Pulsed Dye Laser for the Treatment of Macular Amyloidosis: A Case Report

Maya Barsky, MD; Robert L. Buka, MD, JD

Practice Points

- Macular amyloidosis is benign and nonsystemic but typically results in cutaneous hyperpigmentation.
- Initial treatment with topical keratolytics has limited success rates.
- A second-line approach to treatment with light-based therapies may improve patient outcomes.

Macular amyloidosis causes an eruption of brown pigment in the skin when keratin is altered. The resulting hyperpigmentation, which often leads to patient distress, generally has unsatisfactory treatment options. Among the treatment modalities that have been used for amyloidosis, the pulsed dye laser (PDL) has shown success in the treatment of nodular amyloidosis, and the Q-switched Nd:YAG laser has reduced the appearance of amyloid plaques in macular amyloidosis. We investigated the effects of repeated PDL treatments in a 57-year-old man with recalcitrant macular amyloidosis. The patient was treated with 3 treatment sessions of PDL at 2-week intervals. Based on patient self-assessment and our own photographic analysis, improvement of the lesions was noted with each treatment. Macular amyloidosis can be successfully treated using the PDL, which decreases amyloid aggregation and skin hyperpigmentation. This effect from a decrease in collagen and dermatan sulfate synthesis is similar to the mechanism behind the reduction of size of hypertrophic scars using PDL.

Cutis. 2014;93:189-192.

Dr. Barsky was from Warren Alpert Medical School of Brown University, Providence, Rhode Island, and currently is from Baystate Medical Center, Tufts University School of Medicine, Springfield, Massachusetts. Dr. Buka is from the Department of Dermatology, Icahn School of Medicine at Mount Sinai, New York, New York.
The authors report no conflict of interest.
Correspondence: Maya Barsky, MD, 617 Center St, Ludlow, MA 01056 (maya.barskymd@bhs.org).

Macular amyloidosis causes an eruption of small brown or grayish-pigmented macules that often are symmetrically distributed on the upper back and shoulder blades in a reticulated pattern. Amyloidosis occurs when there is an abnormal extracellular tissue deposition of proteins from keratinocyte amyloidosis,[1] which can be diagnosed based on both clinical characteristics and on histologic findings of skin biopsies. The disease prevalence is greater in women, especially those of Asian, South American, or Middle Eastern descent.[2] It is a chronic disease and generally has poor treatment options.

The most problematic aspect of macular amyloidosis is the resulting cutaneous hyperpigmentation. Treatments that have been described thus far have not yielded satisfactory results for patients. Topical treatment with corticosteroids is recommended, but the outcome still can be disappointing. Laser treatments may hold promising results. We report the case of a 57-year-old man who presented with macular amyloidosis and was successfully treated with a 595-nm pulsed dye laser (PDL).

Case Report

A 57-year-old man presented with signs of macular amyloidosis on the upper back of approximately 1 year's duration (Figure 1A). The patient noted that the lesions were tender and nonpruritic. Physical examination revealed numerous ill-defined, erythematous, brown macules measuring less than 1 cm confluent to a patch on the upper back. He had no systemic concerns and was otherwise healthy.

Based on the patient's clinical presentation, a 4-mm punch biopsy was performed. The patient was prescribed ammonium lactate cream 12% to be applied twice daily and was advised to discontinue use if the area became irritated. After 2 weeks, the initial biopsy confirmed the diagnosis of macular amyloidosis, with numerous amyloid globules observed within the dermal papillae (Figure 2). The patient was encouraged to refrain from scratching. Laser treatments were extensively discussed with the patient to ensure that he understood multiple treatments may be needed and the desired cosmetic outcome was not guaranteed.

