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GAVIN PUBLISHERS

Journal of Surgery

Wang L, et al. J Surg: JSUR-1121.

Research Article

DOI: 10.29011/2575-9760. 001121

The Research about the Micro-Environment of Tuberculosis Wound

Li-wei Wang[1], Chang-qing Wu[1], Zhou Han[1], Ao-ao Bian[1], Hong-jie Tang[1], Mei-ying Wu[2*]

[1]Department of Surgery, Suzhou the Fifth People's Hospital, Jiangsu Province, China

[2]Vice President of Suzhou the Fifth People's Hospital, Jiangsu Province, China

[*]**Corresponding author:** Mei-ying Wu, Vice President of Suzhou the Fifth People's Hospital, Jiangsu Province, China. Tel: +8613906133614; Email: wu_my@126.com; uncle_163@163.com

Citation: Wang L, Wu C, Han Z, Bian A, Tang H, et al. (2018) The Research about the Micro-Environment of Tuberculosis Wound. J Surg: JSUR-1121. DOI: 10.29011/2575-9760. 001121

Received Date: 20 March, 2018; **Accepted Date:** 07 April, 2018; **Published Date:** 13 April, 2018

Abstract

Object: To extenuate the pain of tuberculosis patients, to reduce the healing time of the tuberculosis wound, to improve the life quality of tuberculosis patients, and to probe the mechanism of the tuberculosis wound healing.

Method: We chose 30 cases of chronic tuberculosis wound, and 10 cases of normal wound, collected the wound fluid with drainage gauze. We detected the contents of VEGF, EGF, bFGF in different period of tuberculosis wound, and compared with those in the normal wound. Evaluate the micro-environment transformation of the wound healing.

Result: It spends much more time to heal by the tuberculosis wound than normal wound ($p<0.05$), 2 Days after being wounded, the contents of VEGF, EGF, bFGF in tuberculosis wound are less than those in the normal wound. There is diversity of the contents of VEGF, EGF, bFGF in different period of tuberculosis wound, but wound healing shows no significant association with the contents of VEGF, EGF, bFGF ($p>0.05$).

Conclusion: Tuberculosis wound is such a chronic wound which is hard to heal, the disorder of the wound's micro-environment may cause the delay healing, but there are no significant association between wound healing and the contents of VEGF, EGF, bFGF.

Keywords: EGF; bFGF; Tuberculosis; VEGF; Wound Healing

Introduction

In recent years, along with the widespread implementation of modern tuberculosis control strategy, Tuberculosis (TB) prevention and control work made great progress in China. According to the 2015 national epidemiological investigation and analysis, all kinds of tuberculosis patients in our country, about 7 million people, of which about 20% of extra-pulmonary tuberculosis [1]. Especially extra-pulmonary tuberculosis increased year by year in recent years, such as cervical lymph nodes tuberculosis, bone tuberculosis, renal tuberculosis, etc. The TB infection form cold abscess, when need surgery treatment, tuberculous wound hardly heal, granulation tissue grow slowly. According to previous studies [2], through debridement and drainage, wound healing speed depend entirely on the level of granulation tissue growth [3], the treatment time is quite a long time, at least 2 ~ 4 months, even more than two years, which spent a lot and pushed great psychological pressure to patients. Wound healing need specific tissue micro-environment, including the Epidermal Growth Factor, (EGF), Vascular endothelial growth factor (VEGF) and basic Fibroblast Growth Factor (bFGF), which plays a very important role in the wound repairing [4].

Materials and Method

The General Information

We select the 40 outpatient's cases during Oct 2014 to Oct 2016 in Suzhou the Fifth People's Hospital Surgery Department, between 20 ~ 70 years old, including 30 tuberculous wound cases, and 10 normal wound cases. We choose the exudate of wound drainage in the yarn as the research object.

Group Criteria

Tuberculous wounds: Infected with TB bacilli, pus detect tuberculosis *Mycobacterium* DNA in the wound, either found the caseous necrosis around the wound tissue, or the pathological

results prompt TB infection.

Normal wound: Patients with wound which delay healing due to any other reasons. Through debridement and using drainage yarn, take the exudate of wound drainage yarn in different healing phases [5], detection of growth factor contents, since the 1st surgical intervention of the wound, select 2nd days, 9th days, 16th days, 30th days wound exudates. The drainage yarn in the wound is about 5cm length and 1cm width, absorb the wound exudate, until wound healing. Take the wound exudate of yarn, placed into the centrifuge, isolated the exudate, and mark the collection time, sampling placed on refrigerator cryopreserved -20°c within 8 hours. We used ELISA kits from Enzyme-linked on Shanghai biological technology corp. (batch number: m1027145 m103367, m1023364), detect the growth factors in different wound in respective phases.

Wound Healing Criteria

Skin with scar tissue cover, wound granulation tissue completely filling, no potential under-dermal lacuna. Record the healing time.

