Journal of Clinical Trials & Research
JCTR, 1(2): 27-30
www.scitcentral.com
ISSN: 2637-7373
Mini Review: Open Access

Mini Review of Keloid Formation

Abeer Shaheen*

*Department of Dermatology, Tishreen University, Lattakia, Syria.

Received April 11, 2018; Accepted August 03, 2018; Published October 25, 2018

ABSTRACT

Keloid is a benign fibrous growth, which presents in scar tissue of predisposed individuals. Although the pathogenesis of keloid disease is not well understood, it is considered to be the end product of an abnormal healing process. However, it is possible that several factors such as age of onset, sex, cause of scarring, blood groups, anatomical site, presence of family history, number of injured sites (multiple/single) have an important role in keloid formation. Keloids appear as firm, mildly tender, bosselated tumors with a shiny surface. The main differential diagnosis of keloid is hypertrophic scar. No single therapeutic modality is best for all keloids, so prevention is the first rule in keloid. This study gives a mini review of keloid formation, and this is the object of this study.

Keywords: Keloids, Pathogenesis, Risk factors, Diagnosis, Different diagnosis, Histopathology, Treatment, Prevention

DEFINITION

Keloid is a benign fibrous growth, presents in scar tissue of predisposed individuals, extends beyond the borders of the original wound, doesn't usually regress spontaneously and tends to recur after excision. It is a result of irregular wound healing following skin insults, but sometimes occurs spontaneously [1,2].

PATHOGENESIS

Pathogenesis of keloid formation is not well cleared, but it is the end product of an abnormal healing process [3]. Therefore, are several theories of keloid formation according to induced factor. Some of them implicate certain cytokines like Transforming growth factor beta (TGF-b) [4-6], vascular endothelial growth factor (VEGF) [6], connective tissue growth factor (CTGF) [6] or Platelet-derived growth factor (PDGF) [7]. Other implicates keratinocyte [8]. In contrast, some theories suggest that fibroblasts have the initial disorder [3,9-11]. Recent evidence has indicated the role of type of immune response in keloid formation, or maybe a role of mast cell [12].

EPIDEMIOLOGY AND ETIOLOGY (RISK FACTORS OF KELOIDS)

Several factors play a significant role in keloids formation. They are genetic predisposition, blood groups, melanin, the anatomical site, the type of skin injury, the age of onset and sex [11].

Genetic predisposition

There is a clear genetic component given the correlation with family history, which supported by the following phenomena: (a) Some patients with keloids report a positive family history [13,14]. (b) High occurrence in identical twins [14-16]. (c) Higher predisposition in Blacks, Hispanics and Asians, less frequently in Caucasians [15]. (d) Increased incidence of keloids in patients with some genetic syndromes like Turner syndrome, Opitz-Kaveggia syndrome, Rubinstein Taybi syndrome and Ehlers Danlos syndrome [17,18].

Blood groups

People with blood group A have high probability to develop keloids compared with other blood groups [19].

Melanin

There is a relationship between keloid formation and skin color, as supported by the following phenomena: (a) Colored skin people such as the Negroid and Mongoloid races have a

Corresponding author: Abeer Shaheen, MD, Department of Dermatology, Tishreen Hospital, Jableh, Lattakia, Syria, Tel: 963994044175; E-mail: dr.abeer.a.shaheen@gmail.com

Citation: Shaheen A. (2018) Mini Review of Keloid Formation. J Clin Trials Res, 1(2): 27-30.

a greater tendency to suffer from keloid compared to the Whites (the Caucasian race) [15]. b) The incidence of pathological scarring varies across different parts of the body even in the same individual [6,20]. C) Adolescents and pregnant women are more susceptible to developing keloids [20].

Anatomical site

Several studies indicated to the role of anatomical site in keloid formation, which supported by the following phenomena: (a) Genetically susceptible individuals form keloids after wounding but not at every body site [15]. (b) Generally, keloids tend to occur on highly mobile sites with high tension such as shoulders, neck and presternum [21,22]. (c) There are familial patterns of keloid distribution [23].

Causes of keloids (type of skin injury)

Keloids may develop following any skin insult like burn, trauma, surgery, piercings, acne, vaccinations [13], but not all such insults lead to a keloid scar even in the susceptible individuals [15].

Age of onset: Although keloids could occur at any age, they are rare in first decade, most likely to occur in second and third decades and tend to decrease in older [15,16,19,20].

Sex: Incidence of keloids is usually equal in females and males [16,24-26], but sometime there is higher incidence in female [15,26] or in male [27].

Note: The above risk factors are unmodifiable factors, but there are modifiable factors like delayed healing [28] and hypertension [29].

DIAGNOSIS

Keloids appear as firm, mildly tender, bosselated tumors with a shiny surface. In the Caucasian patient, keloids tend to be erythematous and telangiectatic; they are often hyper pigmented in darker-skinned individuals. Keloids are often pruritic and painful, in addition to significant effects of patient's quality of life, both physically and psychologically, especially in excessive scarring [13].

