

## Cutaneous amyloidosis masquerading as cutaneous metastasis: a rare report with unusual presentation

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### ABSTRACT

**Aim:** To report a case of cutaneous amyloidosis that mimicked metastatic malignancy clinically. **Methods and results:** A 65-year-old-male, presented with nodular cutaneous swellings all over the body extending from scalp to the extremities and trunk with a lesion on tongue. History of tobacco chewing and smoking was present since last 20 years. Fine needle aspiration cytology (FNAC) of the skin nodules and imprint cytology of the tongue lesion showed abundant extracellular material resembling tumor necrosis, with interspersed squamous cells. Positive clinical findings and equivocal FNAC findings favoured malignancy. However, histopathological findings of skin nodules and tongue lesion were consistent with cutaneous amyloidosis. **Conclusions:** Cutaneous amyloidosis mimicking malignancy is rarely reported earlier in literature. This report emphasizes that cutaneous amyloidosis should always be considered in cases of multiple skin lesions, suspected of malignancy with skin metastasis.

**Key words:** Amyloidosis,Cutaneous nodules,masquerading,metastasis

### Introduction

Amyloidosis is extracellular amorphous eosinophilic deposition of amyloid fibrils in various tissues. In cutaneous amyloidosis, the deposition occurs predominantly in the dermis[1]Cutaneous amyloidosis is reported to be of macular, lichenoid and nodular types. Nodular type of cutaneous amyloidosis is rare and reported to be plasma cell derived, consisting of AL type of amyloid fibrils[2].We report a rare case of nodular cutaneous amyloidosis involving multiple skin sites, mimicking malignancy.

### Case Report

A 65-year-old-male presented with complains of multiple nodular skin lesions distributed over scalp (Fig. 1a) neck, trunk and extremities (Fig. 1b) with a lesion on tongue, from the last six months. There was history of tobacco chewing and smoking since last 20 years. No history of fever, significant weight loss, family history or evidence of any chronic systemic

illness, autoimmune disease or drug intake was present. There was no lymphadenopathy or organomegaly. CT scan of the chest and abdomen were unremarkable. Routine hematological, biochemical and urine examination tests were normal. Serum protein electrophoresis and urine protein electrophoresis findings were within normal limits. Autoantibodies, including antinuclear antibody, anti double-stranded DNA, anti-SS-A (Ro) antibody, and anti-SS-B (La) antibody, were all negative. Fine needle aspiration cytology (FNAC) of the skin nodules and imprint cytology of tongue lesion revealed abundant amorphous material resembling tumor necrosis with admixed interspersed squamous cells. In view of positive clinical history of smoking and tobacco chewing and equivocal cytological findings, a diagnosis of malignant tongue lesion with metastasis to skin was suspected. May-Grünwald Giemsa (MGG) staining of the FNAC smears revealed abundant bluish amorphous extracellular material (Fig. 2). Hematoxylin and Eosin (H&E) stained sections of both skin and tongue lesions revealed deposition of extracellular, eosinophilic material in the dermis (Fig. 3). The deposits were also seen in peri-appendageal and perivascular regions. The deposition was found to be Congo-red positive (Fig. 4) and showed characteristic apple-green birefringence under polarizing light (Fig.

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5), consistent with amyloid. Infiltration by inflammatory cells including plasma cells was seen in dermis with accentuation in perivascular regions. Moreover, immunohistochemically, the amyloid in the present case was AL type as the plasma cells showed cytoplasmic positivity to kappa light chain. Based on clinical, FNAC and histopathological findings, a diagnosis of cutaneous amyloidosis (CA) was made. Further, rectal and abdominal fat pad biopsy and kidney biopsy of the patient were then done and looked for any systemic involvement by amyloid deposits but were found to be negative. Also, bone marrow examination was then done, and was found to be negative for any signs of hematological malignancy.

