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Case Series of Pyoderma Gangrenosum Successfully Managed with Biological Dressing

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Abstract

Introduction: *The management of recalcitrant vasculitic ulcers of pyoderma gangrenosum (PG) still lacks an ideal challenging topical agent which promotes optimum healing with negligible side effects. Current scenario of management depends on steroids and other immunosuppressive agents which are more devastating than the disease itself. Conventional treatment such as relief of pressure, wound debridement, local dressing, antibiotic therapy, skin grafting, and supportive therapy are somewhat effective in the treatment of such non-healing wounds. Biological dressings are the ideal dressing for the management of chronic wounds. The newer biological dressings like collagen and growth factors, targets the specific defects in the chronic ulcer environment. Collagen is a natural biological skin substitute, easily available, ready to use, non-antigenic, and non-pyrogenic. Collagen induced healing involve all three phases of the natural wound-healing cascade. Collagen sheets are derived from tissues of bovine, avian, porcine and fish origin, which comprises type I and III collagen.*

Case Report: *We have treated five cases of chronic non-healing leg ulcers of PG with oral dapsone and corticosteroids, in combination with topical wet collagen sheet dressings. In all patients of PG included in our study, the ulcers healed completely within duration of 8 to 10 weeks.*

Conclusion: *This study is being presented to highlight the superior efficacy of biological dressings in chronic vasculitic ulcers of pyoderma gangrenosum.*

Keywords: *Pyoderma gangrenosum (PG), Biological dressing, Wet collagen sheet, Chronic non-healing leg ulcer.*

Introduction

Pyoderma gangrenosum (PG) is a rare disease of unknown etiology which produces severe painful non-healing ulcers. Current treatment strategy for PG depend mainly on two major drugs, corticosteroids and cyclosporine.[1] However, they are poorly tolerated and associated with significant adverse effects. Management of

chronic ulcers like PG requires prolonged hospitalization.

Increased wound chronicity of PG has promulgated the use of biological collagen dressing, in an attempt to obtain wound closure and ultimately both physiological and functional healing.[2] Skin substitutes accelerate wound healing and ensure the physiological functions of skin. Newer technologies have paved the way for bioengineered skin substitutes.

An ideal skin substitute should be nontoxic, immunologically compatible, less antigenic, and should not transmit disease. The skin substitutes minimize water, protein and electrolyte loss. They reduce the bacterial load and provide coverage of the underlying structures, thus prevent desiccation, reduction of pain and restore the function[3].The ideal dressing should ensure that the wound remains moist and free from infection, excessive slough, toxic chemical, particles, and fibers. It should ensure that the wound is at an optimum temperature and pH for healing, and undisturbed by the need for frequent changes.[4]

Treatment options for chronic ulcers include skin substitutes such as autografts, allografts, xenografts, tissue engineered, synthetic, or biologic dressings.[3]Biological dressings offer promise in the treatment of chronic ulcers and in various dermatologic conditions.

Collagen is a natural protein, which plays a important role in all three phases of the wound-healing. Fibroblasts are the major sources of collagen. Collagen stimulates migration of cells and lead to formation of new tissue. Collagen-based formulations stimulate and recruit fibroblasts and macrophages, along the healing process to enhance wound healing. Depending on the delivery system, these materials provide either moisture or absorption. Collagen sheets are easy to apply and remove. Collagen dressings are routinely formulated with bovine, porcine, avian collagen or of fish origin. The newer wound-healing agents like growth factors and collagen, targets specific defects in the chronic ulcer environment.[5]

Wet collagen sheets are produced from bovine tissues comprising mostly type I and III collagen, packed in a neutral glass vial containing sterile liquid medium (admixture of isopropyl alcohol and water) sterilized by ethylene oxide. Wet collagen sheet act as a scaffold for epithelium to grow and arrange itself in the denuded areas.[6]

The role of collagen in chronic wounds

In chronic wounds, there is a decrease in normal collagen deposition and increase in breakdown of collagen. The decrease in collagen deposition is due to slow recruitment of fibroblasts and also decreases in expression of collagen gene in the fibroblasts. Matrix metalloproteinases (MMPs) are enzymes which are involved in degradation of collagen. In chronic ulcers, the MMPs levels are increased and also there is decrease in level of inhibitors of MMPs. This lead to degradation of excessive extracellular matrix (ECM). Elastase is another enzyme, which is involved in healing of ulcers. Their activity is also increased in chronic ulcers. Elastase converts precursors of MMPs to active form (Pro-MMPs to MMPs). Thus, the enzyme heavily contributes to load of MMPs in chronic ulcers. Being a non-specific protease it also degrades collagen. So, collagen in wet collagen sheet act as substrate magnet for both MMPs and elastase.