DIFFERENTIAL DIAGNOSES

The main differential diagnosis of keloid is hypertrophic scar. Hypertrophic scars, which defined as raised scars that remained within the boundaries of the original lesion, often regressing spontaneously after the initial injury and rarely recurring after surgical excision. In contrast, a keloid scar is defined as a dermal lesion that spreads beyond the margin of the original wound, continues to grow over time, does not regress spontaneously and commonly recurring after excision [19].

TREATMENT

No single therapeutic modality is best for all keloids. The location, size and depth of the lesion; the age of the patient; and the past response to treatment determine the type of therapy used.

Standard treatments

These include occlusive dressings, compression therapy and intralesional corticosteroid injections. Occlusive dressings include silicone gel sheets and dressings, non-silicone occlusive sheets and cordran tape [30-32]. Compression therapy involves pressure, which has long been known to have thinning effects on skin. Reduction in the cohesiveness of collagen fibers in pressure treated hypertrophic scars has been demonstrated by electron microscopy [30,33]. Corticosteroids, specifically intralesional corticosteroid injections, have been the mainstay of treatment [30].

Excision: Decreased recurrence rates have been reported with excision in combination with other postoperative modalities, such as radiotherapy, injected IFN or corticosteroid therapy [30].

Radiotherapy: Radiation destroys fibroblasts in the wound, prevents neovascularization, which ultimately leads to a decreased production of collagen [28,34].

Laser therapy: Ablative lasers (Carbon dioxide (10,600 nm), Erbium: Yttrium aluminium garnet laser (Er: YAG) (1064 nm), Argon 488 nm laser) and Non-ablative lasers like Pulsed-dye laser (585 nm), because of its efficacy, safety, and relatively low cost, the PDL remains the laser treatment of choice for keloids hypertrophic scars [30].

Intralesional/topical apply of following drugs

IFN injections [26], 5-Fluorouracil [26], Doxorubicin (Adriamycin) [30], Bleomycin [35], Verapamil [35], Retinoic acid [35], Imiquimod 5% cream [35], Tamoxifen [35], Tacrolimus [35], Botulinum Toxin A [35].

Other promising therapies

The anti-angiogenic factors, including the vascular endothelial growth factor (VEGF) inhibitors (e.g. Bevacizumab). Phototherapy (photodynamic therapy - PDT), UVA-1 therapy, narrow band UVB therapy. Tumor necrosis factor (TNF) alpha inhibitor (etanercept). Recombinant human interleukin (rhIL-10) which are directed at decreasing collagen synthesis [28].

Note: A previous study found that 8% of keloids resolved spontaneously after 5 years [35].

PREVENTION

Keloids may arise from any kind of damage in the papillary dermis, even with small injuries. Therefore, Prevention is the first rule in keloid therapy, so we must take special care in treating patients with a history of keloids [30,36].

REFERENCES

1. Burrows NP, Lovell CR (2010) Rook textbook of dermatology. Volume 3, 8th Edn.

2. Burton CS, Escaravage V (2015) Bolognia text book. Volume 2, 2nd Edn.

3. Shih B, Garside E, McGrouther DA, Bayat A (2010) Molecular dissection of abnormal wound healing processes resulting in keloid disease. Wound Repair Regen 18: 139-153.

4. He S, Liu X, Yang Y, Huang W, Xu S, et al. (2010) Mechanisms of transforming growth factor β1/Smad signalling mediated by mitogen-activated protein kinase pathways in keloid fibroblasts. Br J Dermatol 162: 538-546.

5. Li J, Cao J, Li M, Yu Y, Yang Y, et al. (2011) Collagen triple helix repeat containing-1 inhibits transforming growth factor-β1-induced collagen type I expression in keloid. Br J Dermatol 164: 1030-1036.

6. Robles DT, Moore E, Draznin M, Berg D (2007) Keloids: Pathophysiology and management. Dermatol Online J 13: 9.

7. Hu ZC, Tang B, Guo D, Zhang J, Liang YY, et al. (2014) Expression of insulin-like growth factor-1 receptor in keloid and hypertrophic scar. Clin Exp Dermatol 39: 822-828.

8. Hahn JM, Glaser K, McFarland KL, Aronow BJ, Boyce ST, et al. (2013) Keloid-derived keratinocytes exhibit an abnormal gene expression profile consistent with a distinct causal role in keloid pathology. Wound Repair Regen 21: 530-544.

9. Russell SB, Russell JD, Trupin KM, Gayden AE, Opalenik SR, et al. (2010) Epigenetically altered wound healing in keloid fibroblasts. J Invest Dermatol 130: 2489-2496.

10. Zulato E, Favaretto F, Veronese C, Campanaro S, Marshall JD, et al. (2011) ALMS1-deficient fibroblasts over-express extra-cellular matrix components, display cell cycle delay and are resistant to apoptosis. PLoS One 6: e19081.

