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Research Article

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Wound Healing Efficacy of Re Cell Heal in a Diabetic Foot Infection Patient Diagnosed with Gas Gangrene – A Case Report

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Abstract

Gas gangrene is a rapidly progressive and bacterial infection that produces tissue gas in gangrene. The condition may result from ischemia, infection, or trauma or a combination of these processes. A 72-year-old woman with a 10 years history of type-2 diabetes mellitus (NIDDM) presented to the emergency department with a one-week history of left foot painful, swelling, redness, fever and foul-smelling discharge from wound. Wound infection of the left foot worsening progressing to gas gangrene that remains unhealed after a week to one month. She was diagnosed with Clostridium perfringens and Clostridial myonecrosis. The foot X-ray showed a 13 X 8.5 X 1.75 cm and is surrounded by callus under the 1st to 5th metatarsal heads (Figure 3a & 3b). Computed tomography (CT) scan showed moderate air suggesting deep tissue infection, with multiple tiny gas bubbles within under the first metatarsal heads, concerning for gas gangrene. The patient was treated with Poly Herbal Formulation (PHF), Re Cell Heal 500 mg Capsule (PRANATHI HERBALS; License No. T-2265/Ayur/; Letter No 2884/DA/2018) (p.o) twice a day, in addition to the (Topical) Wound Check Ointment (Letter No 4964/DA/2018) accompanied with debriment over a five (5) months, foot healed without amputation improved therapeutic outcomes, reduce fatalities caused by gas gangrene. Re Cell Heal helps to provide relief in the symptoms like swelling and pain in tissues. Recent scientific evidences and trials conducted on Re Cell Heal is a traditional and alternative medicine in wound therapy, gas gangrene and diabetic related foot problems holds good promise in the future safety without any side effects.

Keywords: Gas Gangrene, Diabetic Foot Infection, *Clostridium perfringens*, Wound Healing, Wound check ointment and Re Cell Heal

Introduction

The global diabetic foot ulcer prevalence rate is 6.3%. The annual incidence of diabetic foot ulcer (DFU) or necrosis in diabetic patients is known to be about 2% to 5% and the lifetime risk ranges from 15% to 20% [1]. The major foot complications include foot ulceration, cellulitis, abscess, wet gangrene, dry gangrene and necrotizing fasciitis, with different pathophysiological concepts behind each of them. Gangrene is a complication of necrosis characterized by the decay of body tissue. There are two major categories: infectious gangrene (which includes necrotizing fasciitis and gas gangrene) and ischemic gangrene (which can arise from arterial or venous obstruction). Gas gangrene is a life-threatening infection where presence of gas at the infection site turns the tissue pale, bronze to purplish-red with development of multiple hemorrhagic bullae. Gas gangrene is rare but dangerous, occurs in patients with any underlying conditions, predominantly in diabetes mellitus. It occurs when infection develops deep soft tissues inside the body, such as muscles or organs. The infection involves deeper tissue such as a muscle, which can lead to a rapidly spreading infection along tissue planes, and patients often present with sepsis. The infection may develop hours to weeks after the initial trauma and inoculation. The bacteria that causes gas gangrene, called *Clostridia perfringens*, release dangerous toxins (alpha and theta) or poisons that wreak havoc throughout the body, along with gas, which can be trapped within body tissue. Wet and gas gangrene spread very quickly. The patient may develop overwhelming shock, sepsis, and death. As the condition progresses, the skin may become pale, gray, and make a crackling sound when pressed, due to the gas within the tissue. Gas gangrene warrants immediate medical treatment. Without treatment, death can occur within 48 hours.

The most common organisms that cause these infections are *Clostridium perfringens*, *Clostridium septicum*, *Clostridium histolyticum* and *Clostridium novyi*. *Clostridium perfringens* cause 80% to 90%, of gas gangrene cases, but other species can also cause infection. *Clostridial myonecrosis* historically was a common war wound infection with an incidence of 5%. Populations at high risk for developing gas gangrene include those with diabetes and

atherosclerosis. Of all amputations on diabetic patients, 85% are preceded by a foot ulcer, which subsequently deteriorates to a severe infection or gangrene [2].

