

## CLINICAL VIGNETTE

# A Life Saving Episode of Low Back Pain -- Discovering an Indolent Multiple Myeloma

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### *Introduction*

Low back pain most often stems from lumbosacral strain or other benign musculoskeletal causes, even potentially in the presence of warning signs. However, such signs may prompt work-up for other etiologies, especially if present with other unexplained new symptoms such as fatigue. We present a case of low back pain that, upon work-up of laboratory abnormalities, revealed a diagnosis of multiple myeloma.

Learning objectives are to recognize warning signs of low back pain that may indicate underlying systemic disease and to utilize an algorithm for sensitive testing for diagnosing multiple myeloma.

### *Case Narrative*

A 55-year-old female with a history of hypertension, treated with amlodipine, presented to the emergency department with a flu-like illness for one week and new onset, severe low back pain for one day.

She noted that over the last week she had had "the flu," which consisted of symptoms of productive cough (yellow sputum) resulting in exacerbation of preexisting stress incontinence, fever (not measured but self-reported), myalgia, sore throat, and non-bloody vomiting, which was slowly improving over that week. Her son, in middle school, was sick at around the same time with similar symptoms after a trip to the beach.

On the evening before admission, she had one episode of emesis that subsequently led to the sudden onset of "shock-like" low back pain that radiated to the right side with associated numbness/tingling, rated as 8/10 in intensity. She "couldn't move" afterwards due to pain and got help to come to the emergency department.

She had no prior episodes of low back pain. She had recently started work in a business consumer alliance, doing mostly sedentary work without much heavy lifting. Her pain did persist at night but did not wake her from sleep. She denied frank weakness, stating that it felt as if her pain limited her movement. She had generalized fatigue with occasional leg cramps in the calves for a few months. She had no urge or overflow bladder or bowel incontinence. She had no weight loss, dizziness, diarrhea, or rashes. The rest of the review of systems was unremarkable. She last had a mammogram 3 years

previously, which was normal, and had no prior PAP smears or colonoscopy.

There was no pertinent past surgical history. Family history was notable for an unknown type of cancer in her maternal grandmother; her father and mother both had hypertension and her father also had hyperlipidemia and diabetes mellitus. She did not smoke or use any illicit drugs.

On examination, her vital signs included a temperature of 40.1 Celsius, heart rate of 111, BP 117/57, respiratory rate of 16 and O<sub>2</sub> sat in low 80s on room air, up to 94% on 3L/min oxygen by nasal cannula. Her pertinent physical exam findings included 4/5 strength on testing of right hip flexion, knee extension/flexion, and foot dorsi/plantarflexion; all were limited by pain with significant tenderness to palpation over the sacral promontory and right paraspinal/gluteal muscles. Straight leg raise was negative on the left and reproduced pain radiating into the right leg at 30 degrees on the right. Her reflexes were symmetric. On gait exam, both her casual gait and toe gait were slow but steady; she deferred heel gait testing.

Given her presentation to the emergency department, new onset low back pain, and generalized fatigue, a complete blood count and basic metabolic panel were obtained, showing a new macrocytic anemia with hemoglobin 7.6 and mean corpuscular volume 101.3 (last values had been Hb 11.3 and MCV 88.5, respectively, over 2 1/2 years earlier). Her creatinine was 1.2 mg/dL, up from 0.8 mg/dL over 2 1/2 years earlier. Calcium was normal. With these new findings, she was admitted for evaluation.

Initial diagnostic concerns were to evaluate urgent etiologies of anemia and acute kidney injury. With older age, obesity, new anemia, new kidney injury, and low back pain, multiple myeloma served as a potential unifying diagnosis.<sup>1</sup> To assist with evaluation of that diagnosis, macrocytic anemia, acute kidney injury, and her respiratory illness, the following tests were done.

Initial imaging included a lumbar X-ray (no fracture or bony lesion) and chest X-ray (peribronchial thickening and increased interstitial markings). Nasopharyngeal swab for PCR revealed influenza B infection. Hepatic function panel was added to her basic metabolic panel to evaluate protein levels, which showed

a total protein of 12.0 g (compared to albumin 3.2g). These results were immediately concerning for hypergammaglobulinemia. Serum protein electrophoresis (SPEP) and serum immunofixation (SIF) were requested with an anticipated delay until results would be available. Quantitative immune globulins (IgG, IgA, and IgM) were checked which showed IgG 5830 mg/dL, IgA 15 mg/dL, and IgM 14 mg/dL. With one monoclonal immune globulin overproduced (IgG in 52% of cases), simultaneous reduction in either of the other Ig's (for example, IgM or IgA in the case of IgG myeloma) occurs in 91% of cases, with both reduced in 73% of cases.<sup>2</sup> Peripheral smear revealed rouleaux formation.

Within a few hours, we had strong support for a diagnosis of multiple myeloma that could at least account for her anemia. Further work-up with urinalysis showed 3+ blood and 3+ protein with FENa 2.58%, suggestive of intrinsic kidney injury. SPEP, SIF, and 24-hour urine for protein electrophoresis, showed significant albuminuria (5712 mg protein with albumin 3370.1 mg and monoclonal protein of 862.5 mg). Her back pain and flu symptoms rapidly improved, and she was discharged with empiric antibiotic coverage for community acquired pneumonia, Oncology follow-up (for outpatient bone marrow biopsy), and nephrology follow-up (to consider kidney biopsy to rule out amyloidosis given nephrotic range proteinuria that was found prior to discharge, and for assistance with management of proteinuria). A bone survey done subsequently as an outpatient did not show any bony lesions. Bone marrow biopsy revealed 80-85% monotypic plasmacytosis, and along with SPEP and SIF demonstrating an IgG kappa monoclonal gammopathy, the diagnosis of multiple myeloma was confirmed.

