

# A case of primary systemic amyloidosis with nail dystrophy

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We hereby report a 79-year-old Iranian man presenting with nail dystrophy and subsequent development of purpuric and ecchymotic plaques, hemorrhagic bullae, and infiltrated papules on the head, neck and trunk. Histological examination of the gingiva, bone marrow aspiration, and biopsy confirmed the diagnosis of primary systemic amyloidosis. In this case, nail dystrophy was the presenting sign of primary systemic amyloidosis, which is a recognized but rare manifestation of this disorder. According to this case report, we could suggest that nail dystrophy may provide a clue for early diagnosis of primary systemic amyloidosis, which would ultimately increase the survival of the patient.

**Keywords:** nail dystrophy, multiple myeloma, primary presentation, systemic amyloidosis

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## INTRODUCTION

Amyloidosis is a rare and potentially fatal disease that occurs by extracellular deposition of insoluble protein<sup>1</sup>. This process causes organ dysfunction and gradually leads to death. This rarity and the variable involvement of different organs and tissues are often responsible for missed or delayed diagnosis, and therefore amyloidosis remains a considerable clinical challenge. Nail dystrophy is one of the manifestations that can lead the physician to the diagnosis of amyloidosis<sup>2-5</sup>.

## CASE REPORT

A 79-year-old man presented with a 2-month history of petechia and purpura on the face and neck. The lesions were mostly seen on the right cheek with some crusted forms on the neck (Figure 1). The patient's chest was also involved intermittently over the last 2 months but there was no lesion at the time of presentation. The patient



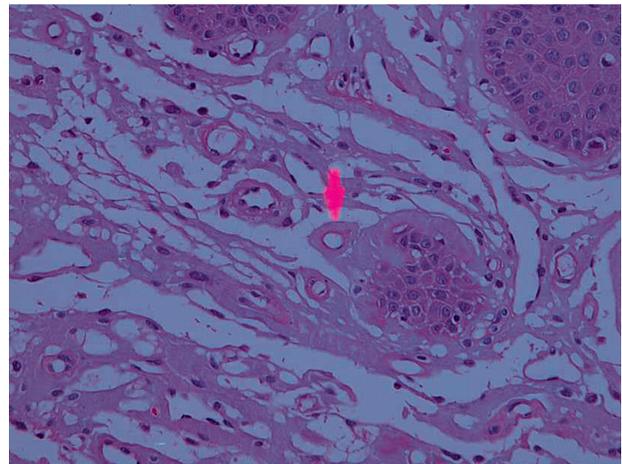
**Figure 1.** Hemorrhagic blisters with infiltrated erythematous and purpuric papules on the face and neck

was HBsAg positive, had a history of coagulopathy and complained of dysphagia recently. He was a smoker (2 pack-years) and had a history of cataract surgery on both eyes 2 years ago. He developed nail dystrophy over the last year (Figure 2). The family history was positive in his daughter only for cutaneous pemphigus vulgaris.