Collagen in wet collagen sheet will reduce elastase levels in a wound environment, disrupting the vicious cycle of chronicity, which is shown in (fig-1). Collagen is retained in the tissue and gradually absorbed by inflammatory cellular activity.[7,8]

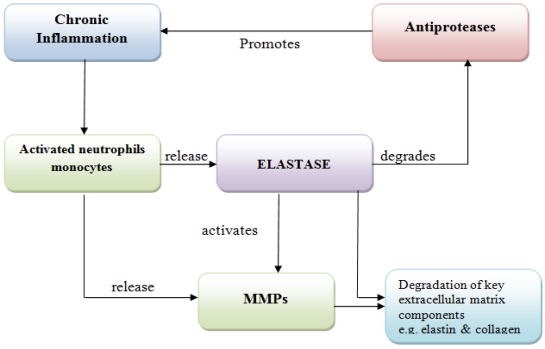


Figure 1 Effect of Elastase on Chronic Wounds

Materials and Methods

Five PG patients were selected as suitable candidates for collagen sheet dressing. Their case details are listed in Table 1.Comorbidities of each patient was noted. Skin biopsy was done for all patients to confirm the diagnosis. Wound bed was cleaned with normal saline without producing further trauma. Debridement is contraindicated in PG because it may produce pathergy phenomenon.

Collagen dressings were done weekly. In each time collagen was applied using appropriate sterile techniques. Collagen sheet with trade name of kollagen or colloskin which was much affordable and available in the market were applied to the wound area. Secondary dressing with gauze pad and roller bandage was done. Depending upon the amount of exudates dressing was changed daily or once in 3 days. The favorable outcomes were: a visible impact on granulation tissue, a reduction in wound surface area and a decrease in wound depth.

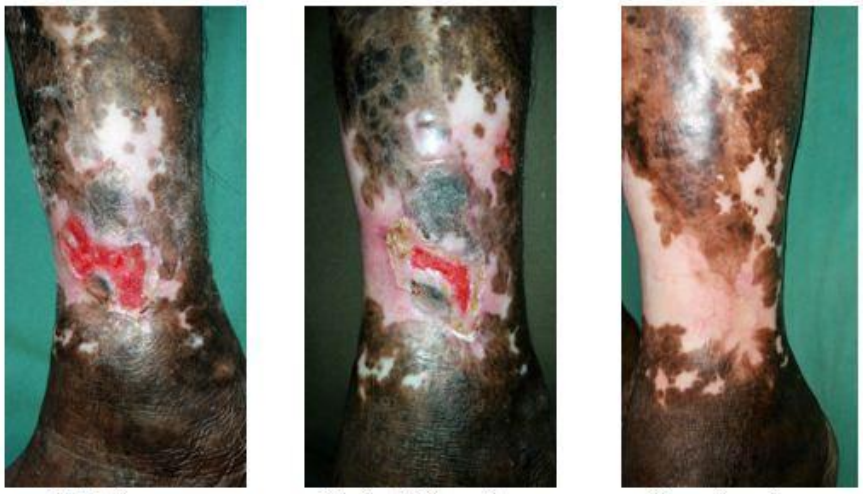
All parameters were measured once in week. Digital photographs of the ulcers were taken before and after collagen dressing and also in subsequent follow up periods. All study cases showing complete closure of wound after serial application of wet collagen sheet shown in Fig.2.

