UC Davis
Dermatology Online Journal

Title
Primary localized cutaneous amyloidosis

Permalink
https://escholarship.org/uc/item/3956j2fh

Journal
Dermatology Online Journal, 19(12)

Authors
Terushkin, Vitaly
Boyd, Kevin P
Patel, Rishi R
et al.

Publication Date
2013

DOI
10.5070/D31912020711

Copyright Information
Copyright 2013 by the author(s).This work is made available under the terms of a Creative Commons Attribution-NonCommercial-NoDerivatives License, available at https://creativecommons.org/licenses/by-nc-nd/4.0/

Peer reviewed

eScholarship.org Powered by the California Digital Library
University of California

Volume 19 Number 12
December 2013

Case Presentation

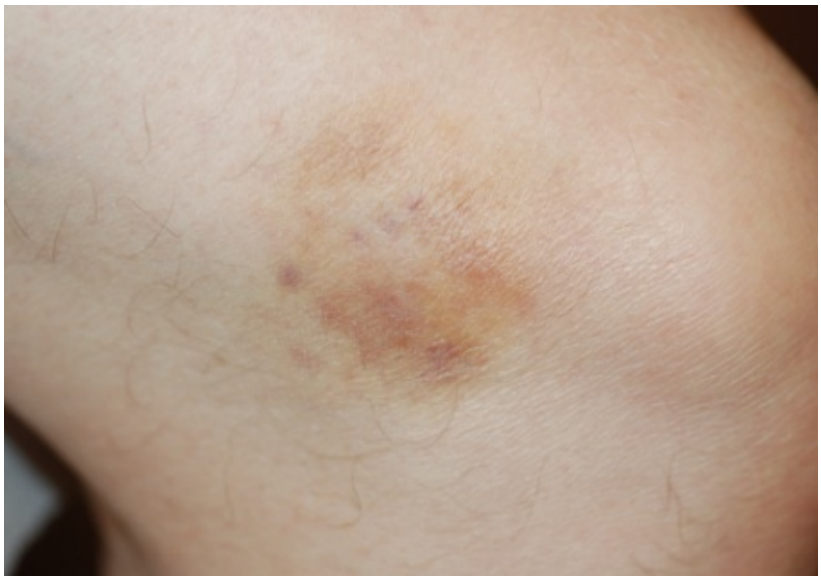
Vitaly Terushkin, MD, Kevin P. Boyd, MD, Rishi R. Patel, MD, and Beth McLellan, MD