### Result and Discussion

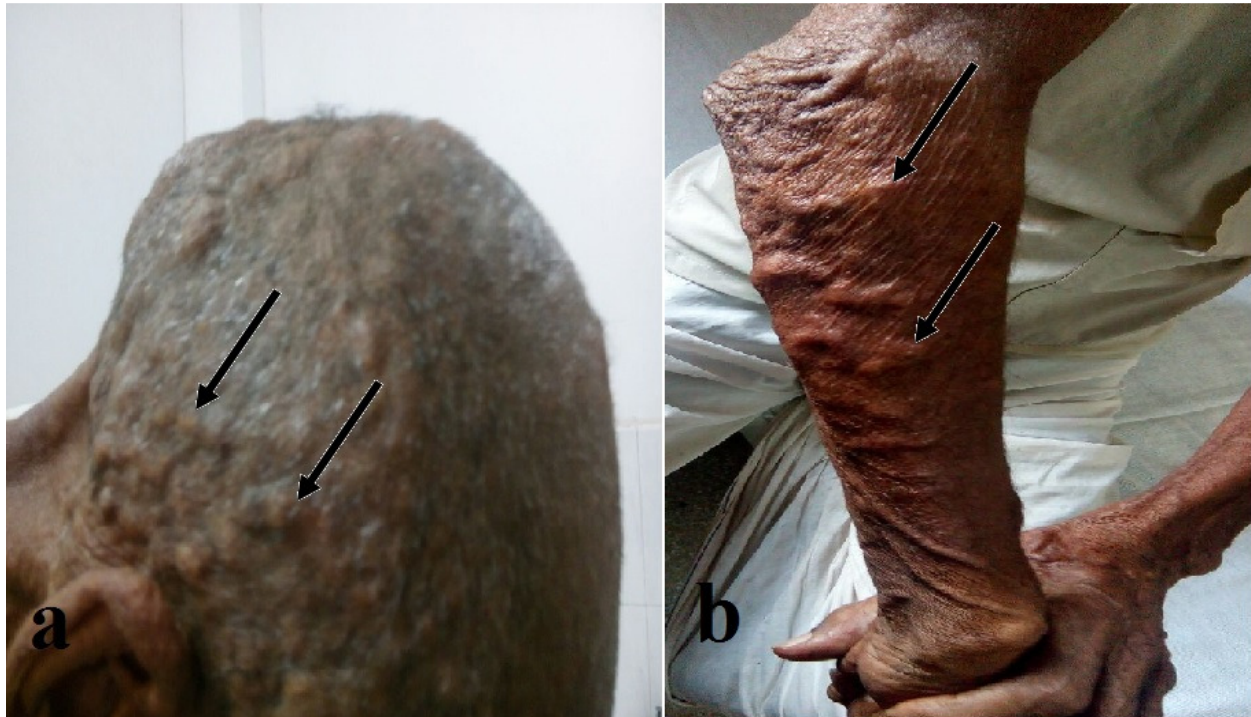
The findings in this case were diagnostic of cutaneous amyloidosis (CA). The amyloidosis in skin has been reported to be of Macular, Lichen and Nodular types. Nodular CA, as was seen in the present case, is typically a benign, asymptomatic disease, limited to the skin[1].The nodular CA is reported to be derived from plasma cells, in contrast to lichenoid or macular amyloidosis, which are keratinocyte-derived[1,2].The plasma cells, in the present case showed immunohistochemical positivity to kappa light chain, confirming the amyloid deposition to be AL type.CA has been reported to be associated with autoimmune disorders[3].Some cases, have history of preceding trauma[4].Presently, no such association with autoimmune disease or trauma was observed. The differential diagnosis in the present case included nodular colloid milium, cutaneous metastatic disease, neurofibromatosis, rheumatoid nodules, cutaneous sarcoidosis, cutaneous leiomyomas, cutaneous lymphoma, nodular kaposi sarcoma and lipomatosis. The findings in this case were diagnostic of nodular CA, distinguishable from these lesions by its distinctive histological features. Nodular Colloid milium or dermal hyalinosis is a rare cutaneous deposit disease of colloid degeneration. It is characterized by the presence of multiple nodules and shows same staining pattern as nodular CA on light microscopy, with deposition in the dermis [5]. However, congo-red positivity and apple-green birefringence on polarizing microscopy in the present case, confirmed the presence of amyloid. Cutaneous metastasis may also present as non-tender, firm, nodular lesions, primarily from a melanoma or metastasis from breast or lung carcinomas. The incidence of metastasis from oral cavity, presenting as nodular skin lesions, as was suspected in the present case, is reported to be only 6.2 percent [6].The present case lacked histopathological

