic heart disease. Liver infiltration is often relatively asymptomatic, but it may be signaled by isolated elevations in alkaline phosphatase. Axonal peripheral neuropathy is also seen in primary amyloidosis; symptoms generally occur in the lower extremities, and sensory changes predominate. However, other neurologic involvement, such as carpal tunnel syndrome or autonomic neuropathy, may also prompt consideration of the diagnosis. Pulmonary involvement is relatively common in amyloidosis but rarely causes symptoms. Infiltration of the thyroid or adrenal gland may also occur and can cause endocrine dysfunction. Because its signs and symptoms are relatively nonspecific, amyloidosis can be somewhat difficult to diagnose. Recognition that the disease is a plasma cell disorder is the key to its diagnosis. Electrophoresis and immunofixation (choice B) of the serum and urine reveal the presence of a monoclonal light chain in about 90% of patients. The presence of a monoclonal protein is a strong clue to the diagnosis, and its absence is a strong negative finding in ruling out amyloidosis. Biopsy can confirm the diagnosis in a patient with clinical manifestations in whom monoclonal protein is detected. Subcutaneous fat aspiration and bone marrow biopsy with Congo red staining of the specimen are relatively noninvasive and have sensitivities of about 80% and 50%, respectively. If neither of these is diagnostic, biopsy of an affected organ may be an appropriate next step. EGD (choice A) is frequently useful in the evaluation of patients with dysphagia (eg, when dysphagia is the result of esophageal carcinoma), and it is not an inherently
incorrect choice. However, because so many of the less common features of amyloidosis are present here, a more directed diagnostic approach (ie, serum protein studies, biopsy) is more appropriate. A radionuclide bone scan (choice C) is a poor test for the evaluation of bone involvement in plasma cell disease. The bone lesions in plasma cell dyscrasias are primarily lytic; thus, in the absence of fracture, bone scans that detect osteoblastic activity will be negative. Plain radiography or MRI would be a better study in this setting. Most patients with amyloidosis are anemic; however, the anemia is a result of marrow involvement rather than of iron deficiency. In addition, this patient's MCV is 96 fl, which makes iron deficiency or related diagnoses very unlikely and iron studies (choice D) of scant usefulness. **Prognosis.** The prognosis for patients with primary amyloidosis is generally poor. Cardiac involvement portends the poorest prognosis, and the median survival of affected patients is 6 months. Once the diagnosis of amyloidosis is established, obtain an echocardiogram to determine cardiac involvement. **Treatment.** The treatment of amyloidosis is evolving. Because it is a monoclonal plasma cell disorder, the history of its treatment parallels in many ways that of the treatment of multiple myeloma. In fact, it may be difficult to differentiate between the 2 diseases in certain patients. Several trials have confirmed that therapy with oral melphalan and prednisone is more effective than no therapy or therapy with colchicine. Unfortunately, the response rates associated with the melphalan-prednisone combination are low, and the time to response often approaches 1 year. More intense chemotherapy regimens have not been uniformly effective. A recent study evaluated the role of high-dose melphalan and autologous stem-cell transplantation in patients with primary amyloidosis. A substantial number of the patients in the study showed significant improvement in 5-year survival and reversal of end-organ disease. **Outcome of this case.** The patient's condition deteriorated over the ensuing weeks; her dyspnea increased to the point that oxygen was required. Eventually, she went into respiratory arrest; intubation was difficult because of apparent infiltration of the larynx and trachea by amyloid deposits, and she was unable to be resuscitated.

**References:**


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