Nodular Cutaneous Amyloidosis in a Female Patient

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Background

Nodular Cutaneous amyloidosis (NCA) is the rarest subtype of a larger subset of cutaneous diseases known as primary cutaneous amyloidoses. Primary cutaneous amyloidoses are defined as skin lesions produced by localized amyloid deposits within cutaneous tissues without any evidence of systemic amyloidosis present. The three subtypes of primary cutaneous amyloidosis are nodular cutaneous amyloidosis, lichen cutaneous amyloidosis, and macular cutaneous amyloidosis. These three conditions can be differentiated from one another through histopathological examination of biopsy specimens. Currently in the literature there are less than 100 confirmed cases of NCA. We report on a confirmed case of NCA at University Medical Center in New Orleans Louisiana.

Case Report

A 59-year-old black female with a past medical history of hypertension presented to clinic for an initial evaluation of a lesion on her back. The lesion had been present for multiple years and featured occasional episodes of pruritis . The patient also noted that the lesion had grown albeit very slowly since she first noticed it. There had been not prior treatment of the lesion. She also denied any history of keloids or other bleeding, ulcerating, non-healing lesions. She does not wear sunscreen or protective clothing daily and attests to a history of high sun exposure and sunburns. On physical exam the patient features a hyperpigmented, reticulated plaque on the right upper back with surrounding reticulated hyperpigmentation pictured in Figure 1. Punch Biopsy of this lesion revealed the interstitial deposition of amorphous pink hyaline material and perivascular plasma cells seen in Figure 2A and 2B. Following these findings, the patient received a serum and urine protein electrophoresis to differentiate an isolated cutaneous amyloidosis from a cutaneous manifestation of a systemic etiology. Both tests returned normal and a diagnosis of nodular cutaneous amyloidosis was made. Upon subsequent clinic visits the patient denied any systemic symptoms, visual changes, neurologic dysfunction, or new cutaneous lesions. She elected not to have her plaque removed surgically

Diagnostics

Serum Protein Electrophoresis:

SPE Total Protein	6.0 - 8.0 g/dl	7
SPE Albumin	3.5 - 5.6 g/dL	3.5
Alpha 1 Globulin	0.1 - 0.4 g/dl	0.3
Alpha 2 Globulin	0.4 - 1.0 g/dl	0.8
Beta Globulin	0.5 - 1.1 g/dl	1
Gamma Globulin	0.5 - 1.5 g/dl	1.4
PROTEIN ELECTRO INTERPRETATION		Normal pattern.

Urine Protein Electrophoresis: Small amount of albumin present with no abnormal bands seen.

Histopathology: 5mm punch biopsy from superior medial back showed skin and subcutaneous tissue with perivascular, periadnexal, and interstitial deposition of amorphous, pink hyaline material. The deposits are highlighted on crystal violet, PAS with diastase, kappa, lambda (weak), and CD34 stains. Increased perivascular plasma cells are highlighted on CD138 and CD79a stains; the plasma cells show a kappa to lambda ratio of ~2:1. PAS stain is negative for fungus. Congo red, Ki-67, S100, CK5/6, CD31, CD68, CD20, desmin, SMA, MSA, Alcian blue, trichrome, iron, and elastic stains are negative. All controls are adequate.

