WHEN ALTERED BLOOD VISCOSITY ALTERS MENTAL STATUS

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Introduction

- Hyperviscosity syndrome (HVS) is an oncologic emergency that classically presents with a triad of neurological deficits, visual changes, and mucosal bleeding.
- While HVS is most commonly associated with IgM monoclonal excess due to its pentamer structure, it can rarely occur with IgA due to its dimeric configuration
- Timely diagnosis of HVS can prevent catastrophic multi-organ failure.
- Here we discuss a patient who presented with acute encephalopathy secondary to HVS with complete symptom resolution with plasmapheresis.

Case Presentation

- A 69-year-old male with a history of type 2 diabetes mellitus and hypertension presented with acute-onset encephalopathy in the setting of subacute progressive cough and worsening diffuse pain.
- Review of systems was overall limited given patient's mental status, though no obvious mucosal bleeding or visual disturbances were appreciated on exam.
- Patient was alert and oriented x2 (unsure of day) and exhibited significant tangentiality.
- Initial labs significant for Hgb 6.8 g/dl (baseline 12), Cr 1.2 mg/dl (baseline 0.9), corrected calcium 15.1 mg/dl, elevated ionized calcium 1.46 mmol/L, low PTH 6 pg/mL, normal PTHrP 0.8 pmol/L, low vitamin D 18 ng/mL, total protein 11.9 g/dl, and a gamma gap of 9.4 g/dl.
- Radiological studies showed a large malignant soft tissue mass on the right lateral chest wall with satellite lesions and extensive rib destruction suggestive of malignancy of hypercalcemia (Figure 2).
- Patient's hypercalcemia was treated with intravenous fluids, diuresis, calcitonin, and bisphosphonate therapy with complete normalization of calcium levels within two days.
- Patient remained encephalopathic despite correction of hypercalcemia, prompting further workup for encephalopathy.

Clinical Course

- A work-up for multiple myeloma was initiated, revealing IgA 6657 mg/dl, IgG 325 mg/dl, IgM < 20.0 mg/dl, two M-spikes of 3.51 g/dl and 1.03 g/dl on serum protein electrophoresis (SPEP), an elevated free kappa of 266.1 mg/L, and an elevated free kappa/lambda ratio of 20 (Figure 1).
- Given overwhelming laboratory evidence for multiple myeloma and elevated IgA levels, HVS was considered as a source of encephalopathy.
- Bone marrow biopsy was obtained. Prior to obtaining results, plasmapheresis (PLEX) was initiated and continued until symptomatic improvement (days 2-4 of hospitalization).
- Repeat IgA levels reduced to 3163 mg/dl with complete resolution of encephalopathy (Figure 1).
- Blood viscosity level drawn from prior to plasmapheresis initiation demonstrated elevation to 2.7 rel to H2O, confirming the diagnosis of HVS.
- Bone marrow biopsy confirmed a plasma cell neoplasm with plasma cells composing 80-90% of cellularity.
- In addition to plasmapheresis, patient received pulse dose dexamethasone and bortezomib prior to discharge with plans for additional daratumumab therapy thereafter.

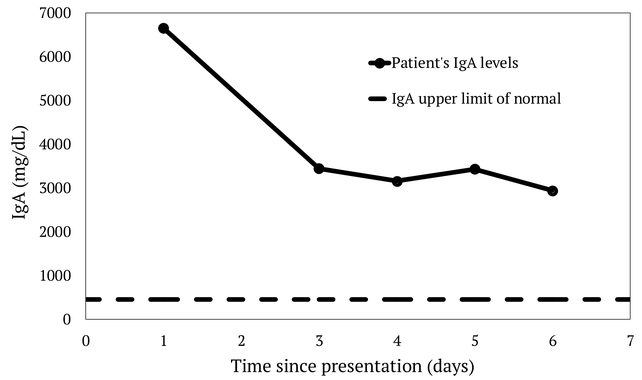

Figure 1. *IgA levels (solid line) during hospitalization with plasmapheresis occurring on days 2-4. Dotted line represents upper limit of normal for IgA levels.*

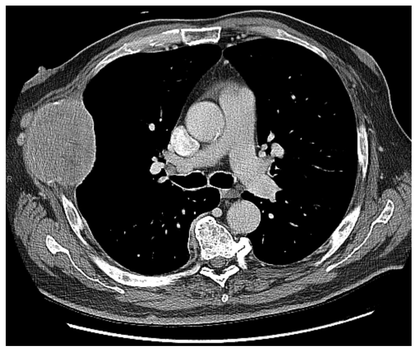

Figure 2. *CT chest demonstrating soft tissue mass along right lateral chest wall measuring 8.5 x 7.0 cm.*

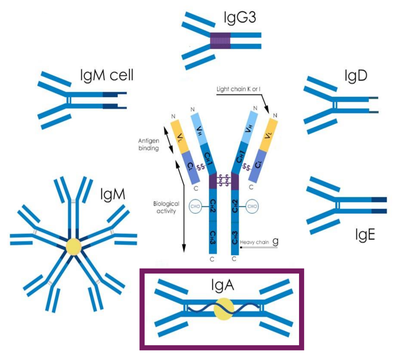

Figure 3. *Illustration of immunoglobulin structure highlighting the dimeric configuration of IgA*

Discussion

- While HVS is typically associated with IgM monoclonal excess due to its pentamer structure (particularly in Waldenström macroglobulinemia), it can rarely occur with IgA due to its dimeric configuration (Figure 3).
- HVS can drive diverse symptomatology at various blood viscosity levels, as the sluggish flow of immunoglobulin-laden blood has the potential to impair the microvascular circulation of many tissues. That being said, the most common and reliable symptoms of HVS are oronasal bleeding and visual disturbances. Our case highlights an unusual case of isolated altered mental status as the presenting feature of HVS.
- In the cases of immunoglobulin driven HVS, it is uncommon for the monoclonal immunoglobulin to be below 4000 mg/dL. Therefore, lower levels should dissuade clinicians from pursuing the diagnosis of HVS.
- Blood viscosity levels are helpful in confirming the diagnosis of HVS, but when clinical suspicion is high, results of testing should not delay treatment.
- While plasmapheresis improves the immediate symptoms and prevents long term ramifications of HVS, it does not treat the underlying disease. Therefore, concurrent initiation of chemotherapy is critical for long term outcomes.

Conclusion

- In the appropriate clinical context, the differential diagnosis for altered mental status should include HVS.
- Early treatment of HVS with plasmapheresis can be critical in preventing multi-organ damage.

References

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