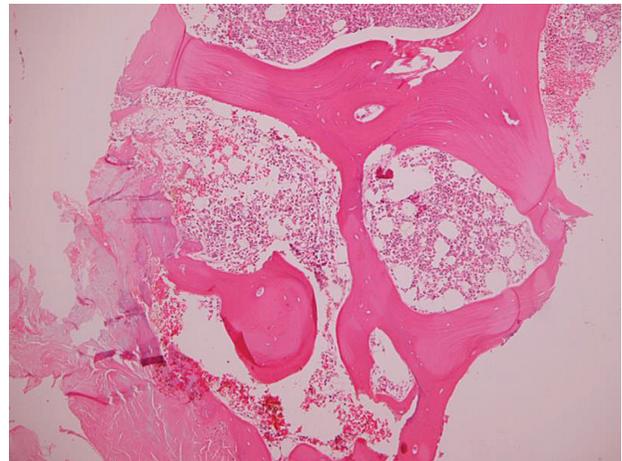
On physical examination of the skin, hemorrhagic blisters with infiltrated erythematous and purpuric papules were observed on the face and neck. Ecchymotic and purpuric plaques were also found on the face and neck. Most lesions were located over the right cheek with bruising around the right eye. Scattered on the lesions were purple nodules seen mainly on the neck. Ecchymoses were also seen on the oral mucosa with infiltrative gingival lesions and macroglossia. Nail dystrophy was found on the fingers and toes, more evident in hands in the form of onychorrhexia, nail plate thinning, and longitudinal ridging leading to nail destruction in some fingers. Abdominal ascites was observed and coarse crackles were heard at the bases of both lungs. The patient had edema in both upper and lower limbs, elevated jugular vein pulse, and decreased heart sounds. With clinical suspicion of primary systemic amyloidosis, biopsy specimens were taken from the gingiva and bone marrow. Gingival biopsy revealed extensive submucosal amorphous amyloid deposition consistent with cutaneous amyloidosis (Figure 3). Bone marrow biopsy and aspiration revealed hypercellularity regarding to the patient's age with normal cellular maturation and significant infiltration of the plasma cells consistent with plasma cell myeloma. There were also tiny foci of deposited amorphous



**Figure 2.** Nail dystrophy in amyloidosis is seen in the form of nail bed thinning, longitudinal ridging and onychorrhexia. There is also a hemorrhagic blister on the index finger.



**Figure 3.** Eosinophilic homogenous and fissured deposits of amyloid are present in subepithelial corium of gingiva in intimate association with a blood vessel (arrow) (H&E\*40).

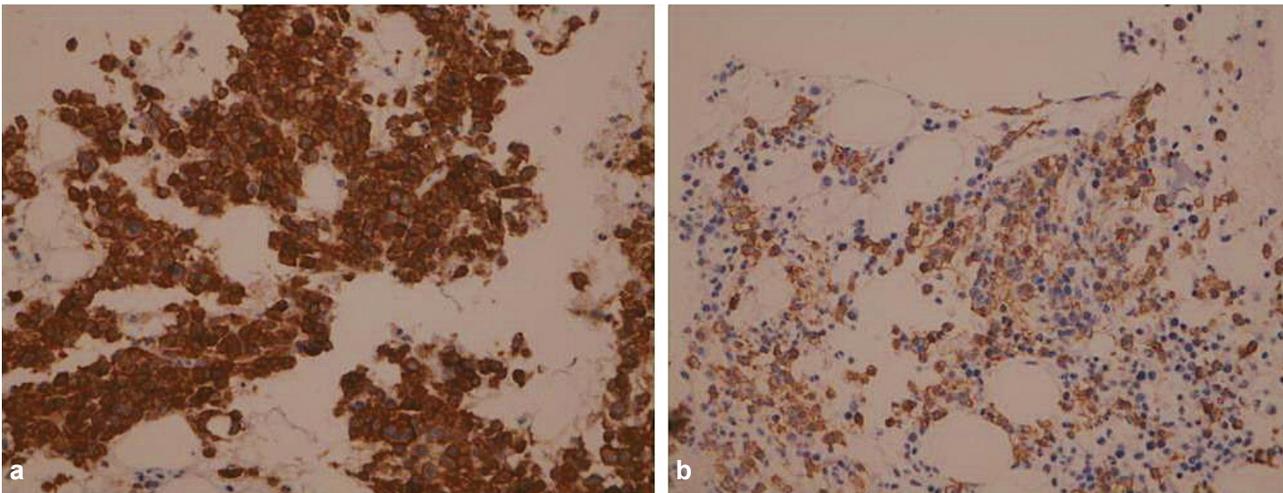


**Figure 4.** Bone marrow biopsy: significant infiltration of plasma cells with tiny foci of deposited amorphous eosinophilic material in stroma (H&E\*10)

