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Complications of Injected Exogenous Growth Factor for Cosmetic Facial Rejuvenation: A Case Series and Sequential Therapy

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Abstract

Background Exogenous growth factor presents promising soft tissue regeneration, but the complications from injectable exogenous growth factor seem to be growing. However, there is no detailed summary of complications and sequential treatment protocols. It is noted that the injection of exogenous growth factor into the soft tissue is an unreasonable or even illegal procedure, which could cause uncontrollable tissue growth and some other complications.

Methods A total of 65 patients underwent analysis retrospectively for complications related to the injection of exogenous growth factor from 2017to 2022 at Xijing Hospital in China. Initially the symptoms mainly consisted of redness, skin temperature arisen, itching, tissue hypertrophy, localized swelling, mass, and lump, with later manifestations including ulcerations and purulent discharge. A comprehensive treatment scheme was formulated based on the location and size of the lumps as well as the type of complication. Post-treatment satisfaction was evaluated over a mean 16-month follow-up (range 6–39 months).

Results A total of 65 patients participated in the treatment. Drug injection therapy was initially performed on all patients. If injections were not effective, surgical treatment (debridement/excision/liposuction) was performed. Twenty-eight patients were managed with intralesional injections alone. Patients reported improved satisfaction in 23 cases (82.14%), full symptom resolution in 3 cases (10.72%), and no improvement in 2 cases (7.14%). Surgery was required for 37 patients. Postoperative improved satisfaction was reported in 30 cases (81.08%), full symptom resolution was recorded in 4 cases (10.82%), and no improvement was seen in 3 cases (8.10%).

Conclusions This study highlights the management of complications arising from exogenous growth factor injections through the implementation of a sequential therapy approach. Specifically, this approach involves the initial administration of drug injection therapy, and if drug injection therapy proves ineffective, then surgical treatment is pursued. In conclusion, the injection of exogenous growth factors into soft tissues should be forbidden.

Level of Evidence IV This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266.

Keywords Exogenous growth factor · Facial injections · Complications

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Introduction

With aging, the loss and redistribution of facial soft tissues contribute to the changes in facial morphology associated with senescence. To postpone aging, injectable fillers, and aesthetic facial recontouring procedures can enhance soft-tissue volume and fill subcutaneous defects. However, presently approved injectable fillers are unlikely to achieve long-term efficacy.

Recently, exogenous growth factors have been receiving increasing clinical attention as an alternative additive. However, the injection of exogenous growth factor into the soft tissue is an unreasonable or even illegal procedure. Currently, exogenous growth factors are only approved for topical application to the wound. Exogenous growth factors are low molecular weight peptides that promote biological functions such as soft tissue regeneration [1]. Currently, available exogenous growth factor components include vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), and basic fibroblast growth factor (bFGF). Only topical exogenous growth factor has been approved by the Food and Drug Administration (FDA) for clinical use [2]. However, some unlicensed practitioners have injected illegally exogenous growth factors into the subcutaneous tissues alone or combined with hyaluronic acid and/or adipose grafts as treatments designed to promote tissue regeneration and achieve a long-lasting effects.

Unfortunately, the prevalence of complications from injectable exogenous growth factor administration seems to be growing, as shown by the numerous reports in the literature [2]. Injection-related complications include redness, pain, itching, hard lumps, and abnormal hyperplasia. A large number of patients developed complications from exogenous growth factor injections, which drew the concern of clinicians. Moreover, the treatment of complications is challenging and has attracted the attention of multiple clinicians. Liao [2] summarized the management of lump formation after exogenous growth factor injection, recommending surgical excision as the primary management. However, there are few standardized statistics and or systematic treatment protocols for managing these complications. In our study, we have summarized the detailed complications associated with exogenous growth factor injections for the first time and have proposed a combination of drug injection treatment and surgical treatment to address these complications.

Through our previous summarization and review of our clinical treatment approach, we evaluated the effectiveness of the treatment for exogenous growth factor complications. The present work treated 65 patients with different complications after the injection of exogenous growth factor in a non-professional setting due to cosmetic reasons. By recording the injection site and detailed symptoms of complications, we formulated a comprehensive scheme for treating complications after exogenous growth factor injections.

Methods

Participants

A total of 65 patients with facial complications due to an exogenous growth factor injection were treated at our institution. All were female, aged 23-56 years (mean 43.7 years old). All were previously healthy and had no history of hypertension, diabetes, immune system disease or facial filler treatment with other materials. Medical history, ongoing medications and concomitant medical conditions were recorded. All patients were screened with an ultrasound soft-tissue examination performed by an experienced operator to produce precise information about the volume, nature, and position of the injected material.

Comprehensive Treatment Involved the Following Procedures

(A) Pre-treatment preparation: detailed history, type, dose and site of the injection and ultrasound detection to clarify the injection layer.
(B) Treatment methods: Injections are administered first. If these are not effective, surgery (debridement/excision/liposuction) can be performed.

