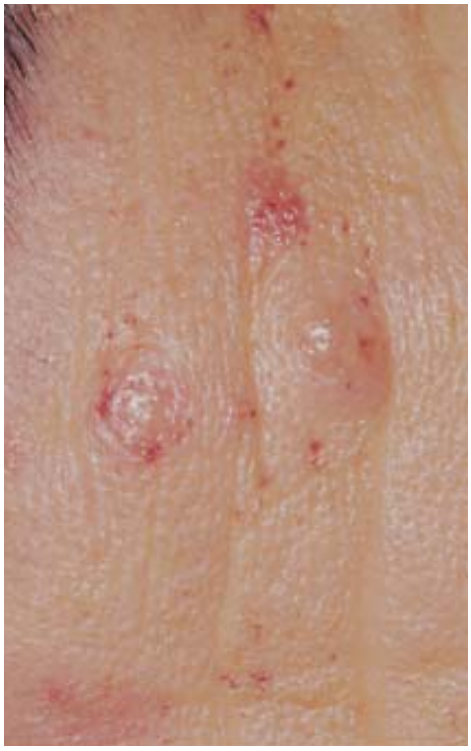
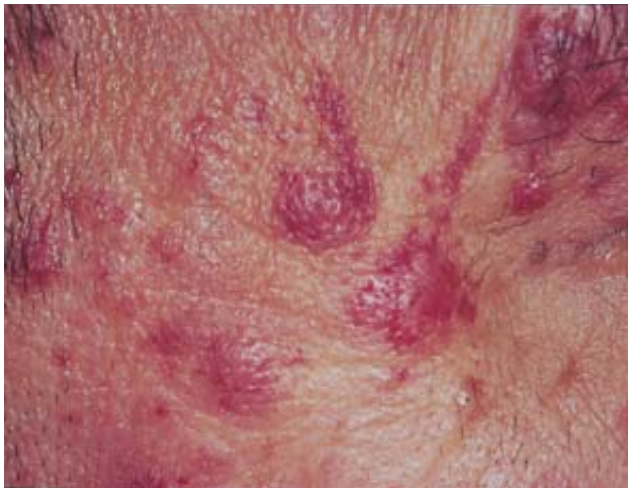
What Is Your Diagnosis?





A 58-year-old Hispanic man presents with a several-month history of asymptomatic, waxy, purpuric papules appearing in crops on his face.

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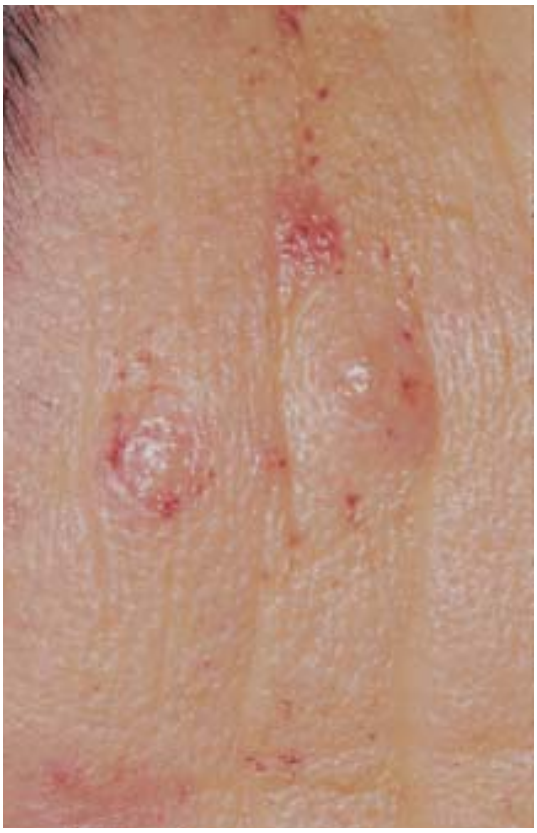
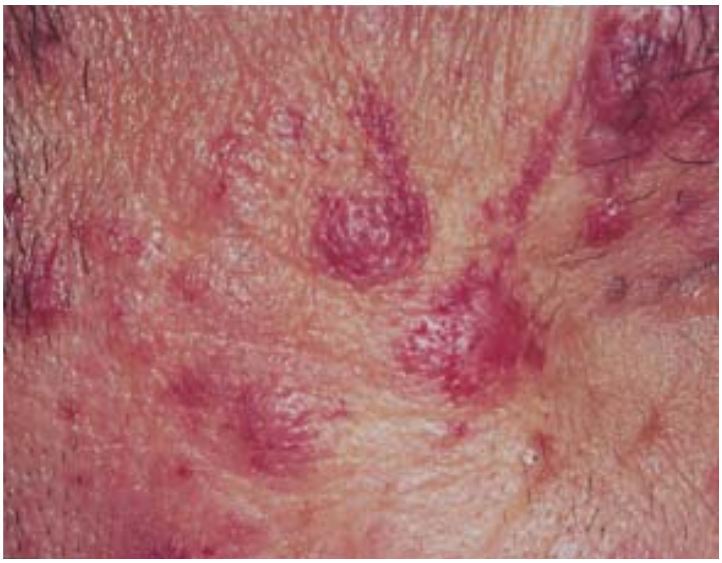
The Diagnosis: Primary Systemic Amyloidosis





Amyloidosis is a general term for a group of disorders with abnormal extracellular deposition of proteins. The protein consists of an amyloid P component along with different types of amyloid fibrils.[1] The various types of amyloids are classified according to the clinical presentation and type of fibril deposit.