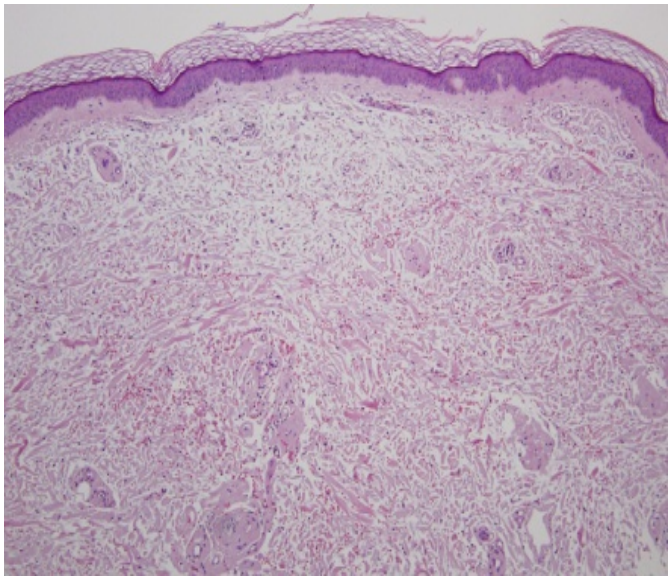
Dermatology Online Journal 19 (12): 7

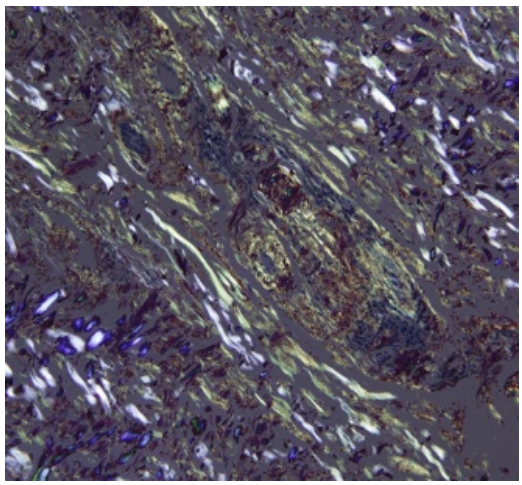
New York University School of Medicine

Abstract

A 61-year-old man presented for evaluation of a bruise-like lesion of the right knee. He was found to have an ill-defined, light brown patch with focal areas of dark red and brown. The histopathologic diagnosis was consistent with amyloidosis. Further subtyping showed that the amyloid protein was AL (κ). A systemic evaluation failed to show internal involvement. Amyloidosis comprises a spectrum of diseases, which range from systemic to localized cutaneous types, and is characterized by the extracellular deposition of amyloidosis protein as beta-pleated sheets. The forms of amyloidosis are differentiated by the specific types of protein-derived amyloidosis fibers. Both nodular and primary systemic amyloidosis can present as nodules on the skin owing to deposition of AL type amyloid protein. Primary systemic amyloidosis, which carries a poorer prognosis than does nodular amyloidosis, also may give rise to ecchymoses and many other cutaneous and extracutaneous findings. Histopathologic features are similar in both cases and involve the deposition of amorphous, eosinophilic material in the dermis. Nodular amyloidosis may progress to primary systemic disease in up to 50% of cases. Because our patient had no systemic involvement and the lesions did not appear nodular in nature, the patient was given a diagnosis of primary localized AL cutaneous amyloidosis. Routine follow-up for this patient is necessary to detect any potential disease progression.







Case synopsis

A 61-year-old man presented to the New York University Dermatologic Associates for evaluation of a focal skin discoloration on the right knee that he had noted for 5 months. He stated that this area periodically became dark and swollen. He had minimal associated pain. The patient had no history of skin cancer or other skin problems. His medical history included benign prostatic hypertrophy, hypothyroidism, and hypercholesteroleremia. The patient brought an ultrasound report which showed possible vasculitis.

The lesion was biopsied by the treating dermatologist. Once the histopathologic diagnosis was confirmed, the patient underwent further evaluation by a rheumatologist, who found no evidence of systemic disease.

Physical Examination: On the lateral aspect of the right knee was an ill-defined, light brown patch with focal areas of dark red and brown. No associated surface changes were appreciated. The lesion was not tender to palpation.

Laboratory Data: A complete blood count, comprehensive metabolic panel, serum and urine protein electrophoresis, C-reactive protein, erythrocyte sedimentation rate, homocysteine, methylmalonic acid, partial thromboplastin time, thyroid stimulating hormone , creatine phosphokinase, lactic dehydrogenase, and hemoglobin A1C were normal.

Histopathology: Within the dermis, there are perivascular and dermal deposits of amorphous, eosinophilic material with scattered surrounding plasma cells and a sparse, interstitial, inflammatory infiltrate that is comprised of lymphocytes, neutrophils, and plasma cells. A Perl stain highlights focal siderophages within the dermis. A Congo red stain highlights the amorphous eosinophilic deposits (red); under polarized light, there is apple-green birefringence.

Diagnosis: Primary localized AL cutaneous amyloidosis

Discussion: Amyloidosis comprises a spectrum of diseases, which range from systemic to localized cutaneous types. It is characterized by the extracellular deposition of amyloid protein as beta-pleated sheets. The amyloid protein consists of protein-derived amyloid fibers, amyloid P component, and ground substance [1]. The systemic and localized cutaneous forms also are further subdivided into primary and secondary types. What separates the various forms of amyloid is the specific type of protein-derived amyloid fibers.

Approximately 1275 to 3200 new cases of primary systemic amyloidosis are diagnosed each year in the United States [2]. This type of amyloidosis usually occurs in patients with plasma cell-dyscrasia related to deposition of protein AL, which is comprised of immunoglobulin light chains. Deposition occurs in organs such as the kidneys, liver, heart, gastrointestinal tract, and skin. In the oral cavity, patients may develop macroglossia and rubbery, nodules of the tongue. Minor trauma to the skin may result in ecchymoses, purpura, and petechiae, particularly around the eyelids, neck, axillae, and anogenital region. Waxy, translucent nodules also may develop anywhere on the skin surface. Performing urine and serum electrophoresis to check for free light chains is one of the first steps in the evaluation of a patient who is suspected of having primary systemic amyloidosis. The prognosis is extremely poor, especially when there is cardiac involvement, with a median survival of 13 months [3]. Treatment strategies are similar to those of multiple myeloma with the use of melphalan and systemic glucocorticoids. One study showed that an autologous peripheral blood stem-cell transplantation after melphalan administration was associated with increased survival [4].

