

Original article

Mycosis Fungoides Skin Wound Management With Skin Graft Post Ultraviolet Radiation therapy.

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Abstract

Objective : To assess the survival rate of skin graft management in skin lesions of mycosis fungoides patients after therapy with ultraviolet radiation.

Methods : Between February. 2011 and June 2015, 89 [8- 81 yrs.] mycosis fungoides patients were followed up at dermatology clinic, the initial investigations were skin biopsy and the most common used therapy is photo therapy with ultraviolet radiation (according to stage in the histopathologic reports)

Results : Of the 89 patients that we followed , 90% treated with phototherapy (80 patients) , 35% of them (28patients) of these patients were managed by skin grafts of skin lesions and ulcers , 10% of them (3patients) the skin graft didn't survive without previous therapy with ultraviolet radiation , 90% (25patients) of them the grafted areas survived after phototherapy of UVA ,UVB radiation to the potential donor site, the other 65% (52patients) of the followed pts were managed without skin graft for the ulcerated skin lesions , 38% of them healed spontaneously , others didn't healed for a long time and need skin graft.

Conclusion: Mycosis fungoides is the most common type of cutaneous T lymphoma, pts who received phototherapy to the potential donor site has proven beneficial for skin graft survival , since ultraviolet radiation A,B ,decrease the cytotoxic T lymphocyte activity and decrease inflammatory cells in both graft and donor tissues , with decrease in the antigen presenting cells expression, which leads to decrease in the delayed type hyper sensitivity reaction and increase graft uptake.

Keywords: *Mycosis fungoides , skin graft , phototherapy.*

Introduction

Mycosis fungoides represents the most frequent type of cutaneous T-cell lymphoma⁽¹⁾. The annual incidence of cutaneous T-cell lymphoma is apparently increasing and currently estimated at 9.6 cases per 1 million person- years⁽²⁾. Male to female ratio is about 2 : 1, while type 4 skin (blacks) have twice the incidence of type 1 skin (whites)⁽³⁾. Most of patients are detected in the fifth and sixth decades (median age 55 to 60 yrs). patients under the age of 18 years are rarely affected . around 1,000 new cases are diagnosed each year in the united states⁽⁴⁾, the usual cutaneous stages of mycosis fungoides are 1. Patch stage , 2. Plaque

stage , 3. Tumor or erythrodermic stage. Were described by Bazin⁽⁵⁾ in 1876 .

The diagnosis is generally made by recognition of clinical manifestations plus routine histopathologic reports after skin biopsy , supported sometimes by immunophenotyping , flow cytometry and T-cell receptor gene rearrangement (TCRGR) analysis. The usual treatment of early stages is psoralen plus ultraviolet type A radiation (PUVA) , Narrow band ultraviolet radiation type B (311 nm) , sometimes interferon alpha -2a or retinoid , topical steroids can be used , or combination of these modalities⁽⁶⁾. Treatment of late stages includes

Extracorporeal Photophoresis , systemic chemotherapy, biologic therapy and Radiotherapy , Also PUVA in combination with interferon alpha can be used⁽⁷⁾ Regarding The prognosis of MF , it's a low grade malignancy with prolonged survival , progression and extracutaneous spread usually takes place over many years or decades⁽⁸⁾ It has been predicted that only 15-20% die of their disease⁽⁹⁾.

skin graft applied to chronic non responding ulcer or skin lesions in patients of mycosis fungoides ,it's the graft technique in which sheets of skin are harvested containing the epidermis and part of dermis (split skin graft) or both the epidermis and dermis (full thickness graft) to cover skin loss⁽¹⁰⁾. It has two purposes 1:reduce the course of treatment needed , 2: enhance the function and the cosmetic appearance of the lesion that receives skin graft⁽¹¹⁾, and regarding the difference of both types see table :1 ,which shows comparison chart of split-thickness and full-thickness skin grafts.

