Myeloma-associated Systemic Amyloidosis with an Extensive Cutaneous Involvement

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Sir,

Amyloidosis refers to a group of disorders characterized by extracellular deposition of insoluble beta-pleated protein fibrils in various organs.[1] Cutaneous deposition of amyloid may represent localized cutaneous amyloidosis or a manifestation of systemic involvement.[2]

Primary systemic amyloidosis (PSA) mostly occurs in the setting of plasma cell dyscrasias.[1] It is difficult to diagnose as it usually presents with nonspecific symptoms.[2] Mucocutaneous manifestations occur in 29%–40% of cases and provide important diagnostic clues.[3] We report an atypical case where an unusually extensive cutaneous involvement provided the first sign of a widespread multiorgan infiltration by amyloid protein and eventually led to the diagnosis of multiple myeloma.

A 56-year-old woman presented with nonitchy, raised confluent lesions over the face of 1-year duration. She complained of an enlarged tongue causing dysphagia and hoarseness of voice for the past 3 months. She also gave 1-year history of numbness of fingertips and severe constipation.

Cutaneous examination revealed numerous skin colored, shiny, infiltrative waxy papules, coalescing into plaques, over central face, involving the eyes, nose and mouth, including the eyelids and lips [Figure 1a]. Similar lesions were identified in retroauricular, axillary, inframammary, and periumbilical areas. Tense, erythematous swelling, and induration of the lateral nail folds of fingers were present [Figure 1a]. Multiple purpuric macules were noted in axillae and groins. Oral evaluation [Figure 1b] revealed a rigid, enlarged tongue pressed with tooth indentations. Subepithelial petechiae were present on the buccal mucosa. Gingival enlargement was observed.

Laboratory investigations showed severe anemia (Hb - 6.2 g/dL), hypoalbuminemia (2.7 g/dL), and hypercalcemia (14.1 mg/dL). Total protein count was normal (6.4 g/dL). Thyroid profile was normal. Erythrocyte sedimentation rate was significantly elevated, 122 mm/h. A 24-h urine test revealed proteinuria, 1.88 g/day. Immunoelectrophoresis demonstrated monoclonal light chains in blood and urine. Radiologic evaluation and abdominal ultrasonography detected no abnormality. Echocardiography revealed restrictive cardiomyopathy.

Histopathological examination of the skin biopsy showed an eosinophilic homogenous material in dermis on hematoxylin-eosin staining [Figure 2a]. The dermal deposits stained strongly with Congo red [Figure 2b] and exhibited green birefringence when viewed under polarized light. Verhoeff-van Gieson stain for collagen and Alcian blue stain for mucin were negative. On bone marrow biopsy, about 60% of total nucleated cells comprised mature and immature plasma cells.

The patient was diagnosed with amyloidosis involving the skin, oral cavity, heart and probably kidney and nerves; associated with multiple myeloma. She was started on the chemotherapeutic regime as advised by hematology department. Four months after diagnosis, the patient developed left-sided heart failure presumably due to cardiac amyloidosis and died.

This case presents a plethora of cutaneous findings which were atypical in the respect that the characteristic purpuric rash was preceded by infiltrative papules on face lacking a hemorrhagic component. Infiltrative lesions coalescing to form large tumified areas with such gross distortion, as in our case, is a rare presentation.

Our first clinical differential, in this case, was papular mucinosis because of the absence of facial purpurae typical
of amyloidosis. However, absence of mucinous deposits ruled out the former. Another differential suggested by cutaneous nodules, macroglossia and hoarseness, is lipoid proteinosis.[1] Although it is a genetic disease, a few rare late-onset cases have been reported.[4] Strong Congo red staining favored the diagnosis of PSA. Finally, the third differential would be the rare variant of localized cutaneous amyloidosis - nodular or tumefactive form. In such a case, aggressive therapy is not required, but complete evaluation and follow-up to detect evolution into the systemic disease are necessary.[3]

The median survival of idiopathic amyloidosis is 2.1 years and is reduced to 5 months when associated with myeloma.[5] Although the current therapy with alkylating agents results in a limited response, newer approaches like autologous stem-cell transplantation may offer possibility of long-lasting response, provided the disease is recognized in early stages.[1]

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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