

THERAPEUTIC HOTLINE

Isolated corymbose collagenoma responding to intralesional triamcinolone acetonide and hyaluronidase injections

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ABSTRACT: Collagenomas are connective tissue nevi with circumscribed hamartomatous proliferation of collagen. Due to their benign nature and lack of any simple medical treatment, they are most often left untreated. We present a case of isolated corymbose collagenoma, a distinct morphological variant not described hitherto that was successfully treated with intralesional injections of combination of triamcinolone acetonide and hyaluronidase.

KEYWORDS: intralesional injection, isolated collagenoma

Introduction

Connective tissue nevi of the skin are circumscribed hamartomatous lesions consisting predominantly of one of the components of extracellular matrix – collagen, elastin, or proteoglycans. Collagenomas are connective tissue nevi composed predominantly of normal collagen tissue. The inherited types, which are autosomal dominant and have a positive family history, include familial cutaneous collagenoma and shagreen patch of tuberous sclerosis; the acquired types include eruptive collagenomas and isolated collagenoma (1).

Isolated collagenoma is a rare acquired connective tissue nevus with abnormal proliferation of

collagen. It has been described over various sites of body and has different morphological patterns. The varied reported presentations include zosteriform lesions at lower abdomen and back (2), cerebriform lesions on palm (3) and sole (4), and papuloliner lesions (5) along the Blaschko's lines. The exact pathogenesis of collagenomas is unknown. It was shown that the increased collagen is of the adult type (type I) and that a local reduction of enzyme collagenase might be the cause of the excess collagen (6). Moreover, the mean population doubling time of the fibroblasts from these lesions is decreased and an enhanced proliferative capacity of the regional fibroblasts may contribute to the accumulation of collagen (6). Histologically, collagenomas are characterized by an excessive accumulation of dense, coarse collagen fibers in the dermis, with a diminished amount of elastic fibers that are abnormally thin or fragmented in some areas. This decrease in elastin possibly

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represents a dilution phenomenon related to the excessive amount of collagen.

There is very limited data regarding the therapeutic options in collagenomas. As they represent benign and nonprogressive hamartomatous proliferation, they are usually left untreated. Treatment is most often attempted for cosmetic or functional reasons. Isolated collagenoma have primarily been treated by surgical excision (7,8). Surgery is difficult in cases of large lesions, multiple lesions, and when collagenoma is present over difficult-to-operate sites. Also, there are inherent complications of surgery. There are two previous reports of treatment of collagenoma with intralesional corticosteroids injections, one with triamcinolone acetonide alone and in other with in combination with hyaluronidase (9,10).

We present a new morphologic variant of collagenoma treated successfully with intralesional injections of triamcinolone acetonide in combination with hyaluronidase.

Report of a case

An 18-year-old girl presented with an asymptomatic skin-colored plaque over her lower back. The lesion was initially noticed by her parents as a single skin-colored papule of 1 cm size when she was 1 year old and since then, it has gradually increased in size. There was no history of preceding inflammation or trauma at the site of the lesion. There were no systemic complaints or similar cutaneous lesion elsewhere on the body. None of the other family member had such complaint.

On examination, there was single large skin-colored plaque (4 × 6 cm) present on the left side of her lower back. There were multiple small satellite papules and nodules in its vicinity. Few of the satellite lesions were coalescing with the main plaque leading to pseudopod-like appearance. Other satellite lesions were small discrete skin-colored papules present within 2 cm of the main plaque. The large plaque had irregular surface with intervening areas of depigmentation and marked atrophy (FIG. 1). It was firm in consistency and nontender on palpation. She had received intralesional triamcinolone acetonide injections every month for a period of about 1 year, which resulted in partial flattening and focal areas of depigmentation and atrophy. The plaque started increasing in size 2 months after stopping this above treatment. Based on the clinical finding, isolated collagenoma and keloid were considered as differential diagnosis, although onset at early age (1 year), spontane-



FIG. 1. Single skin-colored irregular plaque with multiple discrete to coalescing papulonodules in its vicinity (corymbose) and showing depigmentation and atrophy at places.

ous appearance and asymptomatic course were not suggestive of keloid. The histopathological examination of skin biopsy from the plaque showed mild flattening of the epidermis with focal loss of rete ridges. There was well circumscribed proliferation of hyalinized collagen interspersed with small aggregates of inflammatory cells and vessels in the dermis (FIG. 2A). Masson's trichrome stain showed bluish-green staining of collagen bundles (FIG. 2B). Routine investigations, ultrasonography of abdomen, and lumbosacral X-ray were within normal limits. On the basis of clinical and histopathological findings, the diagnosis of collagenoma was confirmed.