Table 1: (Patient Details)

S. No	Age (in years)	Sex	Duration	Initial size of ulcer (in centimeters)	Time required to complete closure
Case 1	58	Male	2 years	Bilateral maximum -5×2	6 weeks
Case 2	48	Male	1 year	Right leg - 8×5	8 weeks
Case 3	60	Male	8 months	Right leg - 7×4	9 weeks
Case 4	27	Female	1 year	Bilateral multiple leg ulcer maximum - 3×2	6 weeks
Case 5	61	Female	1 year	Bilateral leg ulcer maximum -10×7	10 weeks

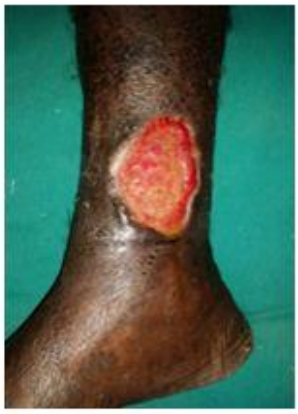
Fig 2: Showing complete closure of wound after serial application of collagen sheets

Case - 1



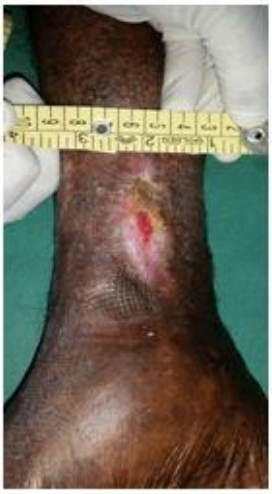
Initial | End of 3rd week | Complete closure (at 6th week)

Case - 2

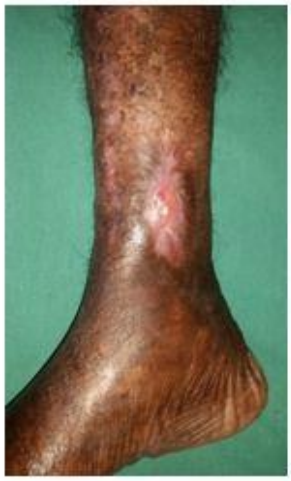


Initial presentation

Application of Collagen sheet

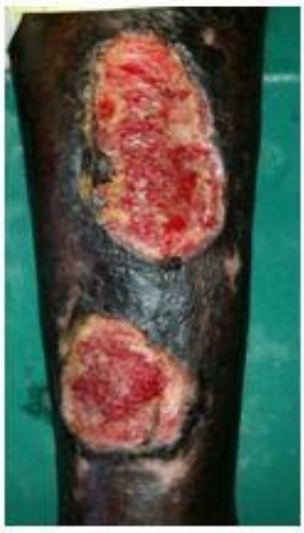


After 6 weeks



Complete closure (at 8th week)

Case - 3



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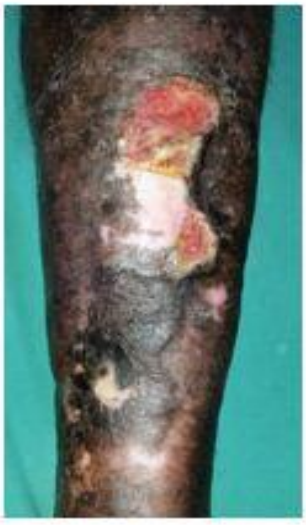
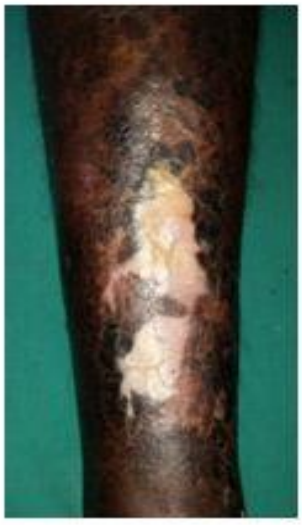
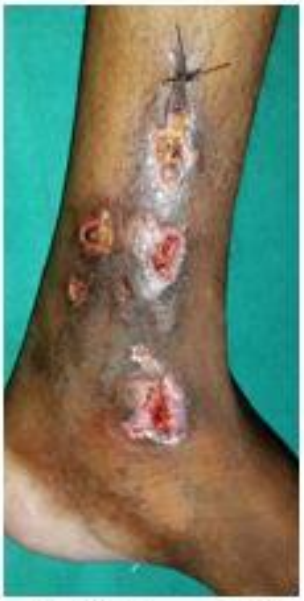


