

Bilateral recurrent facial primary cutaneous nodular amyloidosis (PCNA)

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A rare case of recurrent primary cutaneous nodular amyloidosis (PCNA) involving both sides of the face is being reported from India where the initial lesion on the right side of face was operated upon and recurred in 1 year. Around the same time the patient developed a similar lesion on the left side. The patient refused any treatment after being informed about the relatively innocuous nature of the disease. The importance of regular follow-up was explained to rule out systemic progression. This is the rarest form of primary cutaneous amyloidosis with a very low rate of progression to systemic amyloidosis. We propose that PCNA be included in the differential diagnosis of asymptomatic facial plaques and nodules.

CASE REPORT

A 63-year-old man presented with multiple dark raised lesions on both sides of the face. He had been operated by a plastic surgeon 8 years prior for a skin-colored raised lesion on the right side of face that had developed 12 years earlier and recurred in 1 year. Around the same time he developed similar lesions on the left mandibular area that gradually increased in size. There was no history of preceding trauma. He was a known diabetic and hypertensive on medication. He denied any other systemic systems.

On examination, there were well-defined skin-colored firm nodules, coalescing to form nodulo-plaques with overlying skin showing absence of hair on both sides of the face (Fig 1). A linear scar was visible on the operated site within the plaque that had recurred. There was no sensory deficit, thickening of any peripheral nerves, or any other lesions

on the body. A biopsy specimen revealed a patchy nodular deposit of uniformly pink-staining amorphous material within the whole of reticular dermis and extending to septa of subcutaneous fat. The material was admixed with thickened bundles of collagen in places whereas at other places it was seen as closely packed nodules of the deposit that showed fractured structure (Fig 2). There was no inflammatory infiltrate. The material took up the Congo red stain (Fig 3). It also showed apple green birefringence on polarizing microscopy confirming the diagnosis of cutaneous nodular amyloidosis. The 24-hour urinary protein levels, and urine and serum protein electrophoresis revealed normal findings. Antinuclear factor, anti-Ro, and anti-La were normal. Rheumatoid factor, HIV, and hepatitis B and C serologies did not show abnormalities. Chest x-ray, abdominal ultrasonography, and electrocardiographic examination produced normal results. In view of normal physical examination findings and the above reports, a diagnosis of PCNA was made. After being told the nature of the disease and the expected outcome of various available treatment modalities, the patient decided to opt for no further treatment. He, however, agreed to follow-up every 9 months.

DISCUSSION

Amyloidosis is considered one of the protein conformational diseases.¹ These are diseases where specific peptides or proteins do not adopt or remain in their native functional state and instead get deposited in various tissues as toxic aggregates. Amyloid aggregates get deposited in the skin in various forms of cutaneous amyloidosis.

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Fig 1. Skin-colored alopecic nodules on the right and left side of the face.

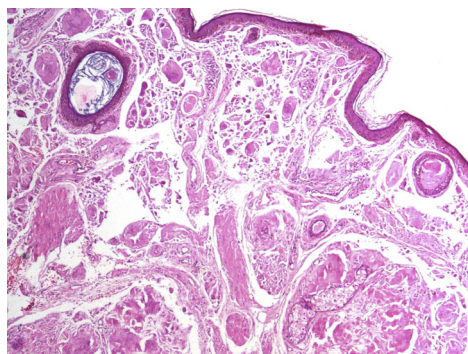


Fig 2. Uniformly pink-staining amyloid throughout the reticular dermis and admixed with thickened collagen bundles.

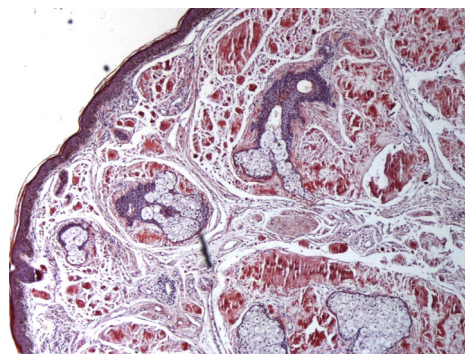


Fig 3. Congo red stain showing pink amyloid material in the reticular dermis and within thickened collagen bundles.