features of malignancy. Patients with rheumatoid arthritis may develop extra-articular subcutaneous nodules, involving deep and superficial dermis, but histologically shows central necrobiotic zone, surrounded by palisading histiocytes, chronic inflammation and fibrosis[7].There was no evidence of such autoimmune process in the present case. However, the fibrosis in rheumatoid nodules may sometimes resemble amyloid on light microscopy, but is congo-red negative and does not show apple-green birefringence on polarized microscopy.Multiple dermal neurofibromas also present with firm, subcutaneous nodules over body and may involve the deep dermis but are usually associated with neurofibromatosis[8]. There were no such manifestations or family history in the present case. Also, histologically, neurofibromas are composed of spindle cells with wavy nuclei in a loose acidophilic stroma.Subcutaneous nodules of cutaneous leiomyomas are differentiable from nodules of CA as these are hyperpigmented and painful and on histology show interlacing fascicles of spindle-shaped cells with fibrillary eosinophilic cytoplasm and blunt-ended cigar-shaped nuclei in contrast to nodular CA[9].Sometimes, cutaneous manifestations of sarcoidosis may present as subcutaneous nodules but it is a granulomatous disease showing characteristic histology consisting of non-caseating granulomas, which was not seen in the present case[10].Lipomatosis can simulate nodular CA clinically and presents with multiple soft subcutaneous nodules on trunk and extremities. It may occur as an autosomal-dominant disease with familial inheritance[11]. Moreover, histologically lipomatosis comprise of multiple vacuolated lipoblasts and is entirely different from nodular CA histologically.Cutaneous lymphoma may also present as multiple skin nodules but is associated with proliferation of abnormal lymphoma cells on FNAC, which was ruled out in the present case.Kaposi sarcoma is a low-grade angio-proliferative neoplasm. Nodular cutaneous manifestations of Kaposi sarcoma may simulate nodular CA. But histologically, the nodular KS exhibits dermal expansion by variably cellular proliferating neoplastic spindle-cells arranged in fascicles with formation of slit-like spaces containing RBCs in contrast to the present case[12].The rate of progression of CA to systemic disease vary from 7 to 50% in various studies[13].Although, various treatment modalities have been recommended for nodular CA in different studies, the use of laser treatment has also been emphasized in recent years. <sup>14</sup> Presently, the treatment option recommended is carbon dioxide laser. The patient is being followed-up for the last six months for progression to systemic involvement and malignancy

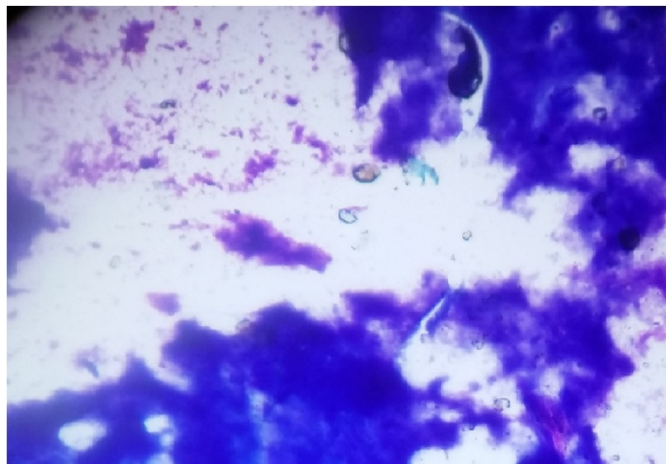
by various tests including complete blood cell count (CBC), complete metabolic profile, serum protein electrophoresis, urine protein electrophoresis, 24-hour

urinary creatinine clearance and bone marrow examination.