End of 6th week



Complete closure (at 9th week)

Case - 4



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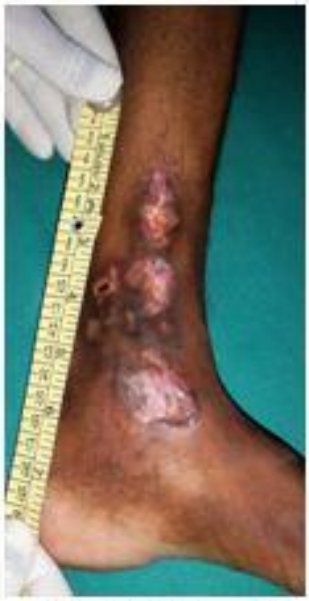
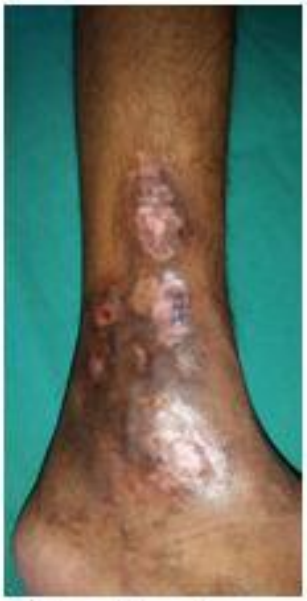


End of 3rd week



Complete closure (at 6th week)

Case - 5

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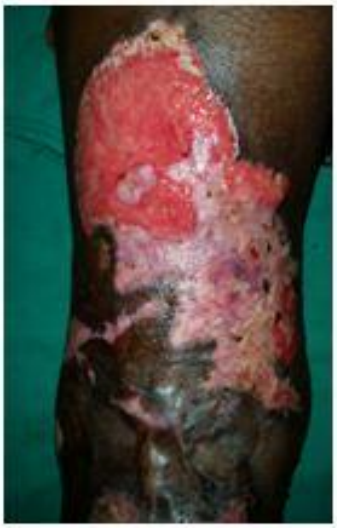
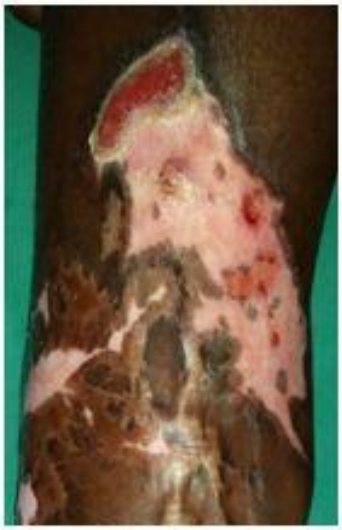


End of 5th week



Complete closure (at 10th week)

Discussion

In this pilot study, we have described how to treat recalcitrant chronic pyoderma gangrenosum with collagen sheets.

This study was done with the aim to evaluate efficacy of wet collagen sheets as a topical wound dressing in a long standing recalcitrant PG cases.

Pyoderma gangrenosum (PG) is an uncommon ulcerative skin disease of uncertain etiology for which current available treatment modality is far from satisfactory. Increased chronicity of wound in PG along with co-existing medical morbidities in a chronically ill patient leads to plethora of the patients with poor healing of the wounds.

This has promulgated the use of biological dressings like wet collagen sheets in an attempt to obtain ulcer closure with physiological and functional healing significantly minimizing the side effects of systemic corticosteroids and immunosuppressant like cyclosporine. Collagens are proline rich proteins that are fibrous with long stiff triple standard helical structure consisting of three α-chains.

The major collagen molecules that give tensile strength to skin or heterotrimeric collagen Type I formed by 2α1(I) chains and one α2(I) chain and homotrimer Type III collagen, formed by three α1(III). The role of collagen in improving wound healing is by stimulating fibroblast activity.[9,10]

Donaghue et al., compared the efficacy of collagen sheets dressings in a non-healing diabetic ulcer patients with the significant reduction of wound healing.[11]

Role of collagen is very crucial in wound healing of chronic ulcers. In chronic non-healing ulcers the level of matrix metalloproteinases (MMPs) and elastases are highly elevated leading to severe extracellular matrix degradation. Collagen is an important component of extracellular matrix, shows an absorptive capacity of MMPs. Collagen decreases pro inflammatory MMPs, resolution of inflammatory state and progression of fibroblast proliferation. It also acts as a scaffold providing faster and effective wound healing.