PCNA is considered the rarest form of cutaneous amyloidosis compared with the other 2 types, macular amyloidosis and lichen amyloidosis.²⁻⁴ The fibrils of amyloid in PCNA are composed of immunoglobulin light chains of either kappa and/or lambda type, called “protein AL” and do not differ from those seen in primary systemic amyloidosis and in multiple myeloma.^{5,6} Unlike in the more common forms such as macular and lichen amyloidosis where the amyloid is formed by degenerating keratinocytes, monoclonal plasma cells in PCNA produce and secrete the immunoglobulin kappa and lambda light chains through an unknown mechanism.^{2,4,7}

Clinically characteristic lesions are single or multiple asymptomatic nodules and plaques of varying

sizes that may coalesce. There is a predilection for acral areas including face, scalp, extremities, and genitalia with majority of lesions occurring on the face.^{2,6,8} Because the lesions develop insidiously they are commonly diagnosed late and the mean time from onset of lesions to diagnosis is 13.5 years.^{2,3,6,9} The median age at diagnosis is 57 years (range 24-87 years) with a slight male predominance. The rarity of the condition is a limitation to estimate the exact rate of progression of nodular localized primary cutaneous amyloidosis (NLPCA) to systemic amyloidosis with estimates ranging from 7% to 50%.^{2-4,10} A 1970 study by Brownstein and Helwig¹⁰ reported a rate of 50%, a figure that was quoted by many.² However, since

then literature seems to suggest the figure to be an overestimate. Fifteen cases of NLPCA by Woollons and Black² have shown the risk of progression of NLPCA to be as low as 7%. In a review of articles describing a total of 65 patients with NLPCA, only 1 patient had progressed to systemic amyloidosis.⁸ Most other literature also suggests that the risk of progression is low but the patient be followed up regularly. There is extensive and diffuse amyloid deposit in deeper parts of the dermis, subcutaneous tissue, and the small dermal blood vessels unlike in the more common forms such as macular amyloidosis and lichen amyloidosis.^{2,4,5,8,10} All of the amyloid material appears as homogenous and eosinophilic in hematoxylin-eosin stain and shows up as a pinkish amorphous mass in more specific stains such as Congo red.

It is imperative to rule out systemic involvement because morphologically identical lesions are found both in primary and systemic amyloidosis.^{2,5,6} There is a strong body of evidence to suggest a genetic basis to development and progression of amyloidosis. Mutations such as oncostatin M receptor-beta on chromosome 5p13.1 and/or interleukin-31 receptor A on the same chromosome have also been documented.^{11,12}

Investigations recommended for ruling out systemic involvement include complete blood cell count with differential and platelet count, serum calcium, blood urea nitrogen, and S creatinine. Serum protein electrophoresis, urine protein electrophoresis and 24-hour urine protein are carried out for multiple myeloma. Ideally, as is practiced in advanced countries, quantitative immunoglobulin levels, serum free light chain, immunofixation, and cytogenetics including fluorescence in situ hybridization should be done but these are prohibitively expensive in India where the average dermatology patient pays for all his medical expenses out of his own pocket and hence these were not done. Other supplementary investigations should include lipid profile, liver function tests, HIV serology, hepatitis B and C serology, chest x-ray, abdominal ultrasonography, and electrocardiogram. Because a significant number of cases of PCNA are associated with Sjögren syndrome, serology should include antinuclear antibodies, anti-Ro/SSA and anti-La/SSB.^{2,5}

There is a tendency for PCNA to recur after attempted intervention. One large study estimates it at 9%.⁸ Various modalities to change the appearance of the lesions include topical and intralesional steroids, dermabrasion, cryotherapy, curettage and electrodesiccation, and excisional surgery.^{2,3,5,9}

Laser modalities such as carbon-dioxide and pulse-dye laser have been tried but lesions tend to recur.^{2,3} More important seems to be meticulous follow-up of the patient in 6 to 12 months to rule out progression of PCNA to a systemic form of amyloidosis.^{2,3,8} Investigations done for this are the same as the ones mentioned earlier. Some centers also recommend periumbilical fat tissue aspiration and rectal pad biopsy for immunochemical analysis of specific amyloid proteins and their quantification. Our documentation of this rare condition is rendered more interesting by the fact that our patient had bilateral lesions and the original one recurred after surgery followed by a lesion on the other side after many years. Trauma of the previous surgery may have led to recurrence as the condition is known to be associated with trauma.⁴ We propose that PCNA be always included in the differential diagnosis of nodular or plaque-type lesions occurring on the face.

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