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Case Report

Treatment of Recurrent Keloid by Surgical Excision followed by High Dose Rate Plesiotherapy: A Case Report and Review of Literature

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Abstract

The term Keloid has been derived from the Greek Language translating to "crabs claw." The condition occurs as a postoperative complication or as a sequela of trauma, which is sometimes worrisome to both the patient as well as the treating surgeon because of its recurrent behaviour. Keloids are a type of scar that can occur after surgery or trauma, and they are characterized by their raised and thick appearance. Patients with keloids may experience physical symptoms such as pain and itching, which can be distressing and affect their quality of life. In addition to these physical symptoms, keloids can also be aesthetically displeasing, causing patients to feel self-conscious or embarrassed about their appearance. The emotional impact of keloids should not be underestimated, as it can have an impact on a patient's mental health and well-being. It is important for healthcare providers to recognize the impact of keloids on patients and to provide appropriate support and treatment options. Generally, keloids have been treated solely through surgery, but due to their high rate and chance of recurrence (45-90%) [1], adjuvant therapy after surgery has been added to aim for reducing the chance of recurrence to a minimum. Among them Surgery followed by low dose Radiotherapy has shown the best results.

Keywords: Keloid; Radiotherapy; Histopathological Examination (HPE)

Case Study

A 19-year-old female patient reported to the out-patient department with complaints of recurrent growth over the Bilateral Lobule of the pinna since 2 months. She had a history of undergoing surgery 4 months back at the same site for the same condition. Patient had no other medical or surgical history. On examination, a well circumscribed, nodular, pedunculated lesion was seen on the lobule of the pinna bilaterally (Figure 1 A, B), which was firm but non-tender on palpation. There was no regional lymphadenopathy. Incisional biopsy was planned for confirmation of the disease. All routine investigations were done, which were found to be within normal limits. Tissue samples collected from both sites by incisional biopsy were sent for histopathological examination (HPE). The HPE report confirmed it to be a case of Keloid Scar tissue. Treatment plan was made which comprised of surgical excision under General Anesthesia followed by High Dose Rate Brachytherapy or Plesiotherapy as the same day of the surgery. Patient was counselled regarding the condition and was informed of its recurrent nature and thus the need for adjuvant radiation following surgery. Upon patient agreeing with the treatment plan, Pre-Anesthetic Checkup was done. Patient underwent excision of the lesion bilaterally, followed by intra-operative placement of a guide wire and a tissue analogue/equivalent under GA (Figure 2 A-D), placement of Brachytherapy tubes (Figure 3) was done, followed by immediate adjuvant Radiation of 16 Gy, 4 fractions within 24 hours (Figure 4). Patient was discharged on Post-Op Day (POD) 2. Patient was recalled for follow up and suture removal was done on POD 7 (Figure 5). Patient was recalled again on POD 30, there was adequate wound healing and grade 1 toxicity. On the 2nd month (POD 60) follow-up (Figure 6 A, B), there was normal scar tissue formation and no evidence of keloid recurrence.

Discussion

Epidemiology

Keloids are a type of scar that can occur after a cutaneous injury, and their prevalence varies depending on region and race.

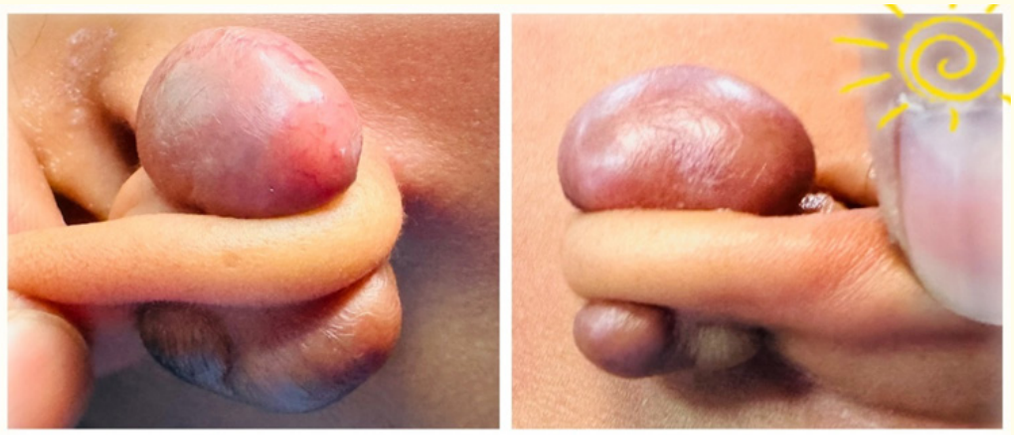

Figure 1(A,B): Showing well circumscribed, nodular, pedunculated lesion over the lobule of the pinna bilaterally.