Data Analysis and Synthesis

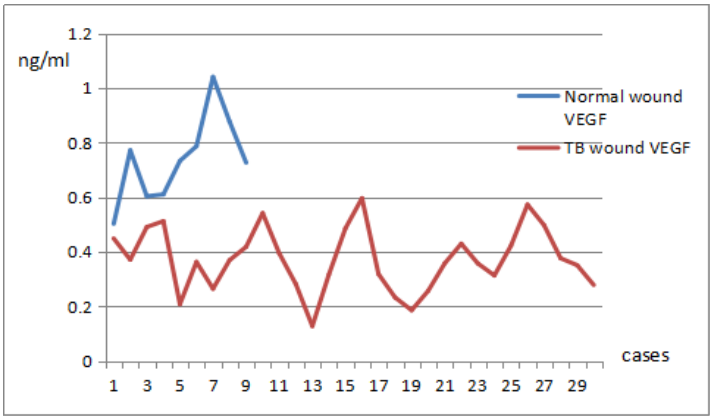
Using SPSS 17.0 software to analyze data, the data between groups using "group t test" and "double variable Pearson correlation test", $P < 0.05$ as the standard instructions shows statistically significant differences between each other.

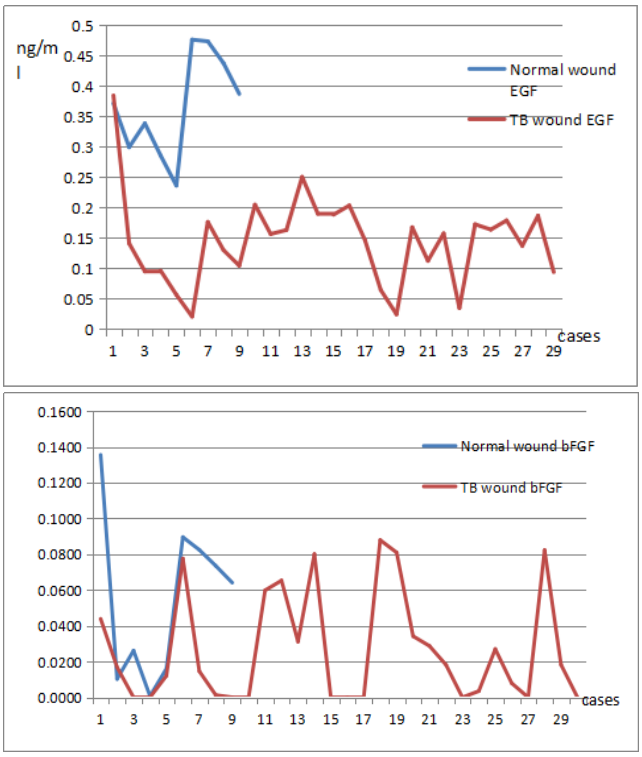
Result

Wound healing phase (Table 1) (Figures 1a-c, 2a-c)

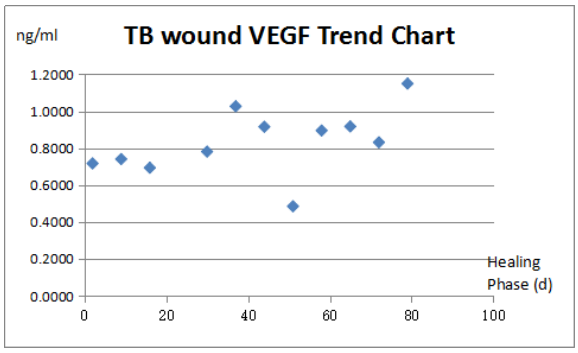
Group	Healing phase (D)
Normal wound	4.67±2.64
Tuberculosis wound	54.43±20.80
t	4.539
P	0.045

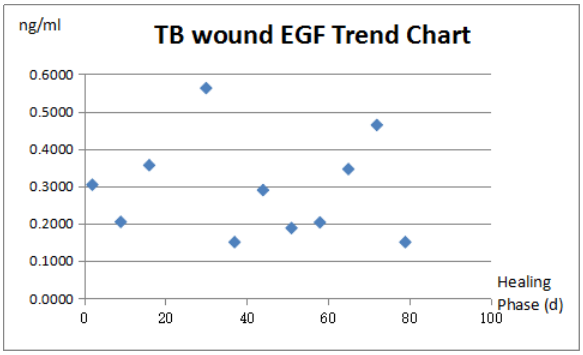
Table 1: Healing schedule.

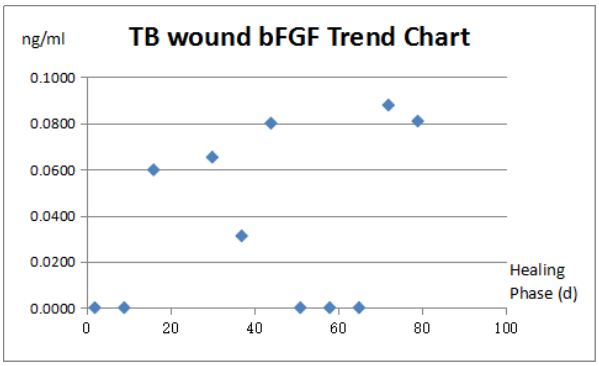




Figures 1a-c: The content of VEGF, EGF, bFGF in the same healing phase (2nd d) between normal wound and TB wound.







