entinedihydrochlorideinthisinterdisciplinarycase. Forthere-
remaininglesions,weofferedliquidnitrogencryotherapyorab-
lative laser resurfacing to the patient. Unfortunately, the patient
was subsequently lost to follow-up.

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gene is a putative copper transporting P-type ATPase similar to the Menkes
2.RobertsEA,SchilskyML;AmericanAssociationforStudyofLiverDiseases
3.IozumiK,NakagawaH,TamakiK. Penicillamine-induced degenerative
4.RosenLB,MuellenhoffM,TranTT,MuhartM. Elastosis perforans serpiginosa
secondary to D-penicillamine therapy with coexisting cutis laxa. Cutis.
5.BardachH,GebhartW,NiebauerG. “Lumpy-bumpy” elastic fibers in the skin
and lungs of a patient with a penicillamine-induced elastosis perforans

Cutaneous Rosai-Dorfman Disease Successfully
Treated With Low-Dose Methotrexate

In 1969, Rosai and Dorfman1 first described a series of pa-
tients with sinus histiocytosis with massive lymphadenopa-
thy, characterized by histiocytic infiltration of lymph nodes and
tissue. To our knowledge, as of 2006, there were a total of 86
reported cases of cutaneous Rosai-Dorfman disease (CRDD) in
the literature,2-3 with several additional cases reported since
then.

Report of a Case | An African American woman in her 50s re-
ported a sudden eruption of dozens of facial papules and nod-
ules 3 months previously and a 7-month history of a groin
plaque. She had been treated with cefadroxil, topical clobeta-
sol, oral prednisone, and a short course of oral isotretinoin
without significant benefit.

Physical examination revealed approximately 75 pink-
domed papules on the cheeks, upper lip, and chin (Figure 1
and dozens of red-brown papules becoming confluent on the
right inguinal and suprapubic skin. Laboratory examination
revealed a mildly elevated erythrocyte sedimentation rate (32
mm/h) and total triglyceride levels (145 mg/dL). Findings of
complete and differential blood cell counts, a comprehensive
metabolic panel, serum protein electrophoresis, and a light
chains assay were within normal limits. Complete computed
tomography of the chest, abdomen, and pelvis revealed no
significant retroperitoneal, mesenteric, or pelvic lymphadenop-
athy. Biopsies from the groin revealed a dense infiltrate of lymph-
cytes and large histiocytes with abundant pale cytoplasm
(Figure 2). The histiocytes showed emperipolesis of lympho-
cytes and occasionally red blood cells. The histiocytes seen in
CRDD stain positively for macrophage marker CD68. The hist-
opathologic differential diagnosis also includes Langerhans
cell histiocytosis. While S-100 may stain positively in both
CRDD and Langerhans cell histiocytosis, findings of CD1a staining
are characteristically negative in CRDD. In our case, cells
did not stain with melanocyte markers Melan-A or HMB45 or
with cytokeratin AE1/AE or CD34 as in epithelioid sarcoma.
Findings of acid-fast bacilli and Grocott methenamine silver
stainings were negative.

The patient’s prednisone dose was tapered, and she be-
gan treatment with oral methotrexate, 15 mg once weekly, and
significant improvement was noted over the next 11 months.
Subsequently, the methotrexate dose was tapered to 5 mg

Figure 1. Clinical Images Showing Gradual Improvement in Facial Papules

A
B
C

Patient observed at 1 month (A), 8 months (B), and 14 months (C) after initiation of treatment with methotrexate.
The exact cause of CRDD remains unknown, the presence of Epstein-Barr virus, human herpesvirus 6 by polymerase chain reaction, and reported eruption after vaccination with spontaneous remission over months to years suggests that CRDD is a benign reactive process involving a particular pattern of immune dysregulation. Early diagnosis remains a challenge in CRDD owing to its nonspecific clinical manifestations, including variable numbers of papules, nodules, plaques, or tumors. Timely diagnosis and initiation of methotrexate therapy may be key to effecting a rapid clinical remission while this disease remains in its active phase.

Discussion | There have been a variety of treatment techniques used for CRDD, including cysterotherapy, surgical excision, irradiation, oral corticosteroids, dapsone, thalidomide, and isotretinoin. To our knowledge, the use of methotrexate alone or in combination with other agents has been reported in 9 cases of systemic Rosai-Dorfman, and a complete or partial response was reported in most cases.4 By contrast, methotrexate therapy has been reported in only 3 cases of CRDD, and partial or no improvement was reported.3,5,6 However, in all of these cases, the eruption had already been present for well over a year. In our patient, a lack of response to prednisone, preexisting diabetes, and significant disease burden prompted the choice of low-dose methotrexate, to which a complete clinical response was seen over 11 months.

Though the exact cause of CRDD remains unknown, the presence of Epstein-Barr virus, human herpesvirus 6 by polymerase chain reaction, and reported eruption after vaccination with spontaneous remission over months to years suggests that CRDD is a benign reactive process involving a particular pattern of immune dysregulation. Early diagnosis remains a challenge in CRDD owing to its nonspecific clinical manifestations, including variable numbers of papules, nodules, plaques, or tumors. Timely diagnosis and initiation of methotrexate therapy may be key to effecting a rapid clinical remission while this disease remains in its active phase.

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Paraproteinemia-Associated Scleredema Treated Successfully With Intravenous Immunoglobulin

Scleredema is a fibromucinous connective tissue disease characterized by symmetric, nonpitting edema and induration of the face, neck, and trunk. Although the pathogenesis remains elusive, associations with infection, diabetes mellitus, and paraproteinemia have been established.1 Paraproteinemia-associated scleredema is typically characterized by a progressive course, for which no standard therapeutic protocol exists.2 To our knowledge, the patient described herein represents the first reported case of scleredema with paraproteinemia successfully treated with intravenous immunoglobulin (IVIG).

Report of a Case | A woman in her 40s presented with a 2-year history of progressive erythema and induration of the face, neck, and upper trunk. She denied a history of preceding infection or diabetes mellitus. Physical examination revealed erythema, brawny edema, and induration of the face, neck, upper trunk, and upper arms. There was significant limitation of neck flexion, extension, and lateral rotation as well as shoulder abduction and internal rotation (Figure A). The patient denied difficulty swallowing or restricted breathing.

A skin biopsy from the upper back revealed dermal thickening with separation of enlarged collagen bundles by Alcian blue-positive mucin deposition, consistent with a diagnosis of scleredema. Findings from a complete metabolic panel, complete blood cell count, and assays for fasting glucose and glycosylated hemoglobin levels were within normal limits. Serum protein electrophoresis revealed an abnormal globulin peak. Immunofixation confirmed an IgA κ-band, and serum IgA level was elevated (933 mg/dL; normal range, 140-260 mg/dL). Investigation for multiple myeloma was negative, with normal findings on skeletal survey, bone marrow biopsy, and urine

Figure 2. Biopsy Specimen Taken From the Patient’s Groin

A dense infiltrate of lymphocytes, neutrophils, and large histocytes with abundant cytoplasm; histiocytes show emperipolesis of lymphocytes (hematoxylin-eosin, original magnification ×40).