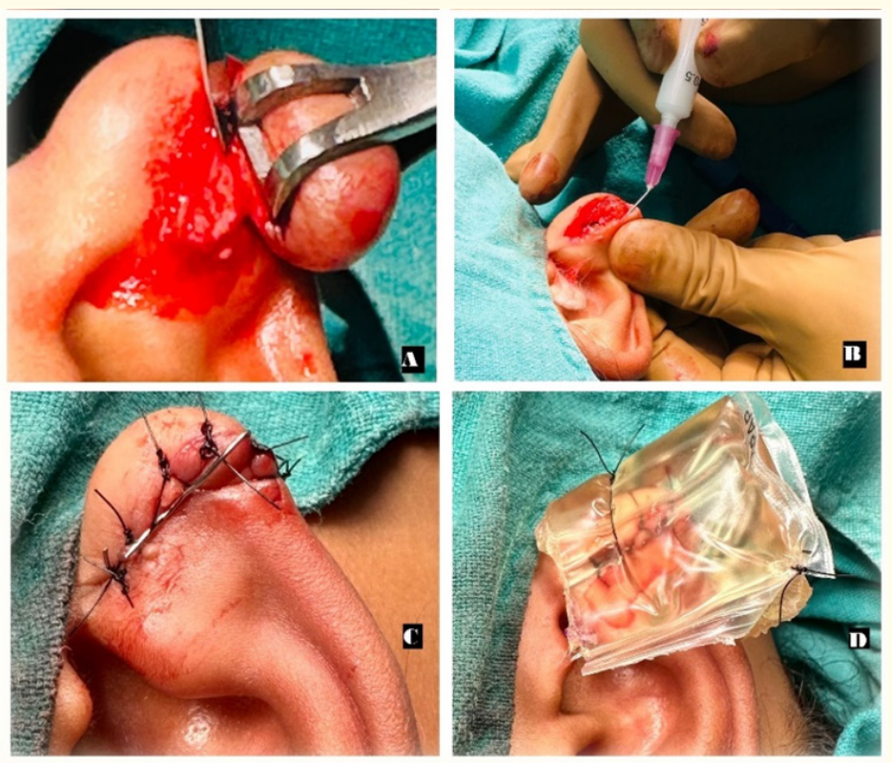

Figure 2(A-D): Intra-operative placement of a guide wire and a tissue analogue/equivalent under GA (Figure 2 A-D).

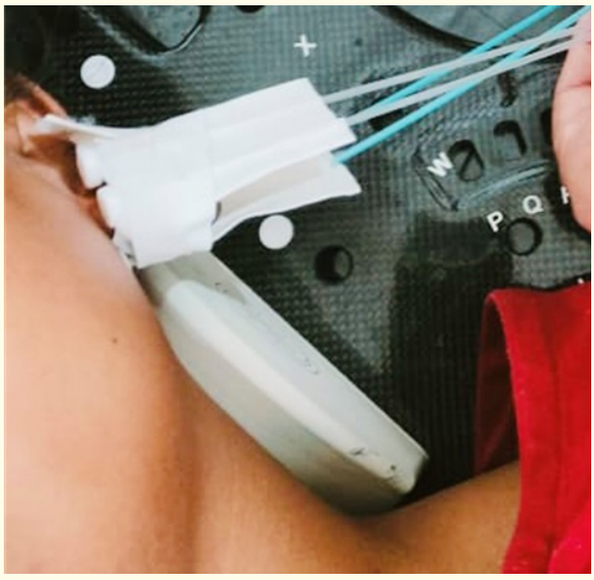

Figure 3: Placement of Brachytherapy tubes.

Figure 4: Surgical excision followed by immediate adjuvant Radiation of 16 Gy, 4 fractions within 24 hours.