Figures 2a-c: The content of VEGF, EGF, bFGF in different healing phase of tuberculosis wound (average of 30 TB wound cases).

The content of growth factor in normal wound is much higher than that in TB wound. Most of normal wound heal within a week, much faster than tuberculous wound healing ($p < 0.05$). At the 2nd d after surgery, the content of VEGF in normal wound is higher than that in TB wound ($t = 4.487$, $P < 0.01$), the content of EGF in normal wound is higher than that in TB wound ($t = 5.438$, $P < 0.05$), the content of bFGF in normal wound is higher than that in TB wound ($t = 3.427$, $P < 0.05$). With the progress of the time, the content of VEGF, EGF, bFGF in TB wound shows no obvious correlation with wound healing ($P = 0.081$, $P = 0.081$, $P = 0.723$).

Discussion

Lymphatic tuberculosis is one of the most common extra-pulmonary tuberculosis, each lymph nodes in the body can infect tuberculosis *Mycobacterium*. Cervical lymph nodes tuberculosis has the highest incidence rate, which is main reason of TB wound. The tuberculosis *Mycobacterium* transmission through lymph and blood, can be divided into nodular type, infiltration type, abscess type and ulcer-fistula type. The abscess type and ulcer-fistula type are much common in clinical work, which are difficult to therapy. Single drug treatment effects poorly, and drainage of abscess also cannot cure TB wound [6]. If we don't perform surgical debridement completely, TB wound need a long term to repair, often costs patients a number of months to several years.

Wound healing includes inflammation, cell proliferation and collagen metabolism and a series of complex path-physiological process, its general divided into four stages, includes blood coagulation, inflammation, proliferation, and rebuilding. The process requires comprehensive control of all kinds of growth factors, cytokines, and so on, to promote wound healing in a certain time [7]. Wound healing needs the blood supply, among the factors of promote new blood vessels, VEGF play an important role. VEGF is a kind of glycosylates secrete peptides, can regulate the formation of new blood vessels in the molecular level, mainly including endothelial cell proliferation, cell chemotaxis, and produce protease [8]. EGF is composed of single polypeptide 53 amino acid residues, have promote cell migration, division and synthesis of interstitial protein, play a key role in the process of promoting cell removing in wound healing [9]. bFGF is erected by fibroblasts, endothelial cells, smooth muscle cells and cartilage cells, etc. its main function is to promote the growth of microvascular endothelial, so as to accelerate the creation of new blood vessels, played a key role in wound vascularization process, at the same time can also increase the collagen content in the wound, improve tissue repair mechanical force [10].

This study found that the content of growth factors (VEGF, EGF, bFGF) in normal wound, is significantly higher than that in tuberculous wound. Seems there are abundant growth factors in normal wound's micro-environment, coordination other wound repair factors, maybe activate some cell signal pathways, both inside and outside the cell, promote restoration and proliferation [11], promote healing in short phase ,and hard to gather all the data. In TB wound, with the progress of time, the growth factors (VEGF, EGF, bFGF) in early phase are generally lower, there is a peak in the middle of the middle phase, then gradually decrease, till wound healing. Tuberculous wound for a long time to heal, investigate its reason, is closely connected with special infected with tuberculosis *Mycobacterium*. Tuberculosis *Mycobacterium* as high metabolize bacteria [12], the energy, protein and other nutrients in the micro-environment are consume too much, which are not enough to wound healing, bacteria cannot be eradicated in the wound, pus accumulated for a long time, the wound micro-environment is adverse for tissue repair [13]. Integrate with this study, seems tuberculosis *Mycobacterium* inhibit some kinds of growth factors, disturb the wound micro-environment, retard the wound healing process. We often use drugs as INH & RFP in clinical application, to destroy tuberculosis bacilli, hope to restore normal wound micro-environment [14]. The complete surgical debridement is vital for recovery, make sure that caseous lesions and stiff tissue are totally removed, it's very important to the wound healing and prevent recurrence.

Surgery has become one of the important of treatment tuberculosis disease, complete debridement to cold abscess can implement in most cases, but TB wound is still hard to cure. Hopefully, there is a suitable wound dressing for TB wound, which could shorten the healing procedure. Tuberculous wound is also found in baby's BCG reaction, curing the wound will last for a long time, bothering the infected babies and their family members. Studies have found that the new dressing "Epidermal Growth Factor (EGF) - hyaluronic acid composite film" "calcium alginate dressings" to promote healing of rat skin, release scar, which have a positive role [15,16]. There are some traditional medicine such as insect poisons (blatt) extract used in wound dressings [17], have achieved good clinical effect. Integrate the study, TB wound is hard to cure, kind of chronic wound, the wound micro-environment disorders may plays key role in the procedure, however there are

many other kinds of factors in the process of wound healing, the interaction mechanism between them is still not very clear. We hope EGF, VEGF, bFGF related wound dressing which can adjust the wound micro-environment could application to clinical work, follow up the next stage of TB wound healing.

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