### **Brief Discussion**

Multiple myeloma is a plasma cell dyscrasia/malignancy of older adults (median age of 66 years at diagnosis) with obesity as a risk factor for development. Seventy-three percent of patients present with anemia and 58% present with bone pain, either from plasmacytoma development or from local osteolytic lesions.

SPEP demonstrates a localized peak in 82% of patients with myeloma, with immune fixation increasing sensitivity to 93%. These are the first two recommended tests given that high sensitivity. Either serum free light chain or 24-hour UPEP (with or without immunofixation) will increase this sensitivity even further to 97%. Either of these studies may be collected with clinical discretion. If urine studies are desired, 24-hour collection is recommended to avoid a false negative spot UPEP in the event that there isn't enough Bence Jones proteinuria that will exceed the proximal tubule's resorptive capacity. As mentioned previously, with one monoclonal immune globulin overproduced (IgG in 52% of cases), simultaneous reduction in either of the other Ig's (for example, IgM or IgA in the case of IgG myeloma) occurs in 91% of cases, with both reduced in 73% of cases. Serum free light chain abnormal ratios occur in 90% of cases.

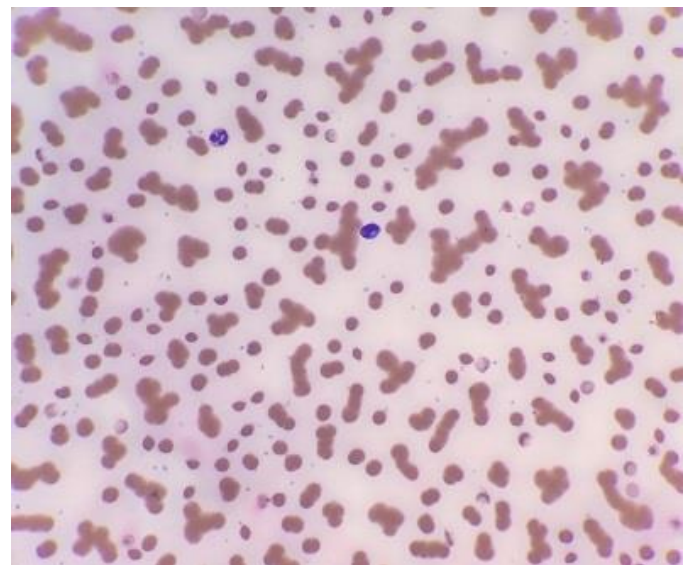
Low back pain may present with other signs or symptoms that are concerning for systemic disease. Features that may be suggestive include a history of cancer, age >50 years, unexplained weight loss, pain lasting over 1 month, nighttime pain, and unresponsiveness to therapy. Injection drug use, recent bacterial infection (especially bacteremia), or fever may increase suspicion for spinal infection (such as epidural abscess or osteomyelitis).<sup>3</sup>

### **Patient Outcome**

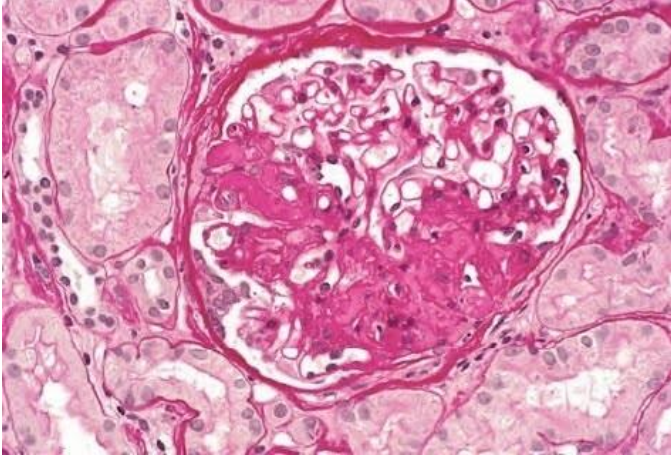
Outpatient kidney biopsy demonstrated focal segmental glomerulosclerosis (FSGS), an unusual finding in myeloma, without evidence of amyloid, light chain deposition disease, or cast nephropathy. There are, however, case reports of temporal and epidemiological links between FSGS and plasma cell disorders.<sup>4</sup> The bone marrow biopsy confirmed the diagnosis of multiple myeloma as above. Subsequent fluorescence in-situ hybridization (FISH) and karyotype studies revealed a high-risk myeloma. She received 6 cycles of lenalidomide, dexamethasone, and bortezomib with no evidence of dyscrasia on repeat bone marrow biopsy. She then underwent mobilization of stem cells and had myeloablative/high dose melphalan with rescue autologous stem cell transplant. She is doing well and has returned to her baseline kidney function, resolution of anemia, and return of her prior functional status.

### **Figures**

**Figure 1.** The patient's peripheral smear shows normochromic anemia with rouleaux formation and leukopenia. In the middle of the figure is a plasma cell; flow cytometry, showed monotypic plasma cells (7% of the total) with aberrant expression of CD20, CD56 and CD117, indicating plasma cell dyscrasia.



**Figure 2.** This is a representative photo of the patient's kidney biopsy.<sup>5</sup> Given the nephrotic proteinuria, which is unusual with myeloma kidney (which is classically Bence Jones cast nephropathy), a kidney biopsy is helpful to evaluate for amyloidosis and other etiologies. This will help with prognosis of kidney function, which will help with management of proteinuria, a known major cardiovascular risk factor.



## REFERENCES

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