Skin graft survival rate was very high in patients who received phototherapy with PUVA , or narrow band UVB . since phototherapy affecting epidermis and dermis , causing suppression of DNA synthesis by formation of DNA photoproducts , and stimulates prostaglandins ,cytokines that play important role in immune suppression. , So infiltrating lymphocytes are strongly suppressed by PUVA and UVB , which leads to increase in graft uptake and high survival rate.

Methods

This retrospective descriptive study was conducted at royal medical services dermatology clinics, Between the period starting February 2011 and ending June 2015 . Approval from the ethical committee was obtained to carry out the study. It included 89 (8 – 81) patients who were diagnosed to have mycosis fungoides (mainly patch stage) . Data were collected from dermatology clinic , histopathology department reports , cosmetic surgery clinic . All patients had their histopathologic reports , and underwent phototherapy with UVA (PUVA) or narrow band UVB , This therapy applied in a large chambers that allowed the whole patients body to get the photoradiation with cover eye glasses (figure 5) . 35% OF Patients treated with (PUVA or UVB) underwent skin grafts for their skin ulcers and lesions.

Related to our policy in Royal Medical Services cosmetic surgery clinics , which is applied as the international protocol guidelines⁽¹²⁾ the skin graft is taken usually from inner thigh or lower back , and grafted as followed 1 : scrubbing and toweling for each donor and recipient site , 2 : debridement of

all necrotic tissues and beds until a healthy vascularized bed is seen , this procedure is done by wike – knife (figure : 1) , 3 : an oil material is called paraffin oil is paint over the donor area then skin graft is taken by the dermatome budget ,with multiple sizes range from very thin to full thickness graft (figure : 2) . 4 : the graft then inserted to be meshed in the mesher that is used to increase the size by (1 – 1.5) , (figure : 3) . 5 : the skin is grafted with the skin facing up . 6 : the graft is fixed at recipient area by metallic clips , then dressed by paraffin gauze (figure : 4) . 7 : the donor area is dressed by antibiotic dressing. Follow up of these patients is done and the survival rate was very good of previously treated patients with (PUVA or UVB) ,and the follow up was done in the next one to two weeks after skin graft to see the results.

Table 1

Comparison Chart of Split-Thickness and Full-Thickness Skin

<u>Grafts</u>		
Characteristics	Split-Thickness Skin Graft (STSG)	Full Thickness Skin Graft (FTSG)
Structure	100% Epidermis & Part of the Dermis	100% Epidermis & Dermis. Also A Percentage of Fat
Graft Endurance	High Chance of Graft Survival	Lower Chance of Graft Survival
Confronting to Trauma	Less Resistance	More Resistance
Cosmetic Appearance	Poor Cosmetic Appearance. Offers Poor Color and Texture Match. This Also Does Not Prevent Contraction.	Better-Quality Cosmetic Appearance. Thicker, and Prevents Contraction or Deformation.
When Performed	Temporarily or Permanently Performed After Excision of a Burn Injury, As Long As There Is Sufficient Blood Supply.	When Aesthetic Outcome Is Important (e.g., Facial Defects).
Donor Site Tissue	Abdomen, Buttock, Inner or Outer Arm, Inner Forearm and Thigh	Nearby Site That Offers Similar Color or Texture To The Skin Surrounding The Burned Area.
Disadvantages	Poor Cosmetic Appearance, a Greater Chance of Distortion or Contraction.	A Higher Risk of Graft Failure. The Donor Site Requires Long-drawn-out Healing Time And Has A Greater Risk Of Deformation And Hypertrophic Scar Formation.