The lesion was large in size and along with multiple papulonodular lesions in its periphery, making surgical excision as a difficult option. We planned to treat her with intralesional injections of combination of triamcinolone and hyaluronidase. The patient was administered intralesional injection of triamcinolone acetonide (40 mg/mL) and hyaluronidase (1500 U/mL) in the ratio of 1 : 1 at multiple points 1 cm apart in the plaque and in the satellite papulonodules within its vicinity. The dose injected at each point was 0.1–0.2 mL depending on the size of the nodule or thickness of the plaque at that site. After first injection, there was almost 20% flattening of the plaque and the surrounding papulonodules (FIG. 3A). Subsequent injections in the same dilution were given at four weekly intervals up to a total of four sessions. Serial lesional photographs were taken at each treatment session (FIG. 3B–D). There was progressive improvement noted at each session, with almost complete flattening of the plaque and satellite lesions after fourth session. She had minor local adverse effects with the treatment like hyperpigmentation, wrinkling and few telangiectasia. Pigmentation

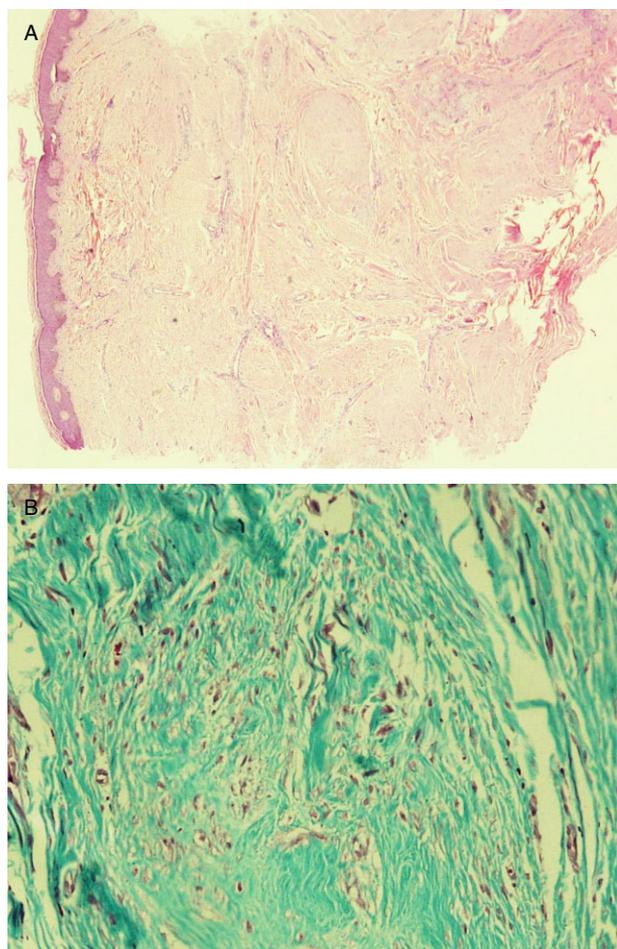


FIG. 2. (A) Microphotograph showing mild thinning of the epidermis with circumscribed nodules of collagen fibers in the mid dermis (H&E $\times 140$). (B) Microphotograph showing bluish-green collagen bundles arranged haphazardly (Masson's trichrome $\times 280$).

was probably related to hyaluronidase injection. The disfiguring patchy marked atrophy at the margins of the plaque which resulted from alone triamcinolone injections given previously did not progress further but persisted. During subsequent follow-up, we observed that the pigmentation decreased in intensity, while few telangiectasia persisted. There was no recurrence during the 1 year of follow-up (FIG. 4).

