Systemic Immunotactoid Deposition Disease: a New Monoclonal Gammopathy of Clinical Significance

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Introduction

- Monoclonal immunoglobulin deposition disease is a rare disorder that causes components of monoclonal immunoglobulins to deposit in various tissues, which could lead to life-altering systemic complications. [1]
- This case highlights a rare presentation of this disorder.

Clinical Presentation

HPI

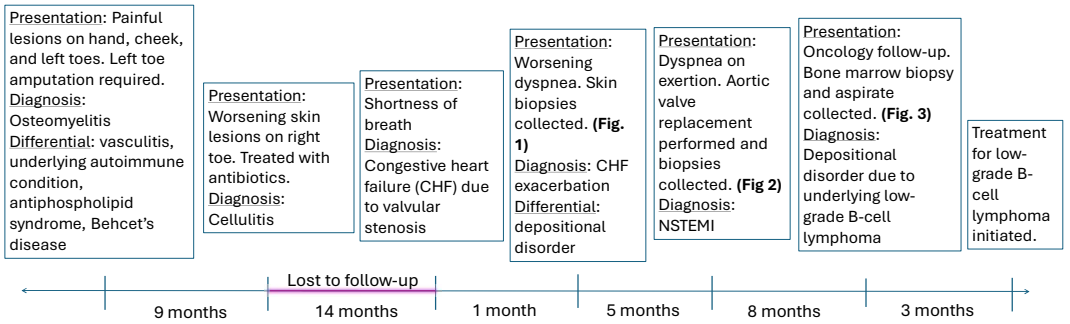
- A middle-aged woman presented with several weeks of progressive exertional dyspnea and unintentional weight loss.
- Physical exam revealed:
  - A systolic murmur
  - Severe hand and foot deformities
  - Numerous papular and nodular skin lesions on her extremities and face
  - Corneal changes
  - Peripheral neuropathy
- Infectious and rheumatologic workups were negative or inconclusive.

PMHx

- History included:
  - Multiple prior hospitalizations for erosive arthropathy with toe autoamputation
  - Untreated low-grade-B-cell lymphoma
  - A remote diagnosis of severe psoriatic arthritis
  - Valvular heart disease
- Prior records noted MYD88-positive lymphoplasmacytic lymphoma diagnosed several years prior but managed with observation due to lack of cytopenias or concerning symptoms.

Imaging

- Hand X-rays - minimal joint destruction, suggesting an extraarticular etiology and contradicting the previous diagnosis of psoriatic arthritis.
- Echocardiogram - diffuse valve thickening, severe aortic stenosis, and heart failure with reduced ejection fraction.
- Laboratory evaluation revealed elevated inflammatory markers:
  - HsCRP – 91 mg/L
  - CRP – 38 mg/L
  - ESR – 35 mm/hr



Pathological Findings

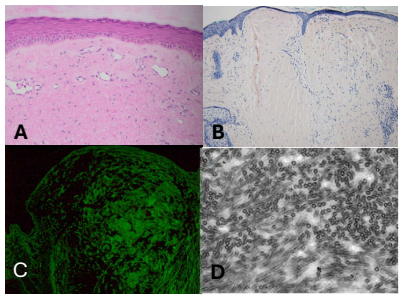


Figure 1. Dermatologic findings upon presentation. **(A)** H&E stain of a red firm papule skin shave from the toe. Centrally eosinophilic amorphous collagen-like fibers surrounded by spindled fibroblasts are present. **(B)** Congo Red stain of cheek skin biopsy. The lack of birefringence suggests no amyloid deposition. **(C)** Immunofluorescence of the left cheek highlights dermal nodules staining for IgG and kappa. **(D)** Electron microscopy (EM) of the toe revealed extensive infiltration of homogenous and elongated microtubules occasionally arranged in parallel bundles.

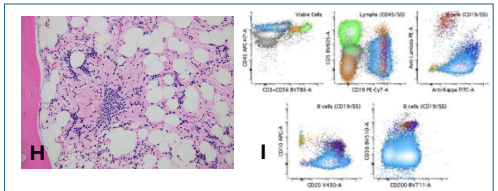


Figure 3. Results from bone marrow evaluation. **(H)** H&E stain of bone marrow. This image revealed MYD88+ lymphoplasmacytic lymphoma, a known underlying clone in IgG1-kappa monoclonal deposition disease. Intermittent areas of increased cellularity comprised of atypical small lymphoid infiltrates. **(I)** Flow cytometry results of bone marrow aspirate revealed abnormal B cell and plasma cell populations with an increased kappa to lambda ratio.

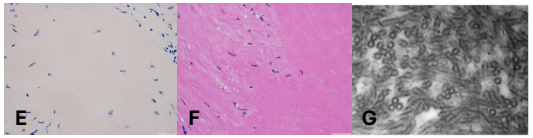


Figure 2. Aortic valve biopsy results. **(E)** Congo Red stain of the aortic valve lacked birefringence, suggesting no amyloid deposition. **(F)** H&E stain shows fibrous tissue with eosinophilic stroma. The biopsy was subject to tandem mass spectrometry (MS) studies to determine the nature of the eosinophilic stromal material. **(G)** EM of aortic valve leaflet. The image shows extensive infiltration of microtubules, formed by IgG1-kappa monoclonal immunoglobulin, bundled in parallel arrays throughout the tissue. These show the same monoclonal immunoglobulin deposition process that was detected in the skin.

Key Highlights

- Immunofluorescence dermatologic findings highlighted restriction to IgG and kappa light chains, suggesting a monoclonal process. **(Fig. 1)**
- A lack of birefringence on both Congo Red stains of the left cheek and aortic valve leaflet biopsy makes amyloidosis not likely. **(Fig. 1, Fig. 2)**
- Results from the EM of the skin and aortic valve leaflet show an identical microtubule infiltration due to IgG1-kappa deposition. This suggests systemic involvement of the patient's depositional disease. **(Fig. 1, Fig. 2)**
- Identification of MYD88+ lymphoplasmic lymphoma, a known underlying clone of IgG1-kappa monoclonal deposition disease, in the bone marrow confirmed its role as the likely causative agent of the patient's systemic symptoms. **(Fig. 3)**

Evidence/ Literature

- Monoclonal gammopathies forming immunotactoids are primarily associated with immunotactoid glomerulopathy [1], with only rare case reports involving extrarenal tissues [3,4].
- The skin findings here mimicked macroglobulinosis, which is typically IgM-associated and lacks immunotactoids [5].

Discussion/ Conclusions

Unique Aspects

- With this disorder, renal involvement is common and significant. Very few cases in the literature report extrarenal involvement.
- This case features systemic, biopsy-proven immunotactoid deposition with multiorgan involvement, broadening the known clinical spectrum of this disorder.

Management

- Initiated 6 cycles of bendamustine and rituximab following identification of IgG1-kappa deposition disease as the likely cause of the patient's systemic symptoms.

Takeaways

- This multisystem presentation underscores the body as an interconnected unit.
- Recognizing extrarenal immunotactoid deposition enabled a unifying diagnosis and individualized therapy, highlighting the value of holistic assessment.
- Access to novel methodologies, like tandem MS, allow for more precise diagnoses which could lead to earlier treatment and halt the disease process before irreversible organ damage occurs.

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