Material and Methods

ReCell Healcapsuleare polyherbal formulation prepared with traditional ayurvedic techniques, (PRANATHI HERBALS) Re Cell Heal each 500mg capsule contains extract of Shunti (*Zingiber officinale* 60 mg), extract of Ashwagandha (*Withania somnifera* 100 mg), extract of Shala (*Shorea Robusta*100 mg), extract of Saptala (*Euphorbia tirucalli* 35 mg), and extract of Kesara (*Crocus sativus*100 mg), Swarna bhasma (5mg) and Shankha Bhasma (100mg). *Zingiber officinale* extract has a variety of effects on the skin that may contribute to improved wound healing, anti-inflammatory, antibacterialand antimicrobial activity against *Staphylococcus aureus* [3]. *Withania somnifera* reported to exhibit antibacterial activities and it shows its activity against both Gram-positive and Gram-negative pathogenic bacteria. Anti-inflammatory effects in a variety of rheumatological conditions, seeds to coagulate milk, applied on open wound, anti-oxidative, anti-diabetic, immunomodulation, reduce cholesterol and triglycerides [4].

However, the leaves of *Shorea Robusta* resin ethanolic extracts also exhibited significant wound healing, antimicrobial activity against Staphylococcus aureus, *S. epidermidis* and *Escherichia coli* [5]. *Euphorbia tirucalli* decoction of leaves applied on affected skin externally. Crushed stem is applied to swellings, wound healing, fresh root or latex used for rheumatism. External applications (mostly for skin diseases, snakebites and wounds) and Antimicrobial activity [6]. Flavonoids, tannins, phenolics and polyphenols present in the plants are found to be effective antimicrobial substances against a wide range of microorganisms, to be toxic to microorganisms. Effect of saffron on burn wound healing at an in vivo model. Saffron was topically applied on burn wounds in rats. *Crocus sativus* possessed antioxidant, antidiabetic, anti-inflammatory, analgesic, dermatological and immunological effects [7]. Swarna Bhasma is anti-inflammatory, antipyretic, antimicrobial, anti-rheumatic, antipyretic and anti-arthritic actions [8, 9]. In Ayurveda, Shankha bhasma is used for treating anti-inflammatory, antioxidant; antacid and calcium supplement [10].

Case Report

A 72-year-old woman presented to the Emergency Department with a one week history of the left foot painful swelling, fever, foul smelling discharge from wound, discoloration of skin like from pale to black, purple, blue, bronze and red. Wound infection of the left foot progressing to gas gangrene that remains unhealed after 1 month. She had past medical history of type-2 Diabetes mellitus poorly controlled with Voglibose, Glimepiride, & Metformin since last 10 years. She was treated with intravenous (IV) antibiotics Piperacillin with Tazobactam 4.5 g Three times a day.

The physical examination of her left foot revealed increased tenderness for 5-6 days, soft tissue edema, erythema with fever, skin discoloration, redness, localized infection includes local warmth or purulent foul smelling discharge with tissue necrosis progressing to gangrene (Figures 1 & 2). Her vital signs were Temp >38.2°C, BP 122/78 mm Hg, HR 101 bpm, Pulse: 110 beats/ min, Respiratory rate: >20 breaths/minute and oxygen saturation 98% on room air, Weight. 60.6kg, Height142.3 cm. Head, Neck, Cardiac, Lung, Neuro and Abdominal examinations were unremarkable.

Figure 1: Dorsal muscles of the left foot revealed soft tissue edema, erythema, skin discoloration, warmth, foul smelling, purulent discharge and tissue necrosis progressing to Gas Gangrene

Figure 2: Dorsal aspect of left foot revealed tissue edema, erythema, skin discoloration, redness, localized infection includes local warmth, tenderness or purulent discharge

Microbiological Data of Wound tissue grew only positive Gram +Bacteria *Clostridium perfringens* and *Clostridial myonecrosis*. Despite surgical debridement and topical application of (Betadine 5% Povidone Iodine Solution) the wound worsened, with the development of purulent secretions and fever to >38.2°C,Pertinent Laboratory Data as drawn in ED,WBC22.3 × 10^9 /L, Platelet 182 × 10^9 /L, hemoglobin (Hgb) 82 g/L, C-reactive protein was (49.0 mg/L), Serum creatinine (Scr) was (152 µmol/L). She was found diabetes (glycated hemoglobin (HbA1c) level, serum glucose (325 mg/dL 10 %) with peripheral neuropathy.