Indications for injection therapy (1) Localized lumps (not the whole face); (2) Obvious surface redness with peripheral infiltration; and (3) No active inflammatory reaction, ulcerations or purulent discharge. *Contraindications*: (1) Liver and kidney dysfunction, hematopoietic system disease or bone marrow suppression; (2) Endocrine disorders; (3) severe damage to important organs; and (4) Recent or impending childbirth.

Detailed methods (Table 1): Corticosteroids combined with 5-FU (5-Fluorouracil): compound betamethasone injection 1mL (Depo-Song, specification: 1ml:5mg:2mg Shanghai Schering-Plough Pharmaceutical Co. Ltd., National Drug Quantifier H20043676) +5-FU0.1mL (specification: 0ml:0.25g, Nantong Essence Pharmaceutical Co., Ltd., National Drug Quantifier H32022246). If the exogenous growth factor was mixed with hyaluronic acid, 1500 units of hyaluronidase can be dissolved into 2mL of 2% lidocaine. Injection intervals were 0.3-0.5cm, with 0.1mL administered at each point with an infiltration range

Table 1 Injection therapies

Injection of formulation	Dose	Injection methods	Course of treatment
Exogenous growth factor	Compound betamethasone injection 1mL +5-FU0.1mL*	Injection intervals were 0.3-0.5 cm, with 0.1mL administered at each point with an infiltration range of 0.5cm.	Four times, at intervals of 4-6 weeks.
Exogenous growth factor combined with hyaluronic acid	Step 1: 1500 units of hyaluronidase with 2mL of 2% lidocaine Step 2: Compound betamethasone injection 1mL+5-FU0.1mL*	Injection intervals were 0.3-0.5 cm, with 0.1mL administered at each point with an infiltration range of 0.5cm.	Hyaluronidase once Step 2 a total of 4 times at intervals of 4-6 weeks.

*This dose was shown in prior clinical trials by our group to increase efficacy and diminish adverse effects

of 0.5cm. Treatments were repeated 4 times at intervals of 4-6 weeks.

We previously used triamcinolone acetonide injections as part of our clinical practice. However, these were not included in our statistics because of serious adverse effects.

Indications for surgery (1) No improvement with injections alone ***Contraindications*** Poor general condition. (severe cardiovascular diseases, severe respiratory system disorders, abnormalities in the immune system or severe immunosuppression, severe liver or kidney dysfunction, and significant bleeding tendencies or coagulation disorders.)

Surgical debridement was immediately performed in the setting of severe ulceration or purulent discharge. The gold-standard surgical procedure was suction with excisions a secondary choice that requires peri-incisional injections to prevent recurrence and scaring. The incision was placed in the most concealed area possible. Excised tissue was routinely sent for pathology, and tissue defects were repaired via flap transfer or fascial implantation.

Results

Clinical Manifestations

The initial symptoms reported by the 65 patients included in this work were the appearance of facial flushing, sensitivity and itching, subcutaneous tissue hypertrophy, abnormal hyperplasia and hard lumps. Hyperplasia extending beyond the normal range affecting facial function and movement was seen at later stages. Nodules and stripes could be clearly palpated. The end stage of the disease process could involve ulcerations and purulent discharge, resulting in significant pain and psychological suffering (Figures 1 and 2).

The included patients were injected at different sites (Figure 3) and presented with different complications (Table 2). All patients had a clinical history of more than 6 months. Local injections, surgical excision, liposuction or debridement were performed based on the course of the disease and the size and location of the lumps. If there was a postoperative skin tissue defect or tissue depression, flap transplantation or skin grafting was immediately performed. Postoperative follow-up ranged from 6 to 39 months, with a mean of 16 months.

Efficacy Criteria

Efficacy after one course of treatment was measured as follows: (1) improved: 81–100% remission of hyperplasia, no redness, sensitivity or itching, no discomfort and no recurrence after treatment; (2) resolved: 61% to 80% remission of hyperplasia, no discomfort; and (3) not improved: slight change after one course of treatment, no relief of symptoms or symptoms reappeared.

A total of 65 patients in this study were followed for 6 to 39 months after treatment (mean 16 months). Twenty-eight patients received intralesional injections alone. Of these, 23 (82.14%) were satisfied. The distribution of the injection sites of the 23 satisfied cases is shown in Figure 4. An additional 3 cases (10.72%) were considered resolved, while 2 patients (7.14%) remained dissatisfied (Table 3).

Thirty-seven patients required surgery after failing injections, of whom 9 required 2 ~ 3 procedures because of residual disease. Thirty (81.08%) were satisfied with their outcome, 4 (10.82%) were considered resolved, and 3 (8.10%) remained dissatisfied (Table 4).

