Minimally Invasive Technologies for Treatment of HTS and Keloids: Low-Dose 5-Fluorouracil

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30.1 Introduction

30.1.1 Hypertrophic Scar and Keloid Information

Keloid is the most difficult pathological scar to treat and cure and it is characterized with uncontrolled growth, invasion into normal skin, and expansion beyond the original wound boundary with severe pain and itching [1]. In addition, high recurrence rate after various therapies is a common feature of keloids. These characters similar to those of tumors render keloids more like a “benign skin tumor” rather than a fibrotic tissue per se. Because of this, anticancer therapies such as chemotherapy and radiotherapy have been applied to keloid treatment.

HTS is another type of pathological scar, characterized with the deposition of excessive amounts of collagen matrix along with significant angiogenic process, which eventually leads to a raised and red scar with severe tissue contracture and painful and itching symptoms. HTS eventually resolves by itself after tissue maturation. Nevertheless, this process can take 1–2 years or even longer with disturbing symptoms and functional disability, which needs to be intervened for improving symptoms and preventing patients from disability. With this perspective, anticancer therapy approaches such as chemotherapy and radiotherapy might be also applied [2, 3].

30.1.2 Chemotherapy for Keloids and Hypertrophic Scar

Intralesional injection is a routine procedure for keloid treatment, and steroid injection alone could lead to recurrence rate higher than 50% [2], indicating the necessity of involving others drugs as a combined drug treatment. Chemotherapy for keloid was tried as early as 1989 [1]. The common drugs for keloid chemotherapy include 5-FU, Bleomycin, and Mitomycin C, etc. [2, 3]. The usual delivery way is intralesional injection of chemotherapy drug alone or combined injection of both chemo-agents and steroids.

In recent years, chemotherapy on HTS has been tried either as intralesional injection or combined with post-laser therapy with positive results [3]. Because of its self-resolving nature, chemotherapy for HTS remains an exploratory area for its balanced value between the efficacy and the side effect. Therefore, most studies of pathological scar chemotherapy focus on keloids and it will be the focus of this chapter as well.

30.1.3 5-FU and Its Combined Use of Steroids

Among the various chemotherapy agents, 5-FU, a pyrimidine analog with antimetabolite activity, might be the most commonly used drug for keloid chemotherapy. Dr. Fitzpatrick R.E. started intralesional injection of 5-FU for both keloid and HTS since 1989 using the concentration of 50 mg/ml with positive results [1]. Later, Gupta and Kalra [4] and Nanda and Reddy [5] also reported their 5-FU applications in keloid treatment with a dose of 50 mg/ml, and the intralesional injection was administered weekly, lasting for 12–16 weeks with positive results. With this dose, pain is the most common side effect and ulceration could occur as high as 21.4% [5].

5-FU intralesional injection was listed as an emerging therapy for keloid and HTS in “International clinical recommendation on scar management” [2], but was listed as a formal therapeutic option for HTS and keloid with monthly injection interval in “Updated international clinical recommendations on scar management: Part 2 – algorithms for scar prevention and treatment” [3]. In addition, a combined use of 5-FU with steroids not only enhanced the therapeutic efficacy, but also reduced pain suffering post-injection [1]. In the literature, high-dose (40–50 mg/ml) 5-FU injection is usually combined with steroid at a volume ratio varying from 9:1 [1] to 7.5:2.5 [6].

According to published literatures [1–6], 5-FU is a safe drug with no obvious side effect for the use in a relatively short time period (such as 2–6 months). However, whether it can be safely used for a long term at the reported dose (40–50 mg/ml) remains unclear because the accumulated effect of chemotherapy agents would be a concern if they are continuously used for a long time.

30.2 The Rational of Using Low-Dose 5-FU Injection for Keloid Treatment

To address the potential concern of 5-FU’s side effects, our group proposed the application of low dose 5-FU for keloid treatment because of the following reasons:

1. Keloid necrosis caused by high dose 5-FU injection should be avoided simply because any new wound will accelerate keloid development and worsen the clinical situation. Inactivating keloid cells and remodeling keloid tissue rather than destroying keloid tissue are the correct strategy for keloid therapy with intralesional injection.

