Cold Agglutinin Syndrome Associated with Solid Tumor Malignancy

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Introduction

- Cold agglutinins are a type of cold-sensitive antibodies that recognize antigens on red blood cells at temperatures below normal body temperature. Classically, cold agglutinin syndrome will cause an autoimmune hemolytic anemia.
- Primary cold agglutinin syndrome occur in the absence of an underlying disorder while secondary cold agglutinin syndromes occur when cold agglutinins arise in the setting of an underlying disorder. Most typically, this is seen in the setting of infections, such as atypical pneumonia due to Mycoplasma pneumoniae or an Epstein-Barr viral infection, autoimmune disorders or lymphoid malignancies. Primary form is rare while secondary form in individuals with underlying infection or hematologic malignancy is much more common.
- The diagnostic criteria include evidence of hemolysis, positive direct Coombs test, and an elevated Cold agglutinin titer.
- We present a case of cold agglutinin syndrome thought to be associated with a nonhematologic malignancy.

Case

Subjective:
69-year male admitted with profound weakness, fatigue and a 60-pound unintentional weight loss over the last 10 months. The patient has a history significant only for smoking (30 pack year history).

Objective:
On initial exam, patient was tachycardic, hypotensive, pale and cachectic. Initial labs were most notable for a profound anemia with a Hgb of 6.4 g/dL. MCV proved high at 106fL, likely reflective of the high degree of reticulocytosis (4.53%). Hemolytic markers revealed a high LDH at 357 U/L, a high bilirubin of 2.9mg/dL and a low haptoglobin at 5 mg/dL. Peripheral blood smear revealed agglutinated red blood cells, schistocytes and a slight spherocytosis. Direct Coombs test was 4+ positive for Anti-C3D and cold agglutinin titers were greater than 1024 dils (reference range 0-64). A bone marrow biopsy was performed and unremarkable for malignancy or lymphoproliferative disorder. CT chest, abdomen and pelvis was remarkable for a hilar mass extending into the mediastinum and partial obstruction of right lower and middle bronchus (image 1 and 2). In the abdomen, there was an 8cm adrenal mass, with a cirrhotic liver and splenomegaly (image 3). CT-guided biopsy of the adrenal mass was unfortunately necrotic with non -viable tissue. Tissue analysis from bronchoscopy revealed squamous cell carcinoma.

Imaging

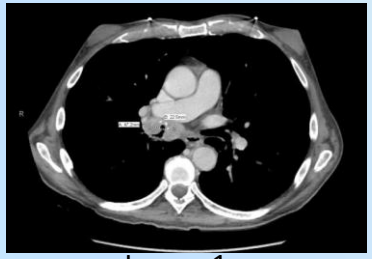
Image 1

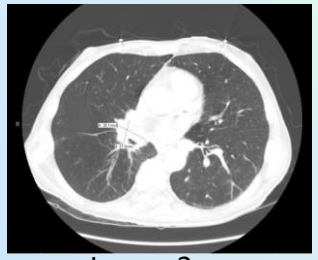
Image 2

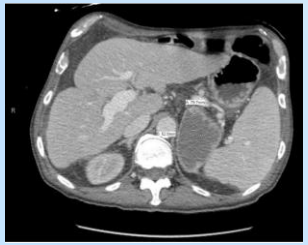
Image 3

Discussion

- Our patient was found to have an autoimmune hemolytic anemia, cold antibody type. In the absence of other data points for a more traditional cause, we believe his disease is attributable to his squamous cell lung carcinoma.
- He was treated with steroids, warmed blood transfusions and started on rituximab.
- This case highlights an interesting presentation of primary lung cancer with symptomatic anemia secondary to cold agglutinin syndrome.