Overall, 53 of the 65 patients were satisfied with their outcome. Seven patients had residual disease and relapsed but were satisfied with their additional treatment protocol or re-treatment. Five patients were dissatisfied after multiple treatments. The total effective treatment rate was 81.54% (Table 5, Figures 5 and 6).

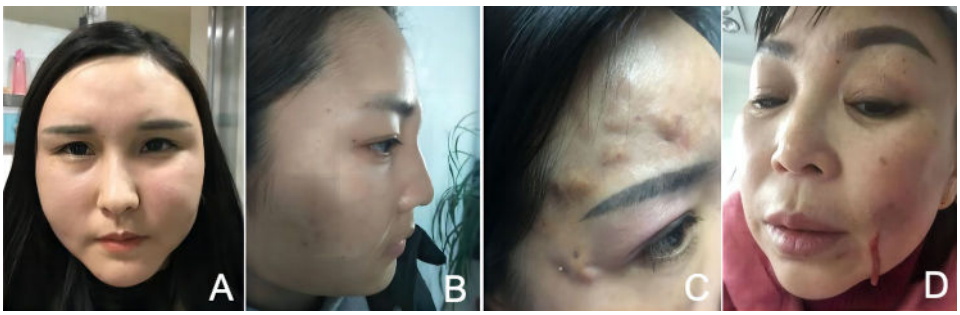
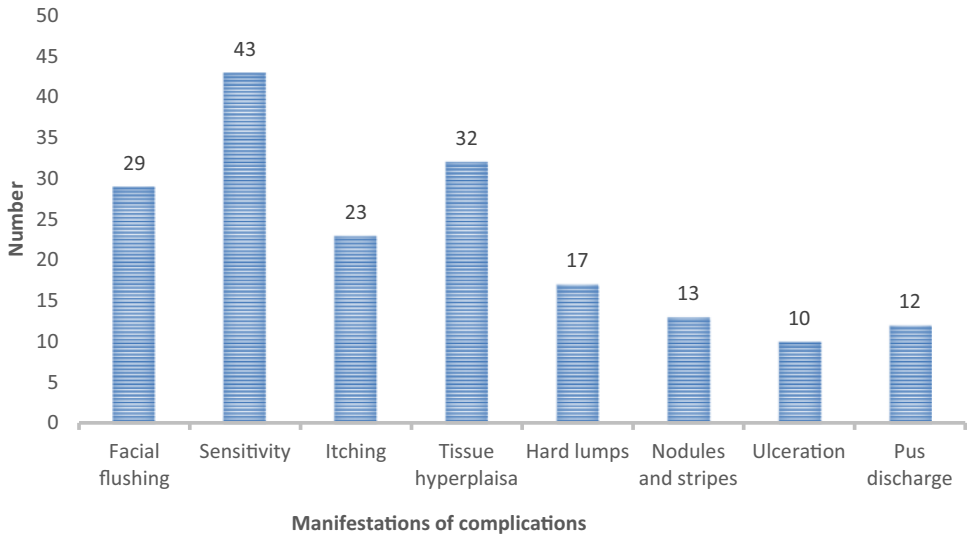


Fig. 1 The typical clinical manifestations of complications following growth factor injection: **A** redness, itchiness and sensitivity throughout the patient's face; **B** prominent hyperplasia between the eyebrow bridge; **C** progressive ulceration of the frontotemporal lumps; and **D** purulent discharge after the lump at the nasolabial fold

Fig. 2 Manifestations of the complications of growth factor injection



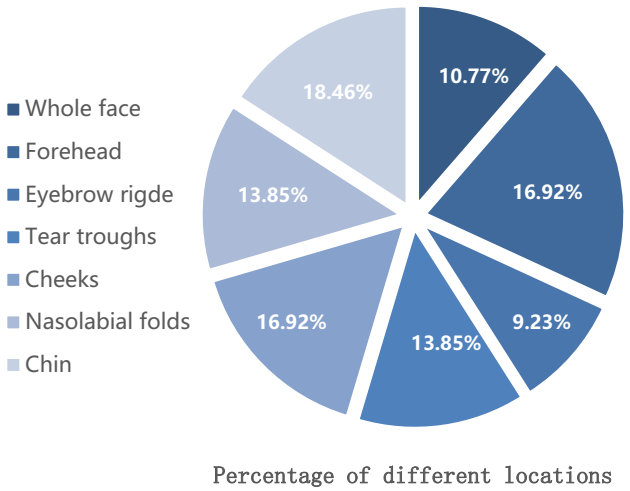


Fig. 3 Injection locations: whole face 10.77%, forehead 16.92%, eyebrow ridge 9.23%, tear troughs 13.85%, cheeks 16.92%, nasolabial folds 13.85% and chin 18.46%.

Patient Examples

Case 1

A 32-year-old female underwent exogenous growth factor injections on the nasal dorsum. After 6 months, she noticed a raised area at the injection site accompanied by redness and swelling. The swelling became more pronounced, forming a noticeable immobile lump with