

A case of paraproteinemia-associated scleredema successfully treated with thalidomide



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INTRODUCTION

Scleredema is a sclerotic skin disease that typically occurs in association with an underlying disorder, such as diabetes mellitus, a poststreptococcal infection, or a paraproteinemia. Twenty-five percent of patients with scleredema are found to have a paraproteinemia-associated scleredema (PAS).¹ A literature search of 3 databases (PubMed, Clinical Key, Google Scholar) did not find a case documenting the successful use of thalidomide treatment in PAS; however, a single case of unsuccessful use of thalidomide did respond to intravenous immunoglobulin (IVIg).² Because our patient was not covered by Part B Medicare for IVIg for PAS, and there is known risk for multiple myeloma (MM) to evolve from monoclonal gammopathy of unknown significance (MGUS), we empirically chose thalidomide as our initial therapy. We report on a patient with an IgA MGUS, whose PAS was successfully treated with thalidomide.

CASE REPORT

An 81-year-old African-American man with ankylosing spondylitis and IgA MGUS presented with 5 years' progressive skin thickening of the thorax, face, and bilateral upper extremities. Movement was limited by woody and indurated areas of the skin. Rheumatologic workup was negative for systemic sclerosis. Serum protein electrophoresis and immunoelectrophoresis showed IgA- κ bclonal pattern; urine immunofixation electrophoresis and

Abbreviations used:

IVIg:	intravenous immunoglobulin
MGUS:	monoclonal gammopathy of unknown significance
MM:	multiple myeloma
PAS:	paraproteinemia-associated scleredema

urine protein electrophoresis showed no monoclonal protein; κ -free light chains were elevated; skeletal survey was negative; and IgA was 2011 mg/dL. Bone marrow biopsy found atypical plasma cells (7%) and normocellular marrow with trilineage hematopoiesis. Flow cytometry found monoclonal plasma cells (2% of total cells) with immunophenotypes of CD138hi, CD45dim⁺, CD19⁻, CD20⁻, CD117⁺, CD56⁻, and cytoplasmic κ . Skin biopsy revealed a thickened reticular dermis with large collagen bundles separated by space containing mucin (Fig 1).

Oral daily thalidomide, 50 mg, was initiated then escalated to 100 mg daily in combination with dexamethasone orally, 20 mg once a week. Mild improvements at 3 months continued, and, after 1 year, IgA levels were consistently less than 500 mg/dL with markedly reduced stiffness, increased mobility, and diminished skin induration (Fig 2).

Total duration of therapy is approximately 3 years to date without significant adverse effects. If the patient continues to tolerate this regimen, then he will continue indefinitely (Fig 3).

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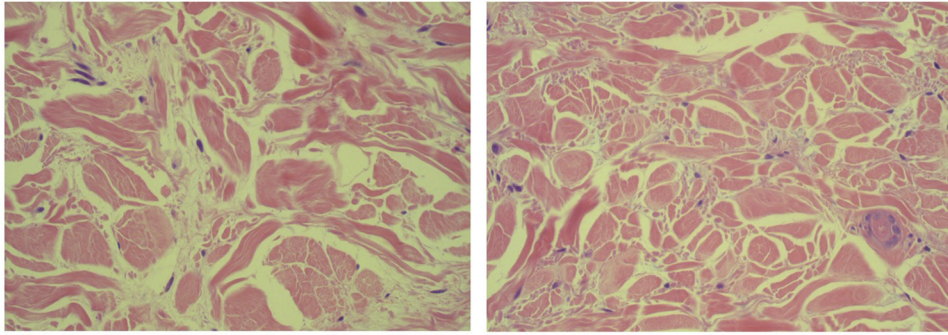


Fig 1. Scleredema histopathologic findings. Histopathologic findings of scleredema include thickened reticular dermis and large collagen bundles separate by space containing subtle evidence of mucin (*blue-grey tinge*).

