Facial Plastic Surgery Controversies: Keloids

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KEYWORDS

• Keloid • Fibroproliferative tumor • Keloid treatment • Keloid risk factors • Keloid prophylaxis

KEY POINTS

- The 3 main barriers to improved keloid treatment outcomes are incomplete understanding of keloid pathogenesis and lack of biomarkers and animal models.
- Keloid risk factors vary by site in the head and neck, and its incidence after head and neck surgery may be lower than reported for other areas.
- The prophylactic treatment of known keloid formers should include a perioperative plan to minimize inflammation, cellular proliferation, and wound tension.
- Keloids are a chronic condition that requires proper disease education and long-term follow-up.
- There are no clear indications for radiation therapy for keloid treatment but it is generally reserved for recurrence, and its usage should be balanced with radiation safety and effectiveness.

Panel discussion

1. What are the barriers to better outcomes for keloid treatment?
2. What are risk factors for keloids in otolaryngology patients?
3. What is your prophylactic protocol for treating known keloid formers?
4. How long do you treat or follow patients after surgical removal?
5. When do you consider radiation therapy for the management of keloids?
6. What is your prophylactic protocol when operating on known keloid formers?

Question 1: What are the barriers to better outcomes for keloid treatment?

JONES

For the more than 11 million people in the world affected with keloids,[1] the goals for better treatment outcomes are evident. I believe patients want return of form and function, respite from physical symptoms and emotional distress,[2] and more reliable results with lower recurrence rates without concomitant treatment mortality and nominal morbidity. I perceive 3 main barriers to improved outcomes for keloid treatment. First, incomplete understanding of keloid pathogenesis; second, lack of biomarkers; and third, the absence of an acceptable animal model.

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Keloids are fibroproliferative tumors that occur after injury to the skin. Their pathogenesis is characterized by overgrowth, which is the result of hyperplasia and increased amounts of extracellular matrix, secondary to increased proliferation and activity of several cell types in the keloid microenvironment.[3] Fibroblasts have been identified as a key player in the pathogenesis of keloids, but the drivers are unkown.[4,5] Moreover, other cell types, such as keratinocytes, play a role through paracrine regulation of fibroblast function.[6] Genetic studies have identified genes that explain only part of the biological or functional changes associated with keloids.[7] Epigenetics, the study of changes in gene expression that occur without changing the DNA sequence, may provide a new direction for the study of keloid pathogenesis.[7] It has been postulated that keloid disease is influenced by aberrant signaling pathways.[8] Research has focused on cytokines, such as transforming growth factor-β and epidermal growth factor, given their implications in other fibrotic disease.[3,9] No clear signaling pathway, however, has been identified. Despite the increased focus on keloid pathogenesis, current approaches of research have yielded some tangible results, albeit with large gaps in understanding of keloid pathogenesis.[4] Overall, a better understanding of the heterogeneity of the mechanisms of keloid formation will allow for development of potential novel therapies for improved treatment outcomes.

Biomarkers identify the presence of disease and can be used for diagnosis and clinical and translational research outcomes. The lack of keloid biomarkers prevents standardized and reproducible data that can be objectively evaluated and compared. For example, keloids and hypertrophic scars are not always easy to differentiate, despite research describing in detail the clinical and morphologic differences.[5] Biomarkers play a critical role in improving drug development[6] and subsequent outcomes for therapy. There are no Food and Drug Administration–approved therapies to treat keloids. Current treatment options are fraught with unacceptable recurrence rates. Nevertheless, some patients benefit from multimodality therapies. Keloid biomarkers would allow for better prediction of outcomes and weighing of risks and benefits of treatment options. Moreover, they would serve as targets and allow for precision therapies that take into account the heterogeneity in keloid formation.

Animal models are also needed to help improve keloid outcomes. Keloids occur only in humans.[7] Current in vitro methods to study keloids do not account for their complexity.[9] Animal models aid in elucidating underlying mechanisms of disease and allow for therapeutic interventions to be studied in a controlled environment.[10] They often represent the last preclinical step in the therapeutic pipeline of translational research. Despite the existence of several animal models to study wound healing, fibrosis, and scarring, none is specific to keloids. Moreover, current in vitro and in vivo models cannot explain why wound healing results in normal, hypertrophic, or keloid scar formation. Better outcomes in keloid treatment will hasten with the advent of an acceptable animal model.

BOAHNENE

Over several decades, keloid treatment failure has remained high and present outcomes are overall unsatisfactory. The quest for better outcomes underlies the wide-ranging variation in treatment regimens and recommendations. Inadequate research funding is always suggested as an impediment to medical discovery and treatment progress and this may be true for keloids. There are, however, additional barriers to understanding keloids and achieving better treatment outcomes. First, keloids are classified as scars that cause mainly cosmetic deformities. As such they do not attract the focused clinical attention necessary to generate significant breakthrough. There are no “centers of keloid treatment” that I am aware of. Perhaps the classification of keloids as mere scars that grow beyond their original boundary should be revisited. Clinically, keloids vary in their behavior but are generally locally aggressive processes capable of replacing normal tissue not so dissimilar to certain neoplastic processes. A change in approach from scar management to treatment of aggressive soft tissue tumor may be necessary to bend the curve in treatment outcomes. Second, there is a major gap in translating the understandings gained from elucidating the pathogenesis of keloid formation from the molecular level to clinical practice. One major reason for this is the lack of an animal keloid model that will allow experimental targeting of potential steps in the disease pathways. Tissue engineering techniques that seek to replicate disease processes ex vivo are shortening the testing of newly developed pharmaceutical products. As desirable replacement of animal experiments, tissue-engineered skin equivalents have recently been applied in microbial and viral infection models. A similar approach to the study of keloids and effectiveness of new therapies holds promise.

BRISSETT

The barriers to improved outcomes for patients suffering from keloids are multifactorial and often