Discussion

Our patient had collagenoma over lower back, the most common site of presentation of shagreen patch. However, the morphology of the lesion was unlike shagreen patch, which presents as discrete thick yellowish irregularly thickened leathery skin

sometimes dimpled like an orange peel. Also, there were no other cutaneous/systemic stigmata or family history to suggest tuberous sclerosis. Corymbose collagenoma would be a more appropriate term to describe the morphology of the lesion in our patient. The term corymbose has previously been used in relation to rare presentation of secondary syphilis lesions where a large central papule or plaque is surrounded by smaller satellite papules (11).

Collagenomas are most often left untreated unless they lead to disfigurement or functional impairment because of their size, number, or location. Their treatment has primarily been limited to surgical excision and not considered amenable to medical treatment. Surgical excision is sometimes difficult or not feasible. There are two previous reports of treatment of collagenoma with intralesional injections. Dawn et al. (9) reported a case of a 41-year-old female with familial cutaneous collagenomas, wherein some lesions that caused irritation to the patient were excised without any recurrence. In the same patient, intralesional triamcinolone acetonide was injected in few lesions, which resulted in reduction in their size. But the author did not provide the details of the dose and frequency of corticosteroids injections. There was no photographic documentation of the response. In another case report of a 17-year-old boy with acquired linear nodular collagenoma, intralesional triamcinolone acetonide (40 mg/mL) mixed with hyaluronidase (1 : 1) was administered at 3 weeks interval, with a maximum dose of 0.2 mL per lesion (10). There was almost 80% reduction in the size of the lesion after three treatments and the improvement persisted after 1 year of posttreatment follow-up.

Our case was interesting because of its distinct morphological features and significant medical treatment history. She had received about 12 intralesional steroid injections (triamcinolone alone) in the past, which resulted in patchy flattening of the plaque. In addition, she developed irregular depigmentation and marked atrophy and dimpling of skin at certain areas within and around the plaque. After stopping the injections, the nodules within and surrounding the plaque reappeared. This could possibly be due to thick bundles of collagen allowing limited spread of the steroid and excessive steroid concentrating in certain areas resulting in localized adverse effects and inadequate response. When we treated her with combination of triamcinolone and hyaluronidase, there was marked flattening of the plaque after first injection only. After four such treatment sessions,