Diagnosis of Gas Gangrene was made, the local infection with erythema (Ulcer) measures (L) 13 cm by (W) 8.5 cm and (D) 1.75 cm 13 X 8.5 X 1.75 cm plantar surface of the foot (Forefoot Metatarsals &Head). Plain radiographs of the affected foot showed foreign bodies, soft tissue gas in the entire foot (Figure 3a & 3b). Computed Tomography (CT) scan showed moderate air suggesting deep tissue infection, with extensive gas bubbles, within dorsal, fore foot with

extensor tendons, metatarsophalangeal joints concerning for gas gangrene (Figure 4).

Figure 3a & 3b: X-Ray of the left Foot showed foreign bodies and soft tissue gas in the entire foot.

Figure 4: Moderate air suggesting deep tissue infection with extensive bubble

The left foot had progressively worsened over a month and then she was transferred to our hospital with the presumptive diagnosis of gas gangrene. After admission, patient was started treatment with Re Cell Heal capsules for 5 months. (July/18/2018 to 13th Dec/2018). She had been taken orally twice in a day Re Cell heal 500 mg capsule along with wound check ointment topically applied, followed by extensive debridement of the remaining necrotic tissue, advanced wound care dressings and close follow-up result in improvement of these wounds. Over 5 months of treatment, her infection resolved and the foot healed without amputation (Figure 5). Without early imaging to elucidate the diagnosis, gas gangrene may rapidly progress systemically to sepsis, shock, or even death.

Figure 5: Over the 5 months of treatment with Re Cell Heal, Gas Gangrene, Wound infection resolved and the Foot healed without Amputation

Results and Discussion

Diabetic foot ulcers (DFUs) are a serious complication of diabetes that results in significant morbidity and mortality. Mortality rates associated with development of a DFU are estimated to be 5% in the first 12 months, and 5-year morality rates have been estimated at 42% [11]. The risk of death at 5 years for a patient with a diabetic foot ulcer is 2.5 times as high as the risk for a patient with diabetes who does not have a foot ulcer. More than half of diabetic ulcers become infected. Approximately 20% of moderate or severe diabetic foot infections lead to some level of amputation. Nearly 415 million people globally have diabetes, with 75% living in low- and middle-income countries. In India about 70 million people have diabetes, and the number is projected to rise to 125 million by 2040 [11]. Foot disease affects nearly 6% of people with diabetes. Between 0.03% and 1.5% of patients with diabetic foot, require an amputation.

Gas gangrene is very rare but at the same time very dangerous and requires immediate medical attention. It is generally caused due to trauma followed by clostridia infection leading to accumulation of toxic gas within the tissue. If left untreated this condition can be fatal in 48 hours. People with diabetes with a foot ulcer or gangrene should be examined with a comprehensive assessment of arterial disease, regardless of age. Gangrene mostly caused by the bacterium *clostridium perfringens*, *Clostridium septicum* which is developed during any injury or wound. In this condition the death of tissues, occur in extremities due to the depletion of blood supply to them. The natural history of a diabetes-related foot ulcer is sobering. Wound infection is a known predictor of poor wound healing and amputation. Despite this, in many cases of *C. perfringens* induced gas gangrene, radical amputation still remains the treatment of best choice [12]. If not controlled, it will always result in systemic toxemia, hypotension, shock, multiorgan failure, and death. The appropriate recognition of infection and treatment with Re Cell Heal in diabetic foot infection is imperative to improve outcomes. The IDSA has outlined specific guidelines for the treatment of diabetic foot infections [13]. The IDSA recommends treatment of wounds with at least two signs or symptoms of inflammation (erythema,

warmth, tenderness, pain, and induration) or purulent secretion. It is recommended that, beforeantibiotictherapy, a deep tissue culture via biopsy or curettage after debridement be obtained. Swab specimens should be avoided, especially in inadequately debrided wounds. It is widely recommended that blood glucose (Glycemic Control) be optimized to improve wound healing and limit adverse effects on cellular immunity and infection. Furthermore, another Cochrane review assessing effects of glycemic targets in type 2 diabetes found that those with intensive glycemic control had a 35% reduction in risk of lower-extremity amputation [14]. With the best care, including early recognition, debriment, and Re Cell Heal capsules and wound check ointment.