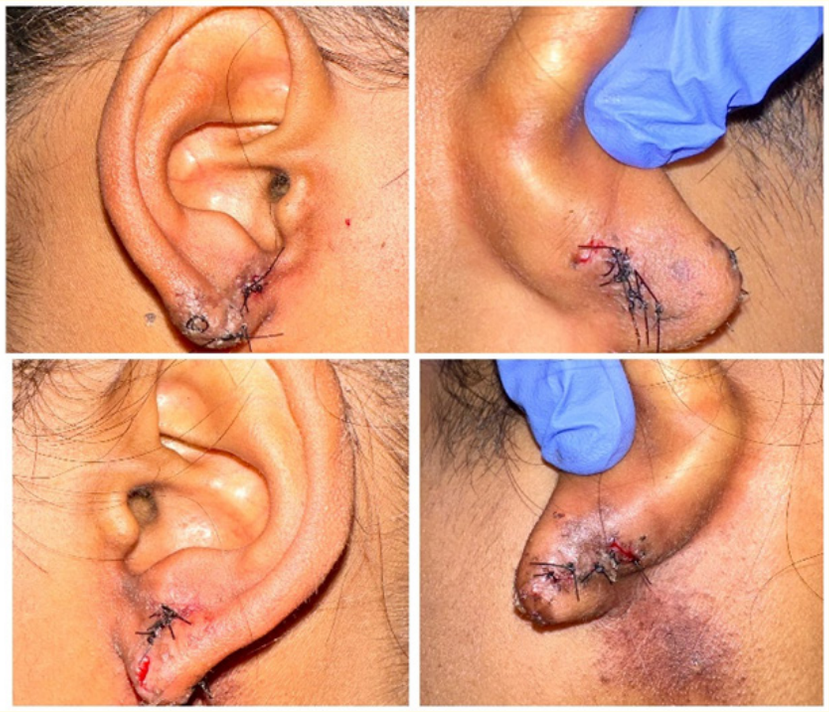

Figure 5: Showing adequate wound healing and grade 1 toxicity after 7 days.

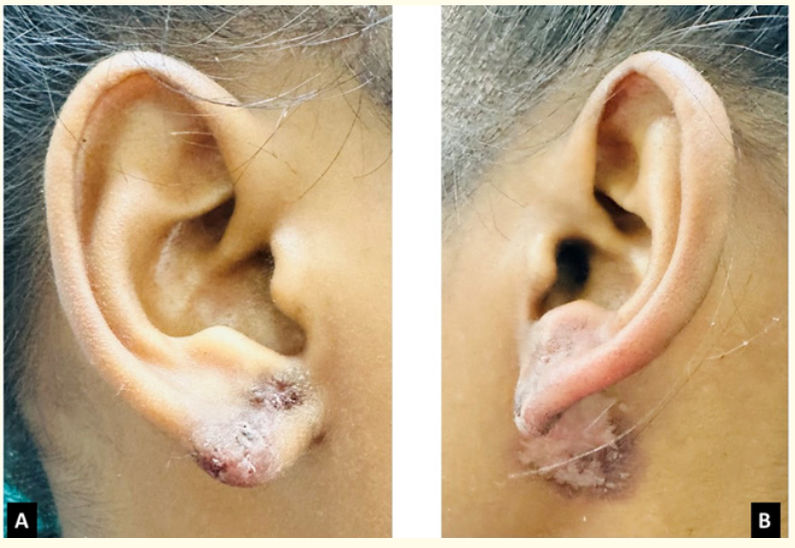

Figure 6(A,B): Showing normal scar tissue formation and no evidence of keloid recurrence after 11 months of follow up.

The prevalence of keloids can range from 30% to 90% of patients, which means that a significant number of people are affected by this condition. Individuals with a darker complexion, such as African Americans, Hispanics and Asians tend to have a higher risk of developing keloids. Having a family history of keloids is also significant in this condition. Commonest age of incidence is between 10 and 30. Hormonal changes occuring during puberty and pregnancy also increass the risk of keloid formation. Blood Group A indivisuals are at additional risk factors for developing keloids [4].

Pathophysiology

Keloid scar formation is a complex process, and its exact cause is not fully understood by medical professionals. While some keloids can form without any apparent cause, most of them occur as a sequela of abnormal wound healing after surgery or trauma. In some cases, keloids can form years after the initial injury, making it difficult to identify the exact cause of their formation. Various factors can trigger the development of keloids, including body piercings, tattoos, mechanical force, vaccinations or surgery. The most common locations for keloid formation are the pinna and sternum or areas where the high skin tension [4].

Keloids are a type of scar that is characterized by an abundance of densely packed unorganized collagen. The collagen bundles in keloids are hypo-cellular, meaning that they have fewer cells than normal tissue. The dermis, which is the layer of skin beneath the epidermis, is infiltrated with inflammatory cells in keloids. The bundles of collagen in keloids are made up of large and wavy type-I and type-II hyalinized fibers. In contrast, Hypertrophic scars are different from keloids by the presence of more delicate and organized collagen bundles that run parallel to the epidermis [4].