(figure : 1) Wike knife



(figure : 2) Dermatoam



(figure : 3) mesher



(figure : 4) paraffin gauze



(Figure : 5) PUVA chambers

Results

There were 89 patients, (45) males , and (44) females , who were included in this study .Their age ranged from 8 to 81 years, and the mean age was 45 years . All patients proved to have mycosis fungoides by skin biopsy and histopathologic reports (mainly patch stage) , and 90% (80 patients) of them underwent therapy by (PUVA or UVB) . 35% of them (28 pts) were managed by skin graft for their skin lesions and ulcers . 90% (25 patients) of the 28 pts had successful skin graft since all of them treated by (PUVA or UVB) ,in the other 10% (3 patients) the skin graft didn't survive since they were not treated with phototherapy (PUVA or UVB) . Regarding the other 65% (52 pts), the skin lesions treated at our dermatology clinic , 38% of them (20 patients) healed spontaneously without complications , in the other 32 patients , the skin ulcers remain chronic and need skin grafts.

Discussion

Mycosis fungoides is a low grade lymphoproliferative disease that involves $CD4^+$ lymphocytes , It is the most frequent type of cutaneous T-Cell lymphoma. The cytotoxic T cells localize to the epidermis and dermis and produce patches , plaques , tumors , or erythroderma⁽¹³⁾ Skin lesions may occur as a result of the disease itself or secondary to its therapy This skin lesions is difficult to be managed . This is mainly due to the presence of a large number of atypical T-lymphocytes and antigen presenting cells (APCS) , which give a harmful effect on wound healing and graft take .

this increase in the pathologic number of T-lymphocytes leads to increase in the immunogenic reaction and then failure of the graft , As normally functioning T-lymphocytes play a major role in inflammation and therefore proper healing .

Treated patients with photodynamic therapy can prolong allograft survival by changing the donor skin antigenicity⁽¹⁴⁾. By depleting the donor antigen presenting cells(APCS) with phototherapy , it has also been shown that UV-B irradiation can decrease the cytotoxic T- lymphocytes activity which leads to a decrease in delayed type hypersensitivities and , so , an increase in graft uptake⁽¹⁵⁾ .

Skin graft in our patients has two aims : it can reduce the course of treatment needed (at a time of hospitalization) , and to enhance the function and the cosmetic appearance of the skin lesion which receives the graft⁽¹⁶⁾. The patient should recover quickly after split – thickness grafting .

Full thickness grafting need a longer recovery time⁽¹⁷⁾. The benefit of split - thickness graft that , it can cover a large areas , it can be meshed , also it can live in area of minimal blood supply , but full - thickness graft , cover the smaller area with plenty of blood supply , so in areas post Radiation treatment Split – Thickness Skin Graft (STSG) is better^(18,19), see the previous table (table :1) .

We used the same principle for managing our patients , Our experience showed that phototherapy irradiation of the donor site (the unaffected body site of the same patient) may , in fact , be beneficial by reducing inflammatory cells in both graft and donor tissue . This lead to a decrease in Antigen Presenting Cells (APCs) , therefore , a decrease in pathological T – lymphocytes and increase in graft take .

Conclusion

Mycosis fungoides is the most frequent type of cutaneous T -cell lymphoma , patients who received phototherapy to the potential donor site , has proven beneficial for skin graft survival ,since ultraviolet radiation (A or B) leads to : a decrease the cytotoxic T lymphocytes activity in both graft and donor tissues , which leads to increase in the graft uptake , this is because psoralens react with cellular DNA ,which leads to inhibition of DNA replication in T- Lymphocytes and keratinocytes , and causes cell cycle arrest, UVB ,exerts its action through direct phototoxic effect on T – lymphocytes⁽²⁰⁾, both stimulates cytokines and prostaglandins that play amajor role in immune suppression⁽²¹⁾.