2. A sustainable and long-term therapy (2–3 years) is usually required for keloid treatment in order to completely cure keloids and prevent their recurrence. To do so, a low dose of chemotherapy agent is necessary not only for safety concern, but also for proper working mechanism of tissue remodeling.
3. Low-dose 5-FU will be sensitive enough for inducing endothelial cell apoptosis/death and destroying neovascular structure during keloid development, and will also be enough to inhibit fibroblast activities such as proliferation, invasion, and matrix production.
4. This therapeutic model provides good basis for other conjunctive therapies including surgery, laser, and steroid injection to remove or to flatten keloid tissue by partial keloid destruction or tissue remodeling. It also avoids host production of risk factors that will trigger keloid development and recurrence, in which growth factors and neovascularization play significant roles.

30.2.1 Background

After careful literature review and exploratory testing, concentrations ranging from 1.5 to 5 mg/ml were decided as the low dose of 5-FU for clinical use with at least monthly injection interval in order to avoid any significant systemic side effect and local side effect such as adverse effect on hemopoietic system and severe pain and tissue ulceration. According to our clinical experience in treating more than 10,000 cases during the past 18 years of clinical practice, this method has been proved safe for patients with a therapeutic time period ranging from 2 to 5 years or even longer, and no severe side effect has ever been observed thus far. In addition, this dose also has the effective rate of more than 97.14% in term of relieving pain and itching symptom, softening and flattening keloid scar, and the recurrence rate is significantly decreased after long term therapy [7]. However, drug resistance to 5-FU was observed in some patients, and for these patients a bit higher doses could also be applied but were always limited to less than 9 mg/ml concentration to avoid significant side effects.

Importantly, low-dose 5-FU injection aims to disrupt or destroy neovascularity of keloid tissue and inhibit fibroblast proliferation, rather than to destroy keloid tissue; thus low-dose 5-FU will not be able to majorly flatten or soften keloid tissues, in which abundant collagen and other matrices need to be degraded with steroid's effect. Therefore, combined injection with steroid is needed in order to flatten and soften keloid tissue. Nevertheless, injected low-dose 5-FU is able to timely demolish neovascularity induced by steroid injection, and thus render treated keloids to become relatively malnourished post-drug injection and thus less possible to reoccur.

Meanwhile, reduced vascularity also allows the longer stay of the injected drug inside keloids due to the reduced drug absorption via tissue capillaries, and thus enhance the drug efficacy and reduce the side effects. The case 1 demonstrates how this strategy could be applied to treat keloid tissue with intralesional injection of combined 5-FU and steroid at a low dose in order to gradually remodel the keloid into normal-looking skin [8].

30.3 Clinical Protocol of Low-Dose 5-FU Injection Therapy

The protocol for intralesional injection of low-dose drugs includes the injection of 5-FU alone or 5-FU combined with steroid. In general, the combined injection of 5-FU and triamcinolone acetonide will be a preferred method, unless the keloid scar is heavily vascularized, which will need 5-FU injection first to demolish tissue vascularity before steroid injection. The key points of this protocol include the following:

1. *Drug preparation:* Triamcinolone acetonide should be mixed with 2% lidocaine, and then 5-FU stock solution can be further mixed with them to maintain the concentrations of 5-FU between 1.5 and 5 mg/ml and steroid between 3 and 9 mg/ml. Low concentrations of both drugs will enable better control of the side effects such as severe pain, tissue ulceration, and atrophy as well as the drug-induced angiogenesis. Also, the volume ratio between the drug and lidocaine should be 3–5:1 in order to reduce the pain suffering during and after the drug injection. As a routine, the concentrations should always start from relatively high (5-FU: 3–4 mg/ml; triamcinolone acetonide at 8–9 mg/ml) and gradually reduced as below described.
2. *Injection procedure:* To avoid pain, 1 ml syringe with 26–27G needles is generally recommended for the injection and multi-entrance manner should be applied. Briefly, each injection should deliver about 0.2 ml volume and then change the injection sites to make sure for even distribution of the drugs. When performing, the keloid tissue should be held between two fingers with pressure in order to prevent drug from oozing into surrounding normal skin. In addition, before injection, blood withdrawal should be tested to avoid direct drug injection into a blood vessel. When injecting, the drug should be pushed hard into the tissue in order to create a pressure in the tissue between the fingers and whiten the injected tissue, this manner will make sure that the injected drugs will deeply infiltrate inside the keloids, but not to noninjected region, and thus to enhance the efficacy and reduce the side effect.

3. *Adjustment of drug concentrations and injectional interval:* Here, an important concept is that this procedure does not try to destroy keloid, but rather to remodel the keloid tissue gradually via inactivating keloid fibroblast and degrading keloid matrices. Therefore, the drug concentration should be adjusted according to the status of treated keloids. The followings are the general principles:
- A. Steroid concentration should be gradually reduced when keloids become softened and flattened as overdoses of steroid will cause tissue atrophy. In addition, sudden withdraw of steroid is well known for causing reoccurrence of other steroid-treated diseases, such as autoimmune disease, and thus the principle of gradual steroid withdrawal should also be applied to keloid treatment.
 - B. 5-FU concentration should be reduced when tissue angiogenesis is significantly inhibited or keloid is significantly inactivated with improved symptoms. Vice versa, a higher concentration of 5-FU should be used when significantly enhanced angiogenesis is observed or keloid remains highly activated and less responsive to the drug treatment.
 - C. Adjustment of drug injection interval: With the progress of drug treatment, injection interval should also be gradually prolonged as a way of gradual withdrawal of steroid and 5-FU, and thus to better prevent keloid recurrence. In general, initial drug injection will be administered every 4 weeks for a few months. Afterwards, the injection can be adjusted for every 6 weeks to 10 weeks for several months, and finally adjusted

to every 12 weeks with further reduced drug concentrations for several repeats. According to our experiences, most keloid will be resolved eventually without a high recurrence rate.

- D. Long-term therapy for localized nodule: As shown in case 1, localized nodule is often observed as the last part of noncured keloid or as the first sign of reoccurred keloid, which needs to be continuously injected with an interval of every 6 to 12 weeks until a final resolution (also see case 3).

30.4 Low-Dose 5-FU-Based Injection Therapy for HTS and Keloids

The best candidate for low dose 5-FU injection is the keloid type that usually exhibits relatively soft and flat but red color with significant signs of inflammation such as severe pain, itching, erythema, and rapid invasion into normal skin (■ Fig. 30.1a). Keloid types that are more like tumors, such as cauliflower-shaped solid tissue with relative dark color, fit better for surgical therapy (■ Fig. 30.1b), but 5-FU-based injection can be well employed as well for preventing keloid relapse after surgical removal.

In general, single or multiple keloids with small sizes (diameter less than 2 cm) and located at various parts of the body are the best candidates for drug injection treatment.

Large-sized keloids will not be ideal candidates for drug treatment by intralesional injection because of potential side effects of both 5-FU and steroids.

■ Fig. 30.1 Keloids are generally divided into two types: **a** inflammatory type; **b** tumor-like type

30.4.1 Important Concepts of Keloid Curing and Relapse Rate for Low-Dose 5-FU-Based Therapy

Insufficient treatment might be the most important reason for not being able to cure a keloid and preventing its reoccurrence

A softened and flattened keloid along with disappearance of the symptom does not necessarily indicate that a keloid is cured and the treatment is completed. Rather, the keloid is in a temporary inactivated stage under the drug pressure. Like cancer therapy, drug treatment can remove most of disease cells but there will always be a portion of cells (residue cells) that survive after chemotherapy and become quiescent and drug resistant [9, 10]. Once the drug pressure is relieved, these cells become reactivated and enter an active stage with rapid proliferation and production of matrices, growth factors, and angiogenic factors, and eventually lead to a reoccurred keloid.