Figure 1A

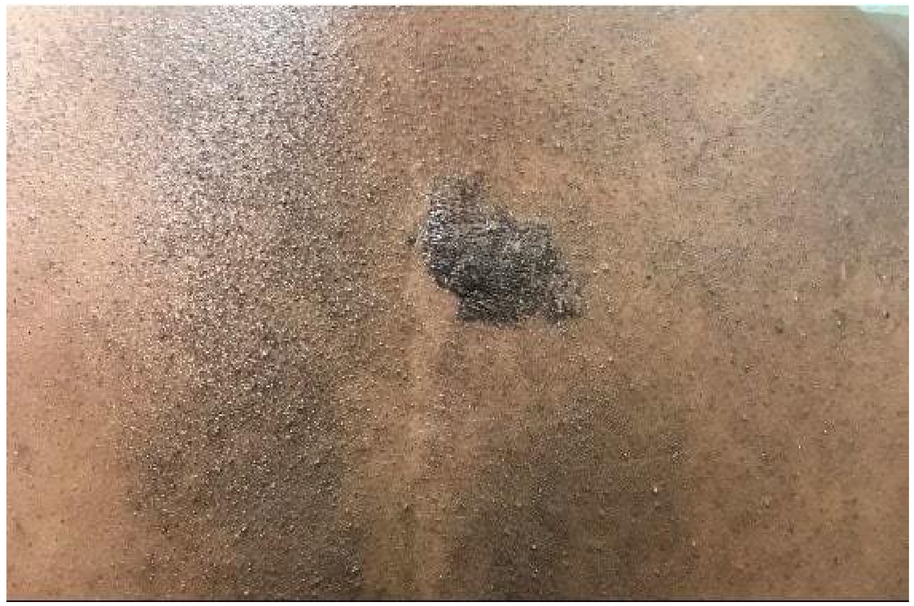

Figure 2A, 2B

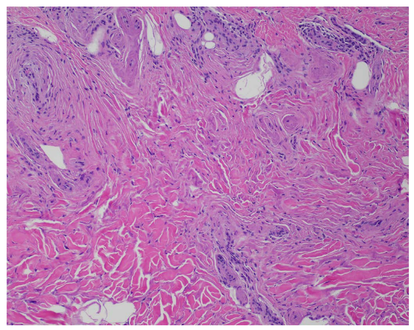

Fig 2A

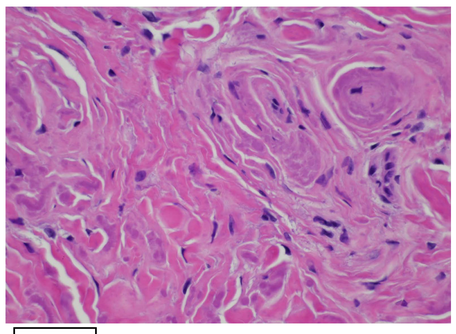

Fig 2B

Diagnosis

The histopathologic findings and absence of systemic symptoms or abnormal serum and urine protein electrophoresis studies confirm a diagnosis of nodular cutaneous amyloidosis in this patient. Histopathologic characteristics that confirm this as a case of nodular cutaneous amyloidosis rather than lichen or macular cutaneous amyloidosis can bee seen in Figures 2A and 2B. Nodular cutaneous amyloidosis is the lone subtype of primary cutaneous amyloidosis which features amyloid infiltration past the dermis into the subcuticular tissues. The perivascular plasma cell infiltrate seen on histopathology can also be used to differentiate nodular cutaneous amyloidosis from the other subtypes of primary cutaneous amyloidosis. This is because macular and lichen cutaneous amyloidosis feature amyloid derived from keratin while the amyloid deposits in NCA are from IG light chains produced from the proliferation of local plasma cells.

Differentiating a primary cutaneous amyloidosis from a cutaneous manifestation of a systemic amyloidosis is also necessary to confirm the diagnosis of NCA. Many conditions such as multiple myeloma can induce a systemic amyloidosis which is able to deposit large amounts of amyloid in cutaneous tissues and present as a skin lesion. These skin manifestation of systemic amyloidosis can be indistinguishable from primary cutaneous amyloidosis and require further testing for a diagnosis to be achieved. This typically involves analysis of serum ad urine protein levels to check for elevations. If no elevations are present such as in this patient a diagnosis primary cutaneous amyloidosis can be made and histopathology can be used to differentiate between NCA, lichen cutaneous amyloidosis and macular cutaneous amyloidosis.

Discussion

The rare nature of the condition NCA makes it extremely important to document whenever it presents. A retrospective literature review conducted in 2008 identified less than 70 total reported cases of NCA since its discovery in the 1950s. The most important focus in the management of a patient with suspected nodular cutaneous amyloidosis or any other suspected primary cutaneous amyloidosis is to rule out systemic causes of cutaneous amyloidosis. Systemic amyloidosis can come from conditions with high levels of morbidity and mortality and need to be identified early in their time course so that appropriate treatment can be administered. NCA has also been associated with a higher risk of other rheumatologic conditions such as CREST syndrome, Sjogren's syndrome , Systemic Lupus Erythematosus and primary biliary cirrhosis. Routine follow-up is necessary in patients with NCA to assess for these conditions as well as the rare but serious possibility of NCA progressing to systemic amyloidosis. The skin lesions of NCA are typically left alone as they rarely cause significant symptoms and have a high likelihood of recurrence when removed. If a patient elects to undergo removal of NCA plaque many different methods such as cryotherapy, intralesional corticosteroids and curettage can be utilized.

References

1. Haycox CL, Odland PB, Olbricht SM, Piepkorn M. Immunohistochemical characterization of dermatofibrosarcoma protuberans with practical applications for diagnosis and treatment. J Am Acad Dermatol. 1997 Sep;37(3 Pt 1):438-44. doi: 10.1016/s0190-9622(97)70146-4. Review. PubMed PMID: 9308560.
2. Ritchie SA, Beachkofsky T, Schreml S, Gaspari A, Hivnor CM. Primary localized cutaneous nodular amyloidosis of the feet: a case report and review of the literature. Cutis. 2014 Feb;93(2):89-94. Review. PubMed PMID: 24605345.
3. Moon AO, Calamia KT, Walsh JS. Nodular amyloidosis: review and long-term follow-up of 16 cases. Arch Dermatol. 2003 Sep;139(9):1157-9. doi: 10.1001/archderm.139.9.1157. Review. PubMed PMID: 12975157.
4. Meijer JM, Schonland SO, Palladini G, Merlini G, Hegenbart U, Ciocca O, Perfetti V, Leijsma MK, Bootsma H, Hazenberg BP. Sjögren's syndrome and localized nodular cutaneous amyloidosis: coincidence or a distinct clinical entity?. Arthritis Rheum. 2008 Jul;58(7):1992-9. doi: 10.1002/art.23617. PubMed PMID: 18576343.