Active constituents of ginger Gingerol (Anti-inflammatory and Anti-microbial activity), Zingerone (Anti-bacterial activity, Anti-inflammatory action and Antioxidant activity), Paradols: (Anti-microbial activity Anti-oxidant activity), Shogaol (anti-inflammatory and Anti-oxidant activity), Zerumbone (Anti-microbial, Anti-tumor activity and infectious diseases, rheumatism and swellings. *Withania somnifera* chemical constituents such as steroidal lactones, alkaloids, flavonoids, tannins, saponins somniferine, somniferine, somnine, with amine, pseudowithamine, withanmine and withanmine. *Shorea Robusta* active principles terpenoids, flavonoids, carbohydrate, lignans, phenols and sterols. *Euphorbia tirucalli* contains terpenes, sterols alkaloids, cardiac glycosides, coumarins, flavonoids, saponins and tannins, etc., *Crocus sativus* contained apocarotenoid glycosides: crocin, picrocrocin, protocrocin, volatile oil, safranal, carotenoids: lycopene, alpha-, beta-, gamma-carotene; fatty oil and starch [15].

Oral medication like *Zingiber officinale*, *Withania somnifera*, *Shorea Robusta*, *Euphorbia tirucalli Latex*, *Crocus sativus*, Swarna bhasma (Clax of gold) and Shankha Bhasma (Clax of conch) are clinically established and practiced drugs in the management of diabetes mellitus and also anti-oxidant, antimicrobial, antibacterial, analgesic, antipyretic, anti-rheumatism and anti-inflammatory actions which help in the prevention of wound infections [9]. *W somnifera* has long been used in traditional and Ayurvedic medicine to cure diabetes and obesity. Recent studies and observations have revealed that, flavonoids found in the roots of *W. somnifera* were able to reduce the high blood glucose level in experimental animals. It was also shown that cells to stimulate the release of insulin. Moreover, it also works for the control of the infection, boosting the immunity, discharge of the pus from the infected wounds and swelling. *Zingiber officinale*, *Withania somnifera*, *Shorea Robusta*, *Crocus Sativusas* a wound healing agent is proved and practiced since decades and its ingredients acts on the various stages of wound healing process thus reducing inflammation, promoting wound contraction, Epithelialization, Granulation tissue formation and scar remodeling [16-19].

Due to the emergence of multi-resistant organisms and a decrease in newer antibiotics, wound care professionals have revisited the ancient healing methods by using traditional and alternative medicine in wound management. Gas gangrene infection is rapidly progressive to septic shock, it is important to treat patients aggressively with Re Cell heal capsule along with wound check ointment and early surgical consultation, which suppresses *Clostridium perfringens* and *Clostridium septicum* release dangerous toxins or poison production, likely helped salvage her foot healed without amputation.

Plants and their extracts have immense potential for the management and treatment of wounds. Recent scientific evidences and clinical trials conducted using traditional and alternative medicine in wound therapy holds good promise in the future. As we look toward a future where many of our current antibiotics may no longer work with the efficacy to which we have become accustomed, I think Re Cell Heal it's important to have alternative strategies in development to fill that gap,"

Conclusion

Gas gangrene still exists and needs urgent attention since it carries a very high mortality rate it requires early imaging to diagnose foreign body with gas gangrene in a high-risk patient with diabetes and to prevent potentially fatal complications. A good glycemic control is required in diabetes patients to avoid future complication. The ReCell Heal polyherbal formulation contains a number of beneficial natural ingredients, which are considered to harbor substantial anti-inflammatory and antimicrobial action, promote synthesis of collagen fibers and increase supply of vital nutrients (amino acids, vitamins and fatty acids) to the wound site. From the Ayurvedic prospective, to manage the problems of gangrene polyherbal formulation (Re Cell Heal capsules), which help to provide relief in the symptoms like swelling and pain in tissues. These help to increase the body's ability to fight against infections and thus support the good immunity. The remedy heals the gangrene, controls infection, and establishes circulation. These natural agents induce healing and regeneration of the lost tissue by multiple mechanisms. Therefore, Re Cell Heal is new hope in this era because Ayurveda focuses on root of disease and manage the symptoms without any adverse effects on health and also safety.

Declaration of patient consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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