To prevent this from happening, a continuous drug pressure should be applied to any of these residue cells to inactivate or remove them once they become activated. In the literature, most studies report the successful treatment of keloid with the criteria of flattening and softening of the treated keloid along with disappeared symptoms of pain, itching, and erythema as judged by Vancouver Score or Patient and Observer Scar Assessment Scale (POSAS). But the cessation of drug injection improperly will likely lead to keloid to reoccur simply because these treatments did not really remove or remodel the residual quiescent keloid cells into normal skin cell phenotype. This might be the key reason why high recurrence rate remains after keloid injection therapy, to which less attention has been paid in the literature.

In our group, it has been observed that 2–3 years are usually required for completely curing keloids by 5-FU and steroid injection in most cases. More importantly, preventive drug injection at a later stage aiming to prevent reoccurrence is essential and is performed by gradual drug withdrawal via reduced doses and prolonged injection intervals. As shown in case 3, there was a large-sized keloid in a woman's abdominal region, and a total of 6.5 years were spent to completely cure the keloid via combined injection of both 5-FU and steroids at a low concentration. During this process, the first 3 years were spent on treatment of the keloid, whereas the last 3 years were spent on preventive therapy to timely treat the reoccurred keloid nodules.

30.5 5-FU-Based Injection Therapy for Recurrence Prevention of Surgically Removed Keloids

Although low-dose 5-FU injection has been proven effective for primary keloid treatment and reoccurrence control, the efficiency would be too low to be an ideal method. As described earlier, the conversion of a keloid tissue into a normal-like skin will be a long-term process. On the contrast, preventing the conversion of normal wound cells into keloid cells would be much easier, in which 5-FU could play an important role.

Surgical excision has now become the first-line keloid treatment in our group because it is an efficient way of keloid treatment. In particular, keloids with a size larger than 2 cm in diameter and possible for primary closure after surgery are the best indication for surgical therapy. Most importantly, the use of low-dose 5-FU injection along with other procedures enables us to prevent the development of new keloids in a surgically created wound. Therefore, the “treatment model” of injection therapy will be shifted to the “prevention model” of surgical treatment, and 1-year time period will be usually long enough to achieve satisfactory results in most keloid patients as shown in cases 4 and 5.

There are three key issues that are essential for the success in this surgical procedure, including (1) anti-tension procedures by proper multilayer suturing and anti-tension device application; (2) wound irrigation with combined 5-FU and steroids during the surgical procedure; (3) post-surgery radiotherapy and combined 5-FU injection. The procedures are described in the following sections.

30.5.1 Surgical Procedure for Keloid Excision

Briefly, after local anesthesia with 2% lidocaine injection, the keloid will be surgically excised followed by multilayer suturing (including fascia and dermal and epidermal layers). 5-FU wound irrigation was reported valuable for preventing keloid recurrence from surgical procedure [11]. Thus, wound irrigation with combined 5-FU (about 3 mg/ml) and triamcinolone acetonide (about 8 mg/ml) should be performed, and excessive drug liquid should be extruded out of the wound before its closure. With the clinical experience over 3,000 cases, no failure of wound healing has even been observed when a wound was irrigated at this dose.

After wound closure, tension-reduction device such as “zipline” should be applied immediately to guarantee a tension-free zone in the wound area. Afterwards, the patients should receive irradiation on the wound within 24 hours post-surgery with a dose of 4–5 grays once a day for a total of 4 days using electron beam as the irradiation source.