In our study, we have employed collagen sheets of bovine origin in the biological dressings of PG wounds because of wet collagen sheets are non-inflammatory, nontoxic and have less immunogenic, minimal biodegradation and well tolerated in clinical trials. There have been no reports of clinically significant immunological or histological response to implantation of collagen sheets, and no reports of rejection to collagen sheets. There is no threat of transferring HIV and hepatitis infection.

Bovine material obtained from countries free of bovine spongiform encephalopathy (BSE) and has long half-lives of five years. Wet collagen sheets are elastic soft supple is impermeable to bacterial migration with tear strength and suturing characteristics.[6]

In our study, we treated five cases of PG with oral Dapsone and Corticosteroids prednisolone 40 mg /day along with weekly collagen dressing. Out of five cases, four cases showed complete closure of ulcers in a span of 8-10 weeks and one case showed marked size reduction attaining near normal wound closure.

This was on par with the study conducted by *Farrey et al(2003*) showed significant resolution of PG wound after therapy with lyophilized bovine collagen matrix on treating a 34-year-old woman.[1]

Conclusion

Collagen dressings provides multiple benefits than conventional dressings by virtue of its ubiquity, low immunogenicity and ability to be molded into strong biocompatible scaffolds plays a leading role in chronic wounds in PG. It shows significant promising rapid wound healing results with reduction of side effects of corticosteroid and immune suppression along with reduced hospital stay.

Although wet collagen sheets in non-healing leg ulcers of PG appear promising, more properly structured clinically controlled trials using a different formulation of collagen in a large scale will be required to confirm these results.

References

1. Farris DR, Schutzer PJ, Don PC, Silverberg NB, Weinberg JM. Resolution of pyoderma gangrenosum after therapy with lyophilized bovine collagen matrix. Dermatology. 2003; 206(3): 284–5.
2. Wahab N, Roman M, Chakravarthy D, Luttrell T. The Use of a Pure Native Collagen Dressing for Wound Bed Preparation Prior to Use of a Living Bi-layered Skin Substitute. J Am Coll Clin Wound Spec. 2015; 6(1–2):2–8.
3. Anish S. Skin substitutes in dermatology. Indian J Dermatology, Venereol Leprol. 2015; 81(2):175.

4. Akingboye AA, Giddins S, Gamston P, Tucker A, Navsaria H, Kyriakides C. Application of Autologous Derived-Platelet Rich Plasma Gel in the Treatment of Chronic Wound Ulcer : Diabetic Foot Ulcer. 2010;20–9.
5. Junkins-Hopkins JM. Biologic dressings. J Am Acad Dermatol. 2011;64(1):5–7.
6. Lazovic G, Colic M, Grubor M, Jovanovic M. The application of collagen sheet in open wound healing . 2005; XVIII (September):151–6.
7. Powers JG, Higham C, Broussard K, Phillips TJ. Wound healing and treating wounds Chronic wound care and management. J Am Acad Dermatol [Internet]. 2016;74(4):607–25.
8. Fleck CA, Simman R. Modern Collagen Wound Dressings : Function and Purpose. J Am Col Certif Wound Spec. 2010;2(3):50–4.
9. Stadelmann WK, Digenis AG, Tobin GR. Physiology and healing dyanamics of chronic cutaneous wounds. Am J Surg. 1998; 176:26S-38S.
10. Schofiel JD, Uitto J, Prockop DJ. Formation of Interchain Disulfide bonds and Helical Structure During Biosynthesis of Pro collagen by Embryonic Tendon Cells. Biochemistry. 1974; 13:1801-06.
11. Donaghue VM, Chrzan JS, Rosenblum BI, et al. Evaluation of a collagen-alginate topical wound dressing in the management of diabetic foot ulcers. Adv Wound Care. 1998; 11:114-19.