When the skin is injured, the body's natural response is to form a scar. This process involves three stages: 1) Inflammation 2) proliferation, and 3) remodeling or maturation. Keloids are a type of scar that forms due to excess dermal fibrosis. Fibroblasts are cells that form the majority of collagen and extracellular matrix (ECM) in the skin. These re the main cellular components that take part in the pathophysiology of keloid formation. Other cells, such as keratinocytes, melanocytes, myofibroblasts and mast cells, also contribute to the development of keloids. Regulatory molecules, including PDGF, VEGF, and proteolytic enzymes, which are involved in the signaling pathways, are important steps that lead to keloid formation. Fibrotic signaling cascades, such as toll-like receptor signaling, SMAD signalling and fibronectin contribute to the development of keloids. Abnormal prolongation of the inflammatory stage of wound healing can cause an imbalance between the destruction and deposition of ECM, leading to an abundance of collagen and other ECM matrix components in the dermis and surrounding subcutaneous tissue. This overabundance of ECM components leads to excessive scarring and the development of keloids [4].

Keloids can be classified into two types - Minor and Major. Minor keloids are small scars having an elevation of less than 0.5 cm, while major keloids are larger and have an elevation of more than 0.5 cm. Both types can infiltrate surrounding tissue and gradually progress in size years after the initial trauma. Keloids generally do not go away without treatment.

Evaluation

- Keloid scars are evaluated using different methods to assess their severity and response to treatment.
- The most common method for evaluation is the use of the Vancouver Scar scale [2], which is a subjective measure that rates the appearance of the scar based on factors such as pigmentation, vascularity, and pliability.
- Another commonly used method is 2-dimensional photography, which provides more objective measures of the scar's size, shape, and texture. This method is useful for tracking changes in the scar over time and comparing the effectiveness of different treatments.
- In addition to these methods, there are other less commonly used techniques for evaluating keloid scars. These include assessing the scar's biochemical properties, such as collagen content and cytokine levels, which can can give a clue into the underlying etiopathology of keloid formation and help guide treatment decisions.
- Ultrasound is another technique that can be used to evaluate keloid scars, particularly in cases where the scar is in a difficult-to-access area or when there is concern about underlying tissue damage.
- Laser-based techniques, such as laser Doppler imaging and laser speckle imaging, can also be used to assess blood flow and tissue perfusion in the scar, which can provide information about the scar's healing process and response to treatment.
- Finally, biopsy may be used in some cases to confirm the diagnosis of keloid and rule out other conditions that may mimic its appearance. This involves taking a small sample of tissue from the scar and examining it under a microscope to look for characteristic features of keloid.

Treatment modalities

Despite the various treatment strategies available, the rate of recurrence is still very high in this condition after surgical excision alone, which has led to the need for combination therapy. Same day radiotherapy given post-operatively has shown to be effective with a success rate of 67-98% reported in some studies. However, the overall control and relapse rates can vary depending on the site of the keloid and the histological confirmation of the lesion. Treatments such as intralesional triamcinalone injections and various reconstructive surgical techniques, have also been recommended for keloids. A meta-analysis conducted in 2016 demonstrated that triamcinolone injection and radiation were both considered effec-

tive treatments for keloids, with no significant difference between them. But, some patients may require adjuvant radiation therapy after triamcinolone injections to prevent relapse. Various other modes of treatment, such as silicone gel, pressure therapy, laser therapy and 5-FU, are either ineffective or lack clinical evidence.

Radiotherapy is a form of treatment that uses radiation energy to destroy abnormal cancer cells. In dermatology, radiotherapy is primarily used to treat non-melanoma skin cancers, mycosis fungoides, lymphomas, and keloids. Adjuvant therapy refers to treatment given after the primary treatment (in this case, surgical excision) to prevent recurrence or improve the chances of a cure. Post-excisional radiation is a type of adjuvant therapy that involves using radiation to treat the area where the keloid was removed. Review of the english literature has shown that post-excisional radiation therapy for keloids can result in excellent outcomes with minimal complications or recurrences. Dermatologists should be familiar with the use of radiotherapy for keloids and consider it as a treatment option for difficult-to-treat cases. Different forms of radiation therapy can be used for keloids, including brachytherapy, superficial radiation therapy, electron beam therapy and orthovoltage radiation therapy.