The patient was treated with a 595-nm PDL using nonpurpuric parameters (7.5-J/cm^2 fluence; 30/10-millisecond epidermal cooling; 10-mm spot size). There was a 10% overlap between treatment pulses with no stacking and a 6-millisecond pulse length. The procedure was repeated at 2-week intervals for a total of 3 treatment sessions. It was well tolerated with no complications. At the end of treatment the patch had decreased in size from 10 cm to 5 cm. Two-week intervals were chosen to aim for a photoacoustic effect to assist with amyloid dispersion and collagen renewal. With each laser treatment there was noticeable improvement with lightening of the brown macules, measured by clinical examination (Figure 1B).

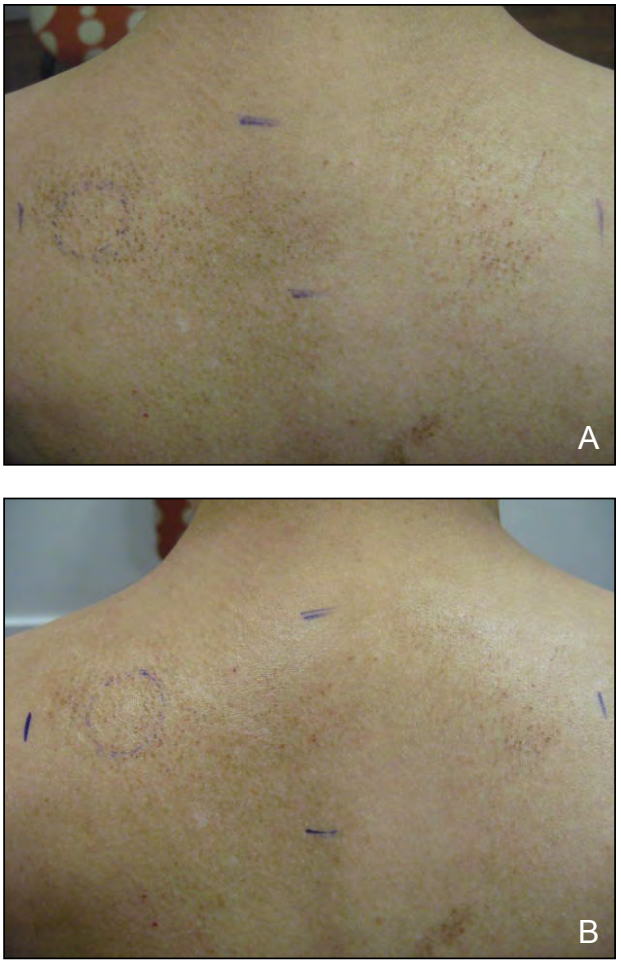

Figure 1. Erythematous brown macules scattered on the upper back showed signs of macular amyloidosis (A). After 3 treatment sessions with the pulsed dye laser, the number of brown macules was reduced and amyloid patches were lightened (B).

Comment

Macular amyloidosis is a type of primary localized cutaneous amyloidosis with deposition of amyloid proteins in the upper dermis resulting in clinical hyperpigmentation.[3] The amyloid deposits have been shown to bind to antikeratin antibodies and contain sulfhydryl groups, suggesting altered keratin as a source for the deposition.[4] Histopathologically, skin biopsies of macular amyloidosis are analyzed either by Congo red staining or methyl violet or crystal violet staining. Thioflavin T–specific binding to amyloid fibrils has been observed with fluorescence microscopy and also has been used diagnostically.[5] The amyloid deposits, which often are found within the dermal papillae (Figure 2), are globular and sometimes can be found in the junction between the dermis and epidermis containing basal cells.[6] They appear as linear aggregates of fibrils arranged in a meshwork. Additionally, they contain a nonfibrillar protein, serum amyloid P component, which is similar to C-reactive protein in the acute phase.[7,8] These properties make amyloid deposits resistant to degradation and phagocytosis.

