When Two Rare Diseases Collide: A Case of concurrent Sarcoidosis & AL Amyloidosis

Tahminah Kausar, M.D., Shivam Singh, M.D., Divya Samat, M.D., Raesham Bukhari, M.D., Sara Khan, M.D.
Department of Internal Medicine

Introduction:

Sarcoidosis is an autoimmune multisystem granulomatous disease with an incidence of approximately 7 to 11 per 100,000 in the US. Light chain (AL) amyloidosis is a connective tissue disorder, with an incidence of 9.7 to 14.0 cases per 1 million person-years, characterized by the production of monoclonal light chains that misfold and are deposited as fibrils in organs or tissues. This case presents a rare coexistence of both conditions.

Case Presentation:

A 72-year-old male with a history of sarcoidosis, diagnosed in 2004 and intermittently treated with Prednisone and Methotrexate, developed new symptoms in July 2020. These included burning sensations in the hands and feet, balance issues, neck pain, and lower extremity edema. He was diagnosed with Immunoglobulin G (IgG) lambda Monoclonal Gammopathy of Unclear Significance (MGUS), confirmed by 4% plasma cells on bone marrow aspirate and 10% by CD138 Immunohistochemistry (IHC), with Fluorescence Insitu Hybridization (FISH) showing lambda predominance. Serum Protein Electrophoresis (SPEP) revealed an IgG lambda M spike of 0.86 g/dL.

A subsequent bone marrow biopsy indicated mild plasmacytosis with lambda predominance, and a PET scan revealed hilar lymphadenopathy consistent with active sarcoid disease. The patient also had significant nephrotic-range proteinuria of 14 grams. As his symptoms progressed, including profound difficulty in ambulating and peripheral neuropathy, the differential diagnosis included amyloidosis or Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal gammopathy, Skin changes (POEMS) syndrome. Despite a negative fat pad biopsy for AL amyloidosis, a renal biopsy confirmed Lambda AL amyloidosis with positive Congo red stain and immunofluorescence. Serum free kappa was 22.8 mg/L, lambda 43.5 mg/L, and kappa to lambda ratio 0.52. Initial treatment with Daratumumab and Lenalidomide was poorly tolerated, necessitating a switch to Pomalidomide. Neurology performed an Electromyogram (EMG)/Nerve conduction study (NCS), which showed length-dependent neuropathy and proximal myopathy, likely attributable to AL amyloidosis rather than sarcoidosis. Despite an ejection fraction (EF) of 75%, his proteinuria and leg swelling worsened, causing shortness of breath, and multiple admissions for diastolic heart failure and pleural effusions.

A fall led to hospitalization, revealing incidental findings of candida esophagitis and erosive gastritis. Ultimately, a massive pulmonary embolism led to the patient's death.

Discussion:

This case underscores the complexity of diagnosing and managing concurrent sarcoidosis and AL amyloidosis, highlighting the necessity of a multidisciplinary approach.

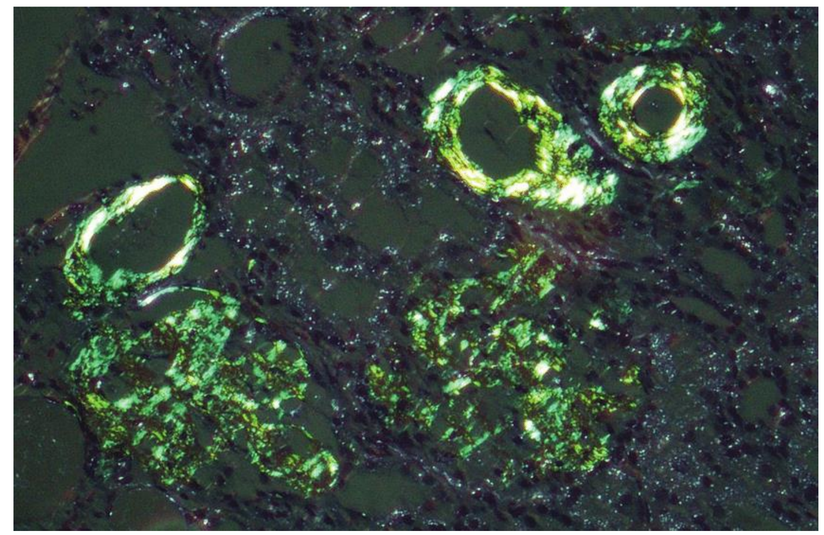

Figure: Histopathology of a kidney biopsy specimen with Congo red stain showing Apple green birefringence under polarized light

References:

- Bui A, Cortese C, Aslam N. Sarcoidosis-associated renal AA amyloidosis and crescentic necrotizing glomerulonephritis. Proc (Bayl Univ Med Cent). 2022 May 16;35(5):680-682. doi: 10.1080/08998280.2022.2072163. PMID: 35991711; PMCID: PMC9373763.
- Agarwal, A., et al. *A rare case of primary amyloidosis in a patient with stage 2 pulmonary sarcoidosis.* CHEST. 2012; 142(4): 1019A.
- Kronen R, Ziehr DR, Kane AED, VanderLaan PA, Kholdani CA, Hallowell RW. Pulmonary amyloidosis as the presenting finding in a patient with multiple myeloma. Respir Med Case Rep. 2022 Mar 18;37:101626. doi: 10.1016/j.rmcr.2022.101626. PMID: 35342704; PMCID: PMC8943293.