Pseudo-electrolyte Disorders in Patients with Cancer: When Seeing Is Not Believing

By Insara Jaffer Sathick and Aisha Shaikh

Pseudo-electrolyte disorders are laboratory artifacts, and failure to recognize this entity can lead to inadvertent treatment. The hallmark of pseudo-electrolyte disorders is that the patient does not exhibit classic signs or symptoms of the underlying electrolyte abnormality. This should prompt clinicians to rule out pseudo-electrolyte disorders before initiating therapy. Here, we highlight pseudo-electrolyte disorders seen in onconephrology practice.

Pseudo-hyponatremia

A *falsely low sodium level* is seen in conditions that reduce the water content of a given volume of plasma, such as 1) severe hyperproteinemia due to paraproteinemia, hypergammaglobulinemia, or intravenous immunoglobulin (IVIG) administration; 2) severe hyperlipidemia due to cholestasis/biliary obstruction; and 3) severe hypertriglyceridemia in the setting of cancer therapy, such as tamoxifen, capecitabine, fluorouracil, docetaxel, and paclitaxel (1–4). In pseudo-hyponatremia, serum osmolality is normal, and measurement of serum sodium by direct potentiometry will confirm the diagnosis.

Pseudo-hyperkalemia and pseudo-hypokalemia

A *falsely high potassium level* can be observed in severe thrombocytosis (>500,000/mm^3) caused by myeloproliferative disorders (5). In thrombocytosis, potassium is released from the platelets after the blood is collected due to in vitro clotting; hence, potassium is falsely elevated in the serum but not in plasma because the serum sample does not contain an anti-coagulant (heparin), whereas the plasma sample does, and the presence of the anticoagulant prevents platelet degranulation in the plasma sample (6). Conversely, reverse pseudo-hyperkalemia is observed in severe leukocytosis (>70,000/mm^3) caused by leukemia or lymphoma (7). This occurs due to fragility of the white blood cell membrane, making it prone to lysis by heparin or mechanical factors, such as centrifugation, pneumatic tube transport, or other mechanical factors. This form of pseudo-hyperkalemia is commonly observed in a plasma sample, hence, the term "reverse pseudo-hyperkalemia." Although this phenomenon can also occur in serum samples, it is less likely to occur in coagulated serum samples, likely because of fibrin clot formation stabilizing tumor cells during centrifugation. To circumvent pseudo-hyperkalemia, when suspected, a whole blood sample can be collected in a blood gas-analyzing vial with rapid transport to the laboratory for potassium measurement, which will help rule out true hyperkalemia. Interestingly, pseudo-hypokalemia, a falsely low potassium level, has also been observed in patients with leukemia and leukocytosis (>100,000/mm^3). This occurs if the blood sample is stored for a prolonged period at room temperature, resulting in increased Na-K-ATPase activity and movement of potassium into the leukocytes (8).

Pseudo-hypocalcemia

A *falsely low calcium level* has been described with the use of gadolinium. (Gadodiamide [Omniscan] and gadoversetamide [OptiMARK] specifically have been reported to cause this.) Gadolinium interferes with the colorimetric assay for calcium measurement, leading to pseudo-hypocalcemia (9). This is a transient phenomenon, as gadolinium is rapidly excreted by the kidneys.

Pseudo-hypercalcemia

A *falsely high calcium level* can occur in severe thrombocytosis and is due to in vitro secretion of calcium from activated platelets (10). Pseudo-hypercalcemia has been reported in patients with paraproteinemia due to binding of calcium to abnormal immunoglobulins. In these disorders, the total calcium is elevated, but ionized calcium is normal (11, 12).

Pseudo-hyperphosphatemia and pseudo-hypophosphatemia

These can also occur in the presence of paraproteins caused by plasma cell dyscrasias and lymphoplasmacytic disorders. They are due to assay interference by the paraproteins. Likewise, liposomal amphotericin B can cause pseudo-hyperphosphatemia and pseudo-hypophosphatemia (13). Pseudo-hyperphosphatemia can also occur if the blood sample is contaminated by heparin or t-PA or with the presence of hyperbilirubinemia and hyperlipidemia. Mannitol infusion can cause pseudo-hypophosphatemia by binding to molybdate, which is used in the colorimetric assay for phosphorus measurement (14).

It is critical to recognize these spurious electrolyte disorders to avoid unnecessary interventions that can potentially lead to harmful side effects. ■

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