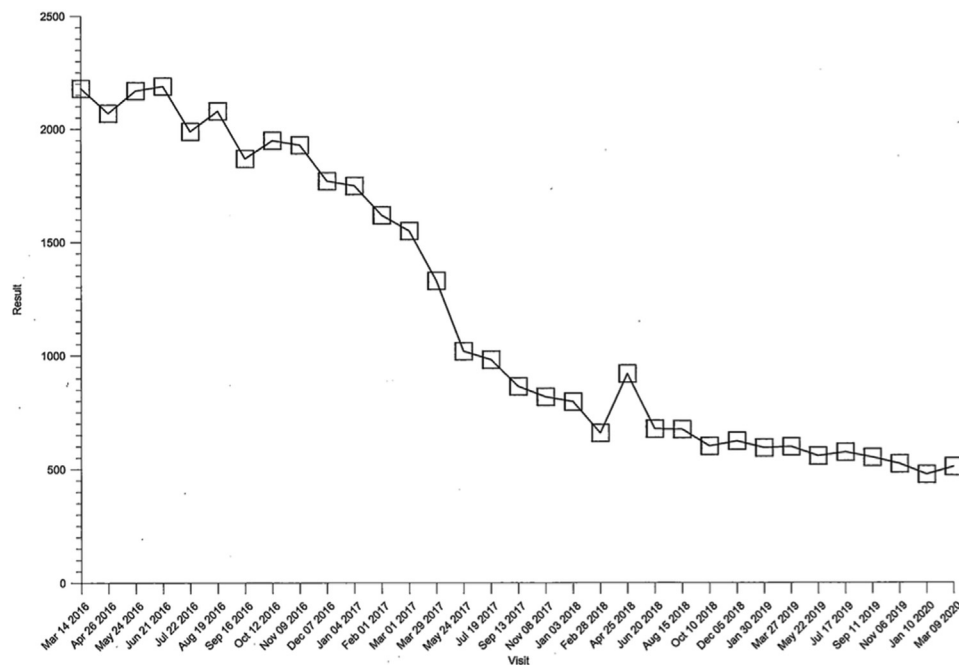


Fig 2. IgA Level (mg/dL) versus time (mos). Graph shows decrease in IgA level over time with thalidomide treatment.

DISCUSSION

The cutaneous diagnosis in our patient was an IgA- κ paraprotein-associated scleredema. Only 40 patients with PAS have been reported to date, and more than 80% have IgG (κ or λ).⁵ We could find only 6 cases of IgA PAS.^{1,2,4-6} Four of these cases were noted in only a tabular form without other clinical information. Only 2 patients were detailed in a clinical case report.

Thalidomide has known activity in plasma cell myeloma. Multiple criteria exist for stratification of patients with MGUS or smoldering myeloma (SM) deemed at high risk of transformation to MM.⁶ Three parameters used to stratify MGUS risk as low versus high are (1) IgG subtype versus non-IgG subtype, (2)

M protein concentration less than 1.5 gm/dL versus ≥ 1.5 gm/dL, and (3) normal versus abnormal serum-free light chain ratio. Our patient had 3 of 3 risk factors indicating a 58% chance of progression to MM over the next 20 years.⁷ In addition, cases of long-standing scleredema in which MGUS progressed to overt MM tend to have a more aggressive course.⁸

Several important factors led us to choose empiric off-label thalidomide for our patient: (1) Neither MGUS nor PAS are currently listed as covered conditions for IVIg by the Centers for Medicare & Medicaid Services. (2) There was a higher risk profile of progression from MGUS to MM in our patient. (3) Thalidomide is recommended as second-line use for



Fig 3. Patient pictures of hands and lower extremities. Pictures of skin show woody induration before treatment with thalidomide.

many types of sclerosing diseases of the skin in patients not at risk of pregnancy.⁹ In light of the gratifying sustained response to thalidomide and the emerging understanding and consensus recommendations for patients with MGUS at high risk of progression to MM, perhaps thalidomide should be reconsidered as first-line therapy in some PAS cases deemed at high risk of progression to MM. IVIg, if a covered benefit, can be reserved for those who do not clinically respond or are intolerant to thalidomide. Ultimately, the results of a long-term trial to assess whether higher-risk MGUS patients will benefit from thalidomide or similar agents may help guide the optimal initial therapy.

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