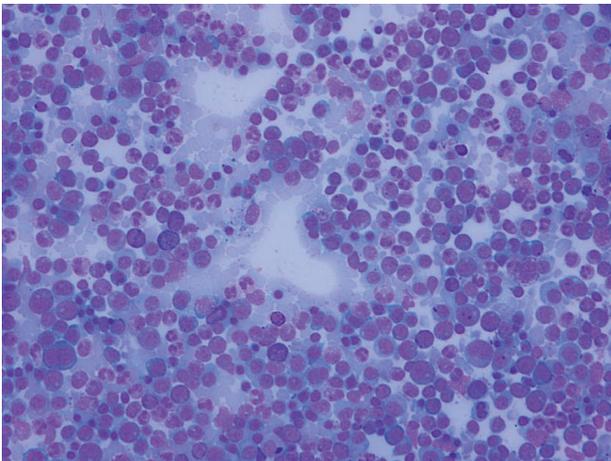
eosinophilic material in the stroma, which was compatible with light chain deposition secondary to plasma cell myeloma. Immunohistochemical study confirmed that the infiltrated cells were positive for CD38 and CD138 markers (Figure 4-6).

## DISCUSSION

Amyloidosis is a rare and potentially fatal disease that occurs as a result of extracellular deposition of insoluble abnormal fibrils derived from the aggregation of misfolded normally soluble protein<sup>1</sup>. This process causes organ dysfunction and if not promptly diagnosed, can lead to death. Systemic amyloidosis, with amyloid deposits in the viscera, blood vessel walls, and connective



**Figure 5.** IHC study of bone marrow. The infiltrating cells are positive for CD38 (a) and CD138 (b).



**Figure 6.** Bone marrow aspiration: a large number of plasma cells in bone marrow smear (Giemsa stain\*40).

tissue, is the cause of about one in every thousand deaths in developed countries. This rarity and the variable involvement of different organs and tissues are often responsible for missed or delayed diagnosis, and amyloidosis remains a considerable clinical challenge <sup>2,3</sup>. Microscopy of Congo red stained tissue specimens under the polarized light show birefringent amyloid, which is typed by identification of the amyloid precursor by immunohistochemistry, amino acid sequencing, or proteomics. Nail dystrophy is one of the manifestations that can lead the physician to the diagnosis of amyloidosis. It is seen in large numbers in other countries but it is as an uncommon presentation of amyloidosis in Iran <sup>4,5</sup>.

Nail dystrophy is a rare clinical manifestation of the disease. A few articles have reported nail

dystrophy as the presenting sign of amyloidosis. A 70-year-old man with a 3-year history of dystrophic fingernails and toenails was reported in an article by Prat et al <sup>6</sup>. Nail biopsy confirms the diagnosis of amyloidosis. A long-term history of nail changes was also present in our patient. Hoshino et al reported a quite similar case with dystrophic nail changes, which was confirmed to have AL amyloidosis after myocardial and skin biopsy <sup>7</sup>. Pink et al reported a case of AL amyloidosis who presented primarily with bulla and later with milia and nail dystrophy <sup>8</sup>. A Japanese man presented with a 4-year history of nail dystrophy and blisters as the only manifestations of myeloma-associated amyloidosis in a report by Fujita et al <sup>9</sup>. Ostler et al reported an 81-year-old woman presenting with nail changes as the only manifestation of amyloidosis, which was confirmed with nail biopsy <sup>10</sup>. In a case report by Derrick et al, bilateral periorbital ecchymosis and nail dystrophy were the main presentations of primary systemic amyloidosis in a 67-year-old man. Confirmation of diagnosis was made by skin biopsy <sup>11</sup>.

Periorbital ecchymosis was also found in our patient in addition to nail dystrophy; however, our patient had other lesions on the face and neck. As we can see from the numerous case reports, there is a long-term history of nail changes in a considerable number of patients before the diagnosis of amyloidosis is made. Some of these patients who did not survive the disease, might live longer if the nail changes raised the suspicion of amyloidosis diagnosis earlier. According to

this case report, we suggest that nail dystrophy may provide a clue for early diagnosis of primary systemic amyloidosis which would ultimately increase the survival of the patient.

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