The mechanism by which the amyloid deposits form is unknown. Hashimoto et al[9] proposed that necrotic epidermal cells are transformed into amyloid by macrophages and fibroblasts through filamentous degeneration. In macular amyloidosis, there is a lack of inflammatory cells that typically clear these deposits. The keratin structure forming β-pleated sheets is not explained by this theory. Chang et al[6] suggested that keratinocyte death can be explained by apoptosis in the dermoepidermal junction, leading to dermal amyloid deposits.

Treatment outcome in patients with macular amyloidosis often is disappointing. Topical treatment with corticosteroids is advised but often is associated with unsatisfactory results. Antihistamines have been used for itch relief, but they have only been found to be moderately effective. There have been contradicting reports regarding dimethyl sulfoxide therapy, some indicating lack of efficacy,[10] and phototherapy showed minimal benefits.[11] Surgical treatments such as dermabrasion and excision of lesions often prompt

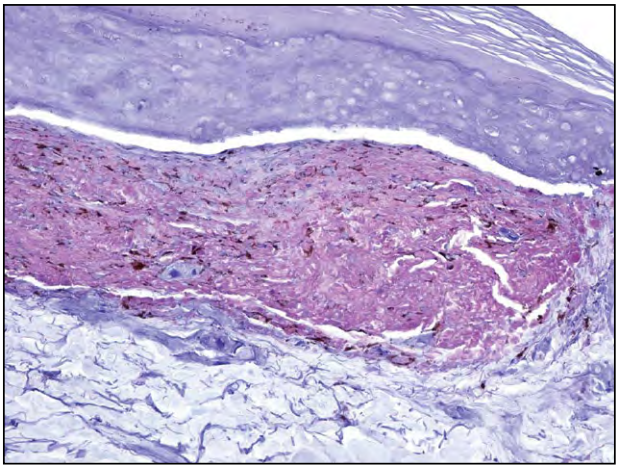

Figure 2. A biopsy specimen showed numerous amyloid globules within the dermal papillae (crystal violet, original magnification ×200).

reoccurrence of amyloid and have mostly been cited for treatment of lichen amyloidosis.[12]

Studies have shown successful treatment of erythematous hypertrophic scars, acne scars, and other vascular lesions using the 585-nm PDL at pulse durations of 1.5 milliseconds and a fluence of 9 to 70 J/cm^2.[13,14] Furthermore, microvasculature destruction causes a substantial decrease in collagen synthesis because of the ischemia at the laser treatment site, which could decrease dermatan sulfate, a component in collagen fiber formation that also is found in macular amyloids.[15,16] Therefore, injury to the cutaneous vessels via PDL could deplete amyloid aggregation. Applying these principles to dermal amyloid patches in macular amyloidosis could demonstrate substantial improvements in the appearance of dark pigmented lesions.

Alster and Manaloto[16] used a 585-nm PDL at 6- to 8-week intervals to determine the clinical and histological response in nodular amyloidosis. There was improvement in color, size, and pliability of nodules, as well as decreased inflammation and dermal collagen due to the decrease in collagen and dermatan sulfate. Both the PDL and the quality-switched (Q-switched) Nd:YAG laser have been used to successfully treat dermal pigmented lesions.[14] Ostovari et al[1] tested the efficacy of the ultrashort pulsed Q-switched Nd:YAG laser in clearing the darkness of skin patches in macular amyloidosis. The study of 20 participants demonstrated effective reduction of the degree of macular amyloidosis patches, with the 532-nm laser citing a good response rate in 90% (18/20) of participants. No side effects were observed, and the pain from the laser therapy was described as tolerable.[1] This positive response was attributed to the destruction of melanin in the dermal layers by the Q-switched Nd:YAG laser,[1] similar to the treatment of hypertrophic scars.[14] Prior studies indicate the efficacy of PDL treatment in nodular amyloidosis and the Q-switched Nd:YAG laser with macular amyloidosis in a single session[1,16]; however, to our knowledge, there has been no research describing macular amyloidosis treated with repeated sessions of PDL. The benefits of PDL treatment include ease of application, minimal scarring, and minimal posttreatment complications.