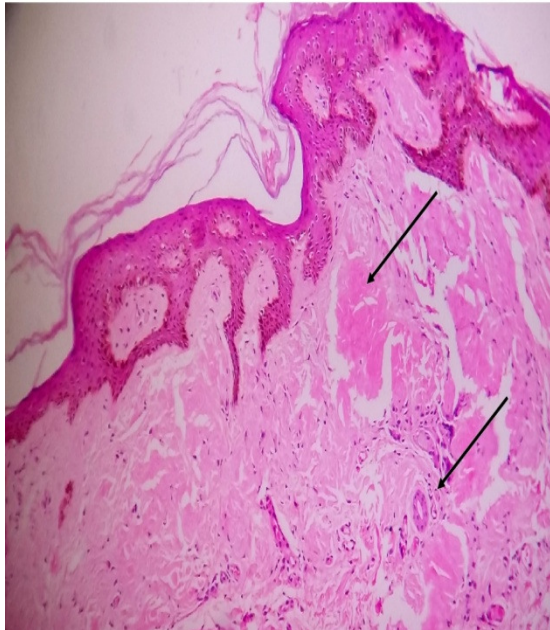
**Acknowledgements:** Patient and his relatives.



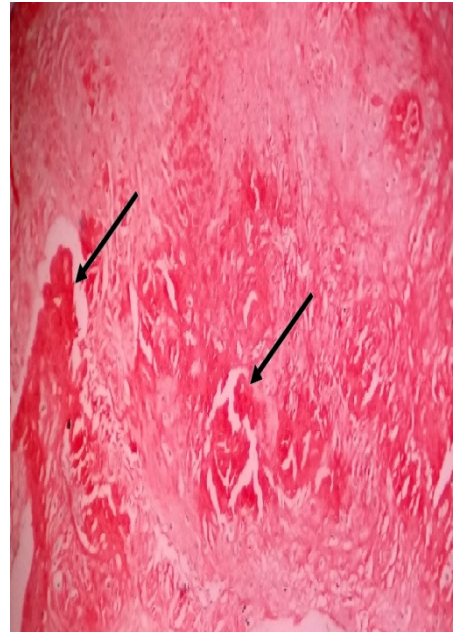
**Fig 1: multiple nodular skin lesions over scalp and upper extremity**



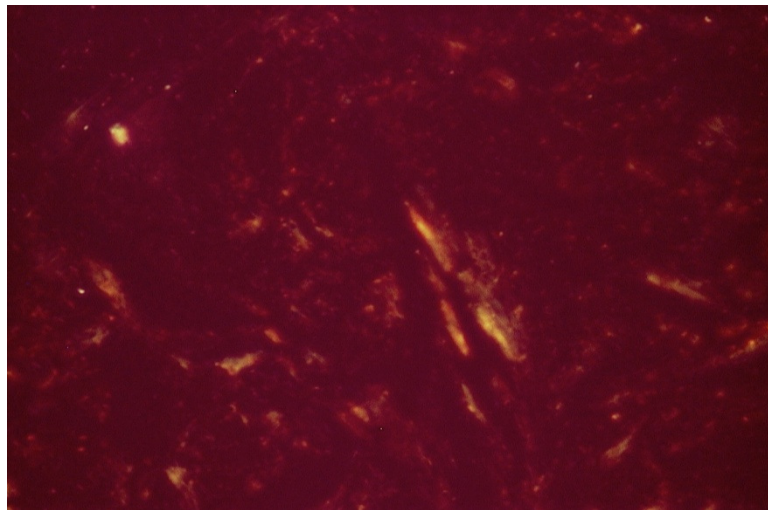
**Fig 2: MGG stained FNAC smear showing bluish amorphous extracellular material**



**Fig 3: H&E stained section showing extracellular, eosinophilic material in the dermis**



**Fig 4: Congo-red positive deposits**



**Fig 5: Deposits showing characteristic apple-green birefringence under polarizing light**

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