Secondary systemic amyloidosis usually develops in patients with chronic infections, such as tuberculosis, osteomyelitis, and pyelonephritis or inflammatory processes, such as rheumatoid arthritis, inflammatory bowel disease, and Beçhet disease. The pathogenesis involves inadequate clearance of a distinctive non-immunoglobulin protein called AA (amyloid A protein) [5]. It is thought that the precursor is an acute phase reactant that is chronically elevated during inflammation. Although internal organs are commonly involved, the skin rarely demonstrates clinical findings. Treatment is aimed at targeting underlying infections or inflammatory processes.

The primary cutaneous amyloidoses are separated into three types: macular, lichenoid, and nodular. In contrast to systemic amyloidosis, the abnormal protein is deposited only in the skin and does not involve internal organs. Both macular and lichen amyloidosis, which are characterized by amyloid that is derived from keratinocytes, are thought to be represent ends of a clinical spectrum. Macular amyloid is described as small, rippled, hyperpigmented macules that are located on the upper back; lichen amyloid is described as hyperpigmented papules that are located on the shins [5]. Both of these conditions are associated with pruritus.

Nodular amyloid is very rare and is characterized by skin-colored nodules that range from several millimeters to several centimeters [1]. The amyloid in nodular amyloidosis, which is similar to that in primary systemic amyloidosis, is comprised of the

AL type of amyloid. It is essential that patients be evaluated for systemic amyloidosis. Multiple studies have shown that the risk of progression from nodular to systemic amyloidosis ranges from 7 to 50 % [6, 7].

On histopathologic examination, all forms of systemic and cutaneous amyloidosis appear similar and exhibit deposition of amorphous, eosinophilic, fissured material in the dermis. Congo red stains the material orange-red. Under polarized light, amyloid has a classic green birefringence. In the case of localized cutaneous forms, the amount of deposition usually separates macular/lichen amyloidosis from nodular amyloidosis because there is a much denser infiltration of amyloid in the dermis and around the blood vessels in nodular amyloidosis. Immunostaining for the type of amyloid can help differentiate macular/lichen amyloidosis from nodular types.

The bruise-like lesion of the patient in this report clinically mimics pinch purpura of systemic amyloidosis. The type of amyloidosis deposited was subtyped as AL (κ) in our patient. Because the systemic work-up was negative, we suggest that this patient's diagnosis be termed primary localized AL cutaneous amyloidosis. Although one may argue that this is similar to nodular amyloidosis, our patient did not have nodules on clinical examination. Therefore, the terminology proposed above is more appropriate. A similar term was proposed over 15 years ago by a group that described a patient with a 20-year history of recurrent, bruise-like lesions on the skin, who eventually went on to develop internal organ involvement [8].

The lesions of our patient are asymptomatic, therefore no treatment is necessary. If the patient were to develop symptomatic nodules, surgical excision, cryotherapy, or electrodesiccation may be used. Most importantly, it is critical that our patient is followed closely for the possible development of systemic disease.

References

1. James WD, *et al*. Errors in metabolism, In: James WD, *et al*., eds: Andrews' Diseases of the Skin Clinical Dermatology. 10th ed., Saunders Elsevier: United Kingdom. 2011:506
2. Falk RH, *et al*. The systemic amyloidoses. N Engl J Med 1997; 337:898
3. Kyle RA, Gertz MA. Primary systemic amyloidosis: clinical and laboratory features in 474 cases. Semin Hematol 1995; 32:45
4. Skinner M, *et al*. High-dose melphalan and autologous stem-cell transplantation in patients with AL amyloidosis: an 8-year study. Ann Intern Med 2004; 140:85
5. Groves RW, Black MM. Amyloidosis, In: Bolognia JL, *et al*., eds: Dermatology, Elsevier: Spain. 2012:699
6. Moon AO, *et al.* Nodular amyloidosis: review and long-term follow-up of 16 cases. Arch Dermatol 2003; 139:1157
7. Woollons A, Black MM. Nodular localized primary cutaneous amyloidosis: a long-term follow-up study. Br J Dermatol 2001; 145:105
8. Chotzen VA, *et al.* Long-term AL primary amyloidosis: a case report. Dermatol Online J 1995; 1