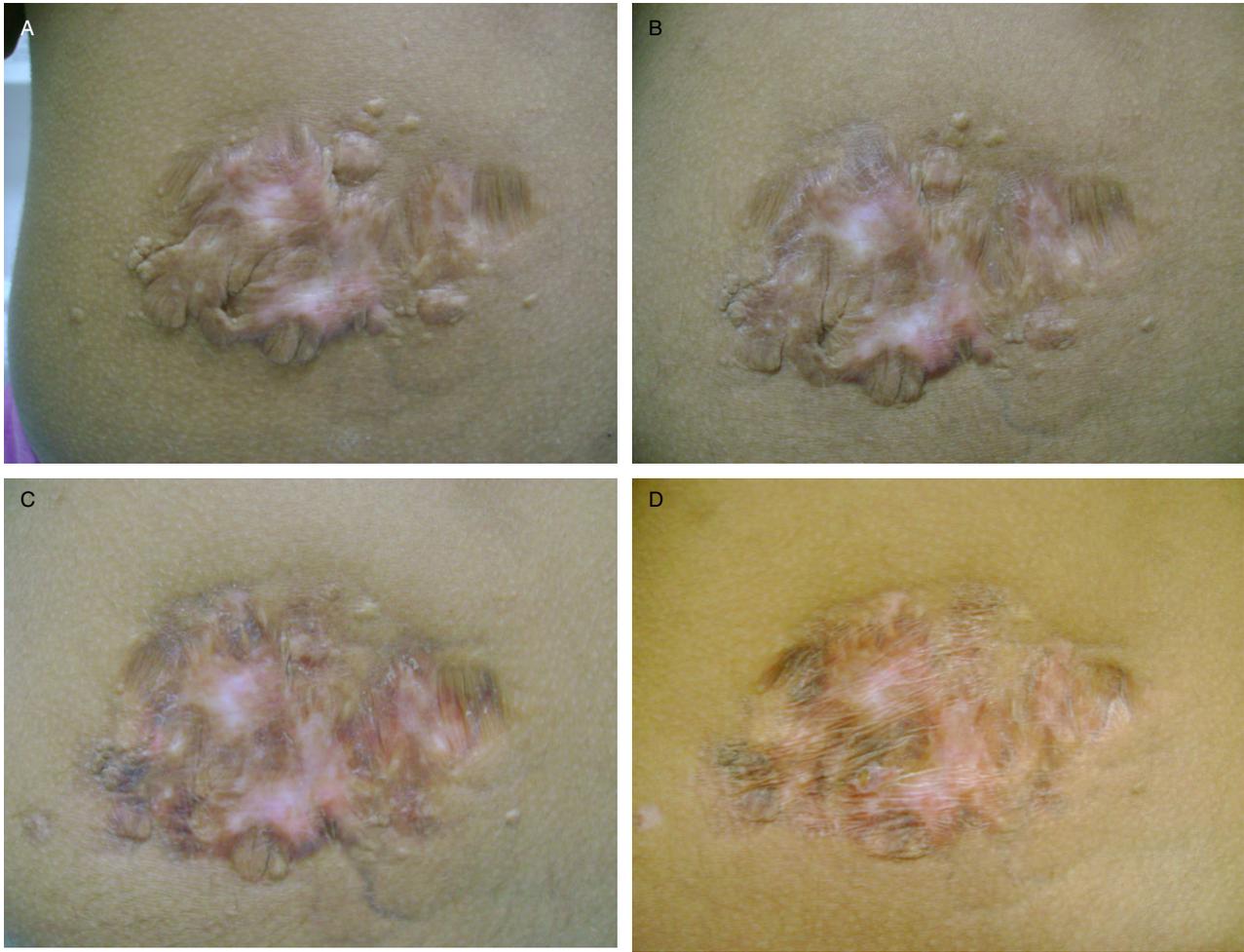


FIG. 3. (A–D) Serial photographs at monthly intervals showing progressive flattening of collagenoma plaque with intralesional injections.

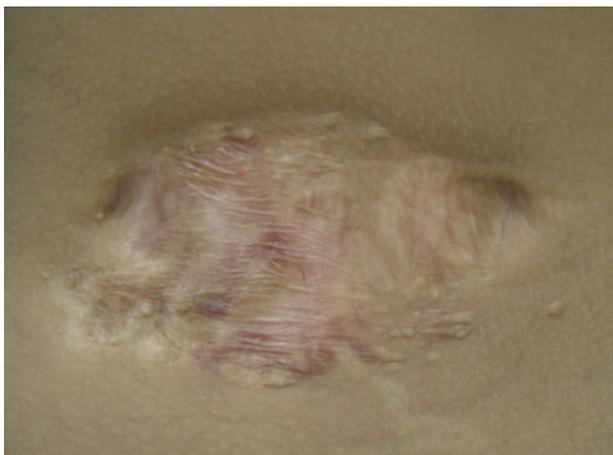


FIG. 4. Collagenoma plaque at 1 year follow-up.

the plaque was almost flat. There were minor adverse effects that partially reversed after stopping the injections. The combination resulted in excellent response, with significantly faster action, minor adverse effects, and no recurrence after 1 year of follow-up.

The response to steroid injections could be a result of the negative effect on fibroblast growth resulting from a decrease in transforming growth factor β 1 production and an increase in basic fibroblast growth factor production in fibroblasts. This mode of action is similar to that in keloids (12). Hyaluronidase is an enzyme that causes hydrolysis of hyaluronic acid, a glycosaminoglycan present in the dermis. This decreases the viscosity of extracellular matrix and increases the diffusion of injected fluids, thus facilitating their absorption and distribution. In our case, the use of hyaluronidase enhanced the penetration of steroid in the dermal collagenous matrix and hence, its inhibitory effects

on the fibroblasts. Addition of hyaluronidase also resulted in smaller dose of steroid injected per session and significantly lesser number of total sessions to produce a substantial response, thereby minimizing the local adverse effects of intralesional steroids.

This case report suggests that medical treatment with intralesional injection is definitely a good therapeutic approach in collagenoma. Small collagenoma may respond to triamcinolone injection alone but it is preferable to treat with combination of triamcinolone and hyaluronidase as it results in markedly faster and complete response. Also, while giving injections, multiple injections should be closely spaced while injecting small amount at each site as spread of intralesional corticosteroid is limited in collagenomas.

Conclusion

Intralesional corticosteroid in combination with hyaluronidase can be considered a novel and promising therapeutic approach for collagenomas.

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