30.5.2 Postsurgical Monitoring and Preventive Injection of 5-FU

After the procedure, the patients are advised to visit the clinic monthly to closely monitor the status of surgical site and silicone gel is generally needed for application on the wound site. In most cases, the above procedure is enough to keep the sutured wound quiescent and non-activated, and the wound tissue will maintain erythema-free and symptom-free for pain and itching (see case 4). If this maintains with no further signs of recurrence, the tension-reduction device can be removed after continuous wearing for at least 6 months.

For high-risk patients, including those who have previous history of postsurgical recurrence, multiple keloids, or previous recurrence after surgery plus radiotherapy, early injection of low-dose 5-FU into the wound subcutaneous tissue should be applied as early as 4 weeks post-surgery, which is maintained for another five injections every 4 weeks until the sixth month post-surgery. Afterwards, 5-FU injection should be given whenever there is sign of pain, itching, and erythema to make sure that early management of recurrence is applied (see case 5).

For non-risk patients, or patient without previous surgery, an indication for low-dose 5-FU injection will be the minor level of erythema and the feeling of pain and itching. The injection should be given one more time after disappearance of these early signs.

30.6 Anti-indications of Low-Dose 5-FU Injection Therapy Combined with Steroids

Children are generally not the candidates for 5-FU-based chemotherapy in both keloid and HTS. In addition, female patients are recommended not to prepare for pregnancy during the treatment time period until 6 months after the cessation of the treatment. In addition, a blood cell count test is recommended every 2 months to monitor potential adverse effects on hematopoietic system. Close monitoring of steroid side effects is needed, and the cessation of the therapy is needed at once in case any side effect is confirmed.

30.7 Representative Case Reports

30.7.1 Case 1. Remodeling of Keloid into Normal-Looking Skin [7] (■ Fig. 30.2)

A 53-year-old woman with 28 years of spontaneous formation and development of her chest keloid with previous history of cryotherapy and steroid injection. The keloid grew rapidly in the last several years with unbearable pain (++++)¹ and itching (++++). Physical examination revealed a big keloid in her chest skin with dimensions 10 cm wide, 7 cm high, and 0.3 cm thick along with severe erythema (++++), and hard tissue texture (++) (■ Fig. 30.2a). The patient was first given nine intralesional injections of 5-FU (mostly 3.45 mg/ml) in 2% lidocaine every 2 weeks in order to control growth and abolish vascularity. The drug injections led to decreased erythema (+), thickness (0.15 cm), hardness (+), reduced itching (+), and also pain disappearance.

Afterwards, the patient received three injections of triamcinolone acetonide in lidocaine (8.3 mg/ml) every other week, resulting in flattened and softened scar with no pain and itching despite the fact that some minor elevated scar areas remained (■ Fig. 30.2b). Due to re-increased erythema (++) caused by injected steroid, the patient received four injections of a mixture of steroid (7.58–7.35 mg/ml) and 5-FU (2.94–2.27 mg/ml) in lidocaine to achieve both drug effects simultaneously, and this further decreased erythema (+), while maintaining flattened and softened scar without symptom (■ Fig. 30.2c). Because of improved symptom and physical sign, the patient was given a much lower dose of combined drugs (steroid: from 2.83 to 2.40 mg/ml, 5-FU from 2.27 to 1.42 to 0.96 mg/ml) for six times with 3–8-week intervals in order to prevent relapse and to remodel the scar. During this time, relatively high dose of drugs remained necessary in some small re-growing areas. When followed up 4 months later, it was surprising to find that some keloid areas became grossly invisible and normal-looking skin had appeared (■ Fig. 30.2d).

Encouraged by this result, another five injections of low-dose combined drugs (steroids: 3.77 mg/ml, 5-FU: 1.42 mg/ml) were administered only to the remaining elevated scar areas with an interval of 4–8 weeks. After another 9-month treatment, scar portion further decreased, and normal-looking skin further expanded with skin color, surface, and texture close to those of normal skin (■ Fig. 30.2e). After 3 years of tissue remodeling therapy, the treatment was completed and

1 Represents the level of pain, itching or thickness of the scar, sort of semi-quantitative analysis.

Fig. 30.2 Case 1: Remodeling of keloid into normal-looking skin at various stages. Black arrows indicate the areas that are under continued tissue remodeling. White arrow indicates reoccurred keloid nodule. (See details in the text)

no further relapse was observed at 14 months post-therapy (■ Fig. 30.2f). Blood cell counts maintained normal during and after therapy.