11. De Felice B, Ciarmiello LF, Mondola P, Damiano S, Seru R, et al. (2007) Differential p63 and p53 expression in human keloid fibroblasts and hypertrophic scar fibroblasts. DNA Cell Biol 26: 541-547.

12. Wulff BC, Parent AE, Meleski MA, DiPietro LA, Schrementi ME, et al. (2010) Mast cells contribute to scar formation during fetal wound healing. J Invest Dermatol 132: 458-465.

13. Gauglitz GG, Korting HC, Pavicic T, Ruzicka T, Jeschke MG (2011) Hypertrophic scarring and keloids: Pathomechanisms and current and emerging treatment strategies. Mol Med 17: 113-125.

14. Halim A, Emami A, Salahshourifar I, Kannan T (2012) Keloid scarring: understanding the genetic basis, advances and prospects. Arch Plast Surg 39: 184-189.

15. Bayat A, Arscott G, Ollier WE, McGrouther DA, Ferguson MW (2005) Keloid disease: Clinical relevance of single versus multiple site scare. Br J Plast Surg 58: 28-37.

16. Ramakrishnan KM, Thomas KP, Sundararajan CR (1964) Study of 1,000 patients with keloids in South India. Plast Reconstr Surg 53: 276-280.

17. Sun LM, Wang KH, Lee YC (2014) Keloid incidence in Asian people and its comorbidity with other fibrosis-related diseases: A nationwide population-based study. Arch Dermatol Res 306: 803-808.

18. Shih B, Bayat A (2010) Genetics of keloid scarring. Arch Dermatol Res 302: 319-339.

19. Shaheen A, Khaddam J, Kesh F (2016) Risk factors of keloids in Syrians. BMC Dermatol 16: 13.

20. Gao FL, Jin R, Zhang L, Zhang YG (2013) The contribution of melanocytes to pathological scar formation during wound healing. Int J Clin Exp Med 6: 609-613.

21. Naylor MC, Brissett AE (2012) Current concepts in the etiology and treatment of keloids. Facial Plast Surg 28: 505-512.

22. Ogawa R, Okai K, Tokumura F, Mori K, Ohmori Y, et al. (2012) The relationship between skin stretching/contraction and pathologic scarring: The important role of mechanical forces in keloid generation. Wound Repair Regen 20: 149-157.

23. Clark JA, Turner ML, Howard L, Stanescu H, Kleta R, et al. (2009) Description of familial keloids in five pedigrees: Evidence for autosomal dominant inheritance and phenotypic heterogeneity. BMC Dermatol 9: 8.

24. Mouhari-Toure A, Saka B, Kombaté K, Akakpo S, Egbohou P, et al. (2012) Is there an association between keloids and blood groups? ISRN Dermatol 2012: 750908.

25. Sharquie KE, Al-Dhalimi MA (2003) Keloid in Iraqi patients. A clinicohistopathologic study. Dermatol Surg 29: 847-851.

26. Philandrianos C, Kerfant N, Jaloux C Jr, Martinet L, Bertrand B, et al. (2016) Keloid scars (part I): Clinical presentation, epidemiology, histology and pathogenesis. Ann Chir Plast Esthet 61: 128-135.

27. Olaitan PB, Olabanji JK, Oladele AO, Oseni GA (2013) Symptomatology of keloids in Africans. Sierra Leone J Biomed Res 5: 29-33.

28. Weledji EP, Ngwane S (2012) The management of keloids and hypertrophic scars. Darlington County Durham Med J 6: 39-45.

29. Ogawa R (2017). Keloid and hypertrophic scars are the result of chronic inflammation in the reticular dermis. Int J Mol Sci 18: 606.

30. Berman B, Elston DM (2016) Keloid and hypertrophic scar clinical presentation. Medscape.

31. Juckett G, Adams HH (2009) Management of keloids and hypertrophic scars. Am Fam Physician 80: 253-260.

32. O'Brien L, Jones DJ (2013) Silicone gel sheeting for preventing and treating hypertrophic and keloid scars. Cochrane Database Syst Rev 12: 1-76.

33. Viera MH, Amini S, Valins W, Berman B (2010) Innovative therapies in the treatment of keloids and hypertrophic scars. J Clin Aesthet Dermatol 3: 20-26.

34. Shejbal D, Bedekoviæ V, Ivkiæ M, Kalogjera L, Aleriæ Z, et al. (2004) Strategies in the treatment of keloid and hypertrophic scars. Acta clin Croat 43: 417-422.

35. Smith OJ, McGrouther DA (2014) The natural history and spontaneous resolution of keloid scars. J Plast Reconstr Aesthet Surg 67: 87-92.

36. Henriquez CB, Costa F (2003) Resident's thesis systematization of treatment of keloid. Proceeding at the Plastic Surgery Unit of the 38th Infirmary of Santa Casa de Misericórdia do Rio de Janeiro.