Pseudohyperkalemia in Chronic Lymphocytic Leukemia: Longitudinal Analysis and Review of the Literature

BY LAUREN KATKISH, MD, TOM RECTOR, PHARMD, PHD, AREEF ISHANI, MD, AND PANKAJ GUPTA, MD; UNIVERSITY OF MINNESOTA DEPARTMENT OF MEDICINE; MINNEAPOLIS VA HEALTH CARE SYSTEM CENTER FOR CHRONIC DISEASE OUTCOMES RESEARCH, NEPHROLOGY SECTION AND HEMATOLOGY/ONCOLOGY SECTION

Pseudohyperkalemia in patients with leukocytosis caused by chronic lymphocytic leukemia (CLL) is well-documented in case studies. However, the incidence of pseudohyperkalemia and its relationship to white blood cell (WBC) count is unknown. Of concern, artificially elevated potassium levels have triggered administration of unnecessary and potentially life-threatening potassium-lowering treatments including emergent dialysis. Either a blood collection and processing protocol to minimize or eliminate pseudohyperkalemia or a reliable method to “correct” potassium levels for the degree of leukocytosis have yet to be determined.

Methods
We studied 310 patients diagnosed with CLL between 1997 and 2014 at the Minneapolis VA Medical Center. Patients with WBC counts ≥50.0 x 10^9/L underwent further scrutiny. Those with alternative causes of hyperkalemia such as recent initiation of a potentially nephrotoxic drug or recent decline in renal function were excluded. WBC counts and potassium levels yielded 1,119 data points over 270 patient-years from 57 eligible male patients. The patients ranged in age from 49 to 95 years at diagnosis and had WBC counts of 5.4 to 282.6 x 10^9/L. Longitudinal fixed-effects linear regression was used to test for a relationship between WBC counts and differences between the measured plasma potassium concentrations and the upper limit of normal (ULN) for the potassium assay.

Results
In our analysis of data on the VA patients, we found overall, 19% of potassium values were >ULN, and 7.3% exceeded the ULN by at least 0.5 mmol/L. For every increase of 100.0 x 10^9 WBC/L, the potassium value increased by 0.5 mmol/L on average. The adjusted odds of a patient’s potassium level being above the ULN increased by 1.4 (95% confidence interval, 1.2-1.5; p <0.0001) with every 10.0 x 10^9 cells/L increase in WBC counts. When the WBC count was below 50.0 x 10^9 cells/L, the median estimated percentage of a patient’s potassium values being above the ULN was low (1.7%; IQR, 0.9-3.45), whereas the estimated percentage above the ULN was 8.1% (IQR 3.9-19) when the WBC count was ≥100.0 x 10^9 cells/L. However, within individual patients, variation in their WBC counts explained only part of the variation in their potassium values. When taken collectively, the trends in the literature were similar to those identified in our study. Studies aiming to determine the mechanism of pseudohyperkalemia had contradictory findings; thus, we concluded no mechanism has been identified and confirmed.

Conclusion
A considerable proportion of measured plasma potassium values are elevated in patients with CLL and high WBC counts. It is likely that the majority of these values represent pseudohyperkalemia. However, a “correction factor” cannot be created to account for pseudohyperkalemia because it is not possible to predict the potassium value based on the WBC count alone. This is likely a consequence of the erratic effect of diverse artifactual phenomena that influence potassium measurement in patients with CLL. Clinical judgment needs to be used when interpreting potassium values in such patients. We recommend that an alert be placed in the electronic medical record system regarding the potential for pseudohyperkalemia in patients with CLL and elevated WBC counts.

REFERENCES
Diffuse Large B Cell Lymphoma Presenting as Transverse Myelitis

BY AIMEE MERINO, MD, PHD, DEPARTMENT OF MEDICINE RESIDENCY PROGRAM, UNIVERSITY OF MINNESOTA

Diffuse large B cell lymphoma is the most common type of non-Hodgkin’s lymphoma, accounting for approximately 25% of cases. The diverse manifestations of this disease and frequent extra-nodal involvement of diverse tissues create a diagnostic challenge.

Case
A 64-year-old man presented to the emergency department after four days of leg weakness and difficulty urinating. On exam he was found to have sensory deficits bilaterally. At that time, MRI of the spinal cord showed edema at T10 to T12, and lumbar puncture was negative for infectious agents but showed a high protein level of 67 mg/dL. The patient was believed to have an idiopathic or post-infectious transverse myelitis and was started on high-dose steroids. His weakness and urinary retention improved initially but worsened when the steroids were tapered.

Further work-up was performed, and a brain MRI showed lesions in the brainstem consistent with demyelination. A lumbar puncture was performed that showed five oligoclonal bands. Given the relapsing nature of his symptoms, MRI findings and oligoclonal bands on lumbar puncture, the patient was diagnosed with multiple sclerosis. Steroid therapy was reinitiated and interferon beta-1a was started. Despite therapy, he continued to have bilateral leg weakness, paresthesia, worsening urinary retention and constipation. An EMG was performed on both legs and showed diffuse axonal sensorimotor polyneuropathy. His steroid dose was increased, and he eventually regained enough strength in his legs to walk using a walker.

Approximately three months after his initial presentation, the patient continued to have urinary retention, constipation and paresthesia in addition to some residual leg weakness. A repeat EMG showed diffuse, bilateral sensorimotor polyneuropathy with primarily axonal involvement. Given his initially acute presentation and his predominately axonal polyneuropathy, he was diagnosed with Guillain-Barre syndrome with spinal cord involvement. The patient was treated with IgG, plasmapheresis and high-dose steroids. After physical therapy, he was able to finally return home with self-catheterization and assistive devices.

A month after returning home, the patient returned to the emergency department with an acute return of weakness to the point of being unable to transfer from his wheelchair. His recurrence of symptoms after treatment with IgG and plasmapheresis in addition to axonal polyneuropathy on EMG prompted a diagnosis of autoimmune inflammatory demyelinating disease. He was started on mycophenolate. Contemporaneously, there was a precipitous rise in his liver function tests with no known etiology. A liver biopsy was performed six months after his initial presentation; it showed diffuse large B cell lymphoma. His neurologic symptoms were determined to be caused by neurolymphomatosis from direct invasion of peripheral nerves and possible lymphoma in the CNS. He was treated with rituximab and dexamethasone until his liver function improved and he was able to receive R-CHOP. His clinical symptoms are improving, and he is again able to ambulate with a walker.

Discussion
This case illustrates the protean presentation of lymphoma and the importance of maintaining a broad differential in patients with unusual symptoms. It is important to remember that lymphoma can arise in almost any tissue and does not always present with typical lymphadenopathy. Recognition of this disease is vital to instituting proper treatment. In this case, treatment with steroids was particularly problematic, as steroids can alter the histopathological characteristics of lymphoma, further complicating the diagnosis.

References