Two years after the cease of the treatment, a small nodule with redness and pain and itching recurred at the left lower corner (■ Fig. 30.2g, white arrowed), and further injections with 5-FU (about 3 mg/ml) mixed

with triamcinolone acetonide (about 9 mg/ml) were given at intervals of every 3–6 months for 2 more years and once a year for another 3 years. The complete cure of the scar was observed at 9 years after the initiation of the treatment except for an even smaller active nodule (■ Fig. 30.2h, white arrowed), which may deserve another therapy modality such as radiotherapy.

Fig. 30.3 Case 2: Intralesional injection of low-dose 5-FU and steroids for the treatment of large-sized keloids before **a** and after **b** treatment. (See details in the text)

30.7.2 Case 2. Intralesional Injection of Low-Dose 5-FU and Steroid for a Large-Sized Keloid

A 50-year-old female patient visited the clinic with a chest keloid spontaneously forming for 5 years, which developed quickly along with the symptoms of pain and itching. The keloid revealed a size of 15 cm in width, 12 cm in length, and 0.5–1 cm in thickness with server erythema (■ Fig. 30.3a). The patient was treated with intralesional injection of combined 5-FU and triamcinolone acetonide at low doses as described earlier. This big-sized keloid was divided into four regions, and the injectional therapy was given in a manner of region by region that lasted for 4 years and eventually resulted in a completely remodeled scar that was flattened and softened without erythema and symptoms (■ Fig. 30.3b). Afterwards, the keloid was generally stable and inactive except for some minor nodules that needed occasional injection.

30.7.3 Case 3. Sufficient Therapy Is Essential for Curing Keloids

A 22-year-old female patient with a large-sized keloid (18 cm in length, 6 cm in width, and 0.5–1.5 cm in thickness) in the abdominal area visited the clinic for her keloid treatment (■ Fig. 30.4a). The total keloid was roughly divided into three regions for one-by-one treatment. Due to high vascularity of the keloid, the patient was first given 5-FU injection alone at the dose about 3 mg/ml every 3–4 weeks for three times to reduce the vascularity via inducing endothelial cell apoptosis. Once the scar became darker with less erythema, combined

5-FU (2.6 mg/ml) and triamcinolone acetonide (7.5 mg/ml) was used for intralesional injection every 4 weeks. At the seventh-month posttreatment checkup, the top two-thirds of the keloid had already become softened and flattened with the disappearance of pain and itching and reduced erythema (■ Fig. 30.4b). The patient was further treated for the rest of the keloid in a similar way and the total keloid area became completely softened and flattened without symptoms and with further reduced vascularity at the 24th-month posttreatment (■ Fig. 30.4c). Then, reduced drug dose (2.6 mg/ml for 5-FU and 4.5 mg/ml for steroids) and prolonged injection interval (6–8 weeks) were applied to focus on remodeling keloid and improving tissue texture. At the 32th-month posttreatment, completely remodeled keloid with tissue texture similar to normal skin and minimal level of redness was observed, except for a few isolated active keloid nodules which remained over-vascularized at the bottom region (■ Fig. 30.4d). Afterwards, the treatment focused only on activated keloid nodules with an injection every 6–8 weeks and whole keloid was completely remodeled when observed at the 68th-month posttreatment except for a few nodules located at the stitch markers that remained activated at the 63th-month posttreatment (■ Fig. 30.4e). Following that time point, the nodule treatment remained and most nodules were completely remodeled after another 15 months of treatment with 3-month interval. The whole keloid has been completely remodeled, which became stably inactivated with whitened color and soften tissue texture when observed at the 78th-month posttreatment (■ Fig. 30.4f). Afterwards, the whole keloid never reoccurred, and the treated nodules also completely inactivated after several more injections. After more than 6 years of treatment with low-dose 5-FU, the patient delivered a completely healthy child at 2 years post-

Fig. 30.4 Case 3: Sufficient therapy is essential for curing keloids with image presentation of an evolved keloid treated with low-dose 5-FU and steroid injection. (See details in the text)

cessation of the treatment. This exploratory treatment indicates the importance of sufficient treatment for preventing keloid reoccurrence.