The extracellular deposits resulting from amyloidosis can be widely distributed throughout the organs of the body as in systemic amyloidosis, or they can occur as primary localized cutaneous lesions. Primary localized cutaneous amyloidosis consists of 3 subtypes: macular amyloidosis, lichen amyloidosis, and nodular amyloidosis. The systemic forms of amyloidosis consist of primary systemic amyloidosis (AL amyloidosis) and secondary systemic amyloidosis (AA amyloidosis).

AL amyloidosis is a manifestation of plasma cell dyscrasia. The accumulated amyloid deposits originate from monoclonal immunoglobulin light chains, most commonly of the λ type, produced by an abnormal population of plasma cells. AA amyloidosis occurs secondary to chronic inflammatory disease, such as leprosy or familiar Mediterranean fever. Clinically, patients with AA amyloidosis show few or no characteristic skin lesions, but skin biopsy may be helpful in establishing the diagnosis.[2]

AL amyloidosis can begin with a nonspecific pattern of vague complaints, such as fatigue, weight loss, carpal tunnel syndrome, or dyspnea. The most common cutaneous findings result from amyloid deposits in blood vessel walls; the walls become fragile, resulting in purpura occurring spontaneously or in areas of trauma. Referred to as pinch purpura, such lesions occur commonly on the eyelids. Periorbital purpura can occur following increased pressure from coughing, sneezing, or other Valsalva-type maneuvers and may be noted following proctoscopy. Other characteristic lesions are smooth shiny papules, plaques, and nodules in flexural areas. Deposits on the tongue result in macroglossia, with characteristic molding along the teeth. Dysphagia and dysphonia also may occur.[3] Less common cutaneous findings in AL amyloidosis include chronic paronychia, palmodigital erythematous swelling, and induration of the hands.[4] Sclerodermalike changes also have been reported.[5]

In cases of AL amyloidosis, results of skin biopsy specimens stained with hematoxylin and eosin reveal amorphous, eosinophilic, fissured masses that may be separated from the epidermis by a thin zone of collagen.[6] Deeper aggregates can occur, which surround and commonly involve blood vessel walls, sweat glands, and fat cells. Thioflavin T is a highly sensitive fluorescent stain for amyloid.[7] Amyloid stains orange with Congo red and exhibits an apple-green birefringence when polarized.[8]

AL amyloidosis affects men more often than women and usually occurs in individuals older than 40 years. Multiple myeloma occurs in about 30% of cases. The prognosis for AL amyloidosis is poor—death often results from cardiac or renal failure within approximately 2 years after onset.[9]

The treatment for AL amyloidosis is problematic. Overall survival of patients with AL amyloidosis is significantly reduced when amyloid deposits involve more than 2 major organ systems and when there is predominate cardiac involvement.[10] Two major trials using different regimens of intermittent oral melphalan and prednisone have supported the efficacy of these drugs in the treatment of AL amyloidosis.[11] Treatment with high-dose melphalan in combination with autologous blood–stem-cell support can result in complete remission of the plasma-cell dyscrasia.[12] However, high mortality rates have been reported—reaching 40% in some series. This high rate appears to be related to multiorgan failure of amyloid-infiltrated tissues.[13]

High-dose dexamethasone with interferon has been reported to be effective in treating patients with AL amyloidosis without cardiac involvement. However, the response rate to this therapy is less than 15% and, thus, it should only be considered when alternatives do not exist.[14] Reports from Japan have shown that the use of daily oral dimethyl sulphoxide in combination with chemotherapy can decrease the number of plasma cells in the bone marrow and improve some of the manifestations of AL amyloidosis.[15]

Newer studies have focused on the serum amyloid P component targeting the inhibition of fibril precursor proteins with resultant regression of the amyloid deposits.[16] Anthracycline 4′-iodo-4′deoxydoxorubicin has an affinity for amyloid fibrils and may interfere with or reverse the amyloid deposition.[17] Clinical effects of anthracycline 4′-iodo-4′deoxydoxorubicin have not been shown to sufficiently alter the course of AL amyloidosis, and only a small number of patients with the disease respond.[18] The durability of remission and the effect on survival remain to be determined.

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