Conclusion

Our case report presents the efficacy of multiple sessions of PDL treatment in the setting of macular amyloidosis. We were encouraged by prior successful PDL treatment of dermal pigmented lesions as well as the success of different laser options in the treatment of primary amyloidosis. Based on clinical photographs demonstrating treatment progress, patient self-assessment, and physician reports, it was determined that the amyloid patches in our patient lightened in color with each PDL procedure. These results indicate that PDL treatment has a positive outcome in macular amyloidosis. Other treatments used for macular amyloidosis have been disappointing, and with the successful results of PDL treatment, we believe there is now an option to relieve the discoloration and severity of amyloid patches.

REFERENCES

1. Ostovari N, Mohtasham N, Oadras MS, et al. 532-nm and 1064-nm Q-switched Nd:YAG laser therapy for reduction of pigmentation in macular amyloidosis patches. *J Eur Acad Dermatol Venereol*. 2008;22:442-446.
2. Rasi A, Khatami A, Javaheri SM. Macular amyloidosis: an assessment of prevalence, sex, and age. *Int J Dermatol*. 2004;43:898-899.
3. Breathnach SM. Amyloid and amyloidosis. *J Am Acad Dermatol*. 1988;18(1, pt 1):1-16.
4. Inoue K, Takahashi M, Hamamoto Y, et al. An immunohistochemical study of cytokeratins in skin-limited amyloidosis. *Amyloid*. 2000;7:259-265.
5. Khurana R, Coleman C, Ionescu-Zanetti C, et al. Mechanism of thioflavin T binding to amyloid fibrils. *J Struct Biol*. 2005;151:229-238.
6. Chang YT, Wong CK, Chow KC, et al. Apoptosis in primary cutaneous amyloidosis. *Br J Dermatol*. 1999;140:210-215.
7. Breathnach SM, Bhogal B, Dyck RF, et al. Immunohistochemical demonstration of amyloid P component in skin of normal subjects and patients with cutaneous amyloidosis. *Br J Dermatol*. 1981;105:115-124.
8. Li JJ, McAdam KP. Human amyloid P component: an elastase inhibitor. *Scand J Immunol*. 1984;20:219-226.

9. Hashimoto K, Ito K, Kumakiri M, et al. Nylon brush macular amyloidosis. *Arch Dermatol*. 1987;123:633-637.
10. Lim KB, Tan SH, Tan KT. Lack of effect of dimethyl sulphoxide (DMSO) on amyloid deposit in lichen amyloidosis. *Br J Dermatol*. 1988;119:409-410.
11. Jin AG, Por A, Wee LK, et al. Comparative study of phototherapy (UVB) vs. photochemotherapy (PUVA) vs. topical steroids in the treatment of primary cutaneous lichen amyloidosis. *Photodermatol Photoimmunol Photomed*. 2001;17:42-43.
12. Savant SS. Therapeutic regional dermabrasion in papular lichen amyloidosis of shins. *Indian J Dermatol Venereol Leprol*. 1995;61:196-201.
13. Goldman MP, Fitzpatrick RE. Laser treatment of scars. *Dermatol Surg*. 1995;21:685-687.
14. Bowes LE, Nouri K, Berman B, et al. Treatment of pigmented hypertrophic scars with the 585-nm pulsed dye laser and the 532-nm frequency-doubled Nd:YAG laser in the Q-switched and variable pulse modes: a comparative study. *Dermatol Surg*. 2002;28:714-719.
15. Manuskiatti W, Wanitphakdeedecha R, Fitzpatrick RE. Effect of pulse width of a 595-nm flashlamp-pumped pulsed dye laser on the treatment response of keloidal and hypertrophic sternotomy scars. *Dermatol Surg*. 2007;33:152-161.
16. Alster TS, Manaloto RM. Nodular amyloidosis treated with a pulsed dye laser. *Dermatol Surg*. 1999;25:133-135.