De Bearman and Gourgerot were the first to describe the use of X-rays for treating keloids in 1906. In the 1940s to 1950s, post operative radiation was described as a proactive approach in preventing keloid recurrence. The dose-dependent approach was first reported in a study at New York, demonstrating a 60% regrowth at controlling rate and a nonsignificant time-dose relationship at controlling symptoms. Another study conducted in Melbourne indicated potential dose-dependent results. Kovalic and Perez [5] followed 75 patients with 113 keloids for a mean time of 9.75 years and demonstrated an overall control rate of 73%. One study presented a total recurrence rate of 2.4% out of 393 keloid sites on 250 patients within 50 years, documenting cosmetic results such as the size, margins, pigment and textures of keloids after radiation therapy [5].

X-ray irradiation was gradually replaced by electron beam irradiation as medical technology advanced. Irradiation given post-surgical excision of keloids up to a dose of 15 Gy successfully prevented the formation and recurrence of keloids. Asians with keloids reported a relatively lower recurrence rate after the transition to electron beam irradiation. High-dose-rate (HDR) brachytherapy is an alternate form of external radiation therapy for patients resistant to adjuvant external beam radiation therapy or corticosteroids. HDR brachytherapy combined with repeated excisions lowered the recurrence rate of refractory keloids. The cosmetic results of this therapy were excellent, with a satisfactory rate of 86.9%, except for mild skin pigmentation and telangiectasia [4].

External beam radiation and internal radiation or brachytherapy are the 2 significant methods of delivering ionizing radiation to apply energy to the targeted area. With the emergence of advanced linear accelerators, higher dosage delivery and normal tissue sparing has been achieved [4].

In 2017, Jing Xu., *et al*. published a study comparing effectiveness; unconstraint, feasibility, and safety of each type of radiation therapy were taken into consideration for this comparison. The concept of biological effective dose was used to enable this cross-sectional comparison, which takes into account the biological effects of radiation on the body. However, most of the current literature recommendations were based on retrospective studies rather than prospective studies, which may limit the validity of the findings. Additionally, the difficulty in clinically distinguishing between keloids and hypertrophic scars and the lack of histopathological confirmation may further decrease the credibility of these studies. Therefore, there are no specific treatments for keloids in specific sites due to these limitations. Treatments such as superficial and orthovoltage X-rays therapy and brachytherapy were all proven to be helpful. Both the effectiveness and complications of each type of radiation therapy were considered for this comparison. The study concluded that:

- Combination therapy of surgical excision and adjuvant radiation therapy is considered as the last resort for keloid treatment.
- The α/β ratio of lower fractions and higher doses is relatively low and is presumed as the choice of treatment.
- High biological effective dose was accomplished through a linear particle accelerator.
- Early radiation intervention should be applied within 48 h after the surgery, ideally within 24 h.
- The dose in one single fraction should be >12 Gy to end with reliable clinical outcome, but <20 Gy might cause more adverse effects.
- Two fractions within 1 week are recommended as a standardized method to guarantee lower recurrence rate and less adverse effects.

Various radiations used show no difference in efficacy, but each has their own disadvantage.

- **X-RAY:** Low-energy X-ray resulted in more acute skin side effects. Hyperpigmentation is a major complication of radiation therapy, with a reported rate of around 30%. Other major post-irradiation complications include delayed wound healing, dermatitis, and skin ulceration60 kV and 120 kV beams achieved homogeneity of two separate but close lesions treatment, with a satisfaction rating of 4.7/5, especially in homogeneous earlobe sites [4].
- **Electron beam:** Superficial ionizing irradiation is a more appropriate treatment for keloids than traditional X-ray therapy. Narrower and more concentrated radiation deposition is better for treating local superficial lesions like keloids. The steeper the dose fall-off, the more targeted is the radiation deposition and lesser damage to the normal tissue [4].
- **Brachytherapy with iridium-192 or cobalt:** The recurrence rate of keloids after treatment with X-ray or electron beams was estimated to be around 20%, which was a concern for surgeons. Brachytherapy with iridium-192 or cobalt was found to be an alternative treatment option that provided more targeted irradiation towards the lesions, resulting in increased sparing of normal tissues. Brachytherapy has become the preferred treatment due to its effectiveness and tolerability. Low-dose-rate (LDR) and high-dose-rate (HDR) brachytherapy were both found to be effective and tolerable compared to other therapy methods. The recurrence rate after treatment with brachytherapy with iridium-192 was found to be lower than 13% after the year 2000, which is lower than the recurrence rate after treatment with X-ray or electron beams. HDR brachytherapy achieved the lowest mean recurrence rate, better than LDR brachytherapy, which might be explained by the shorter interval between surgery and HDR brachytherapy. HDR brachytherapy was found to be more tolerable, no hospitalization is required, which is necessary for LDR brachytherapy due to lead-coated facilities. [4].
- **Superficial and orthovoltage radiation therapy:** Superficial radiation therapy (SRT) has a depth of penetration of 5mm and is used to target the skin, avoiding deeper tissues. In a large study by Speranza., *et al*. 234 keloids were treated 24-hour post-excision with orthovoltage radiation therapy using a dose of 15Gy divided into three daily fractions. With this regimen, 60 percent of patients reported a satisfaction level of 8 or higher on a 10-point scale. Twenty-seven percent of patients developed telangiectasias as a late adverse event [2].