References

1. Hwang ST, Janik JE, Jaffe ES, et al; Mycosis fungoides and Sezary syndrome. *Lancet*. 2008 Mar 15;371(9616):945-57.
2. Criscione VD, Weinstock MA. Incidence of cutaneous T-cell lymphoma in the United States, 1973–2002. *Arch Dermatol* 2007;143: 854–859 .
3. van Doorn R, van Haselen CW, van Voorst Vader PC, et al. Mycosis fungoides: disease evolution and prognosis of 309 Dutch patients. *Arch Dermatol*. 2000;136:504-510 .
4. Morales-Suarez-Varela MM, Olsen J, Johansen P, et al; Occupational risk factors for mycosis fungoides: a European multicenter case-control study. *J Occup Environ Med*. 2004 Mar;46(3):205-11.
5. Weberschock T, Strametz R, Lorenz M, et al; Interventions for mycosis fungoides. *Cochrane Database Syst Rev*. 2012 Sep 12;9:CD008946. doi: 10.1002/14651858.CD008946.pub2.
6. Chiaron-Sileni V, Bononi A, Veller Fornasa C, et al. Phase II trial of interferon- α -2a plus psoralen with ultraviolet light A in patients with cutaneous T-cell lymphoma. *Cancer* 2002; 95:569-575 .
7. Whittaker SJ, Foss FM .Efficacy and tolerability of currently available therapies for the mycosis fungoides and sezary syndrome variants of cutaneous T-cell lymphoma. *Cancer Treat Rev* . 2007;33(2):146-160.
8. Fink-Puches R, Zenahlik P, Bäck B, et al. Primary cutaneous lymphomas: applicability of current classification schemes (European Organization for Research and Treatment of Cancer, World Health Organization) based on clinicopathologic features observed in a large group of patients. *Blood* 2002;99: 800-805 .
9. Horwitz SM; Novel therapies for cutaneous T-cell lymphomas. *Clin Lymphoma Myeloma*. 2008 Dec;8 Suppl 5:S187-92
10. Scherer-Pietramaggiori SS, Pietramaggiori G, Orgill DP. Skin graft. In: Neligan PC, ed. *Plastic surgery*. 3rd ed. Philadelphia, PA : Elsevier; 2013: Chap 17.
11. Smith BD, Wilson LD. Management of mycosis fungoides. *Oncology*. 2003;17:1281–8.
12. Barret-Nerin, Juan; Herndon, David N . (2004) . *Principles and practice of Burn surgery*. New York : Marcel Dekker.
13. Boyce DE, Jones WD, Ruge F, Harding KG, Moore K. The role of lymphocytes in human dermal wound healing. *Br J Dermatol*. 2000;143:59–65 .
14. Obochi MO, Ratkay LG, Levy JG. Prolonged skin allograft survival after photodynamic therapy associated with modification of donor skin antigenicity. *Transplantation*. 1997;63:810–7 .
15. Tamaki K, Iijima M. The effect of ultraviolet B irradiation on delayed type hypersensitivity, cytotoxic T lymphocyte activity, and skin graft rejection. *Transplantation*. 1989;47:372–6 .
16. Jones, JE; Nelson, EA; Al-Hity, A (Jan 31 , 2013). " Skin grafting for venous leg ulcers." . The Cochrane database of systematic reviews.
17. ^emedicine > Skin Grafts, Author: Bengamin C Wood. Coauthor(s) :Christian N Kerman.updated Jan.29,2010.
18. ^"Skin Grafting : Aftercare" . Encyclopedia of surgery. Retrieved sep 19 , 2012.
19. Dipietro , Lusia A. , and Aime L . Burns, eds. *Wound Healing: Methods and protocols*. Totowa, NJ : Humana Press, 2003.
20. MERMELSTEIN FH, ABIDI TF , LASKIN JD , *Mol pharmacol* , 36 (1989)848.
21. Wolf, P., D. X. Nghiem, J. P. Walterscheid, S. Byrne, Y. Matsumura, Y. Matsumura, C. Bucana, H. N. Ananthaswamy, and S. E. Ullrich. 2006. Platelet-activating factor is crucial in psoralen and ultraviolet A-induced immune suppression, inflammation, and apoptosis. *Am. J. Pathol*. 169: 795–805