30.7.4 Case 4. Low-Dose 5-FU for Preventing Keloid from Reoccurrence After Surgical Excision

A female patient who had a chest keloid (3 cm in width, 2 cm in height, and 0.5 cm in thickness) with severe pain and itching visited the clinic to request keloid treatment (■ Fig. 30.5a). The patient received surgical excision

of her keloid, and then the wound was irrigated with combined 5-FU (2.6 mg/ml) and triamcinolone acetonide (7.5 mg/ml) followed by primary wound closure with multiple tissue-layer suturing. A tension-reduction device was immediately applied on the closed wound and the patient was asked to keep wearing the device for at least 6 months after the surgery. The patient received radiotherapy within 24 hours post-surgery with a dose of 4 grays per time and per day for total 4 days. The patient was followed up every 4 weeks post-surgery with no sign of reoccurrence, and a linear white scar was observed at 13 months post-surgery without any sign of reoccurrence (■ Fig. 30.5b).

Fig. 30.5 Case 4: Low-dose 5-FU for preventing keloid from reoccurrence after surgical excision. **a** Before the surgery; **b** 13 months post-surgery. (See details in the text)

Fig. 30.6 Case 5: Low-dose 5-FU for combined chemoradiotherapy to prevent keloid from postsurgical reoccurrence. **a** Before the surgery; **b** 2 years post-surgery with multiple 5-FU injections. (See details in the text)

30.7.5 Case 5. Low-Dose 5-FU for Combined Chemoradiotherapy to Prevent Keloid from Postsurgical Reoccurrence

A female patient with multiple keloids on her neck, chest (Fig. 30.6a), and left arm visited the clinic and requested keloid treatment. Her chest keloid (4 cm in width, 2 cm in height, and 1 cm in thickness) was heavily vascularized with severe pain, itching, and rapid growth (Fig. 30.6a). The patient received surgical excision, wound irrigation, and closure and radiotherapy similarly as in case 4. However, relapse signs of itching and pain occurred early at 1 month post-surgery. Thus, the patient was given injection of low-dose 5-FU alone (about 3 mg/ml) at 1 month, 8 months, 10 months, 13 months, 16 months, and 19 months post-surgery and

no further treatment after 19-month time point. At the 24th month post-surgery follow-up, a whitened linear mature scar was observed at the operational site with no sign of relapse (Fig. 30.6b).

30.8 Conclusion

Intralesional injection of low dose 5-FU combined with steroids for keloid and HTS treatment has been practiced by the authors since 2002 with more than 10,000 cases and proven safe and effective. The use of low dose drugs is to keep this procedure safe and sustainable for long term therapy that is essential for reducing the post-therapy recurrence. Gradual adjustment of drug dose and injection interval time and the management of reoccurred keloids at the earliest possible time are the keys for the success of this procedure.

Take-Home Messages

- Intralesional injection of low dose 5-FU (1.5–5 mg/ml) combined with steroids has been used for keloid treatment with proved safety and efficacy.
- The working mechanism is to inactivate keloid fibroblasts and to gradually remodel keloid tissue, rather to cause keloid necrosis which is a trigger for keloid recurrence.
- The procedure can be used for treating primary keloids or for preventing recurrence of surgically removed keloids.
- Sustainable long-term treatment with adjusted drug dose and injection interval and early management of reoccurred lesions are the keys for keloid successful treatment and recurrence prevention.

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