Case discussion

In the discussed above case, there was already history of recurrence of the keloid. Thus, the treatment plan was devised so that the chance of recurrence could be minimalized. The lesion was pedunculated and present on both the anterior and posterior surface of the lobule of both pinnae, thus it was imperative that the excision is done carefully to remove as much of the keloid tissue as possible, so as to minimize the amount of tissue that needs to be irradiated. After excision, the metallic guide wire was cut and placed at the site and then suturing was done in a fashion so as to secure the wire. This was done to enable pinpointing of the target window/portal for irradiation. Then the site was sandwiched between 2 layers of tissue analogue/bolus/equivalent which were again fixed using sutures.

Bolus is a material used in radiation therapy to reduce or alter dosing for targeted radiation therapy. To ensure that the patient receives the required dose, the bolus must be of the right thickness and placed correctly.

FSD is the distance between the radiation source and the patient's skin surface; it is an important parameter in radiation therapy as it affects the dose delivered to the patient's tissues. This is important to ensure dose homogeneity, which means that the dose is evenly distributed throughout the treated area.

There are 2 types of boluses: (i) pliable e.g. paraffin gauze (ii) rigid e.g. Perspex. In this case Perspex was used due to it being transparent and resistant to change in dimension.

After completion of this step the tubes for brachytherapy were positioned and fixed. And 4 fractions of 16 Gy radiation was administered within 24 hours. This is in compliance with high dose rate irradiation for keloids.

The patient was administered empirical antibiotic and analgesic therapy. Patient was kept for 24 hours for observation and discharged on POD 2. Patient was recalled on POD 7 for follow-up. The wound was adequately healed. Patient had maintained adequate hygiene. There was no evidence of an infection. The brachytherapy tubes, guide wire and sutures were removed. Patient was recalled again on POD 30 and POD 60. At 11 months post-op, there was very little scaring and no evidence of recurrence of keloid. For long term follow-up patient was asked to be on follow up every 6 months for the next 2 years and then continue with yearly follow-up.

Complications

Complications can be divided into two categories: acute skin reactions and late complications.

According to a review by Sakamoto., *et al*. the overall positive adverse effect rate was 19%, and this rate was apparently dose related [12].

Normal tissue shielding is crucial in preventing carcinogenesis and preventing other skin complications, both functionally and cosmetically. Therefore, it is important to carefully consider the dose and site of radiation therapy, as well as the patient's individual factors, to minimize the risk of complications and achieve the best possible outcome.

One of the major concerns that patients might have about radiation therapy is the risk of developing cancer. Many authors have addressed this issue, but there is no conclusive consensus on the matter. Previous studies conducted before 1990 in the X-ray irradiation technique have mentioned a null carcinogenicity rate. Cutaneous cancers arising from keloid affected sites are rarely reported [2].

Ogawa., *et al*. have published a review regarding the relationship between radiation therapy and carcinogenesis. Most of the singular case reports indicated only suspicion of the relationship between radiation therapy and carcinogenesis over a period of 10 years later post treatment [11].

Only one case reported by Biemans [13], which is a patient having fibrosarcoma derived on the same sites of excised keloid tissue, might indicate over irradiation-related carcinogenesis.

Conclusion

Although for decades keloids have been regularly treated solely by surgery alone, catering to its high incidence of recurrence should also be kept in mind. Due to recent advances of guided radiotherapy, surgeons should work alongside radiation oncologists as a team to ensure total cure. Thus, although radiation therapy is associated with risk of carcinogenesis (although rare), surgery followed by adjuvant HDR radiotherapy is a good modality of treatment of Keloids and ensure minimal chance of recurrence.

Conflict of Interest

Authors have no conflicts of interest to declare.

Informed Consent

Written informed consent was obtained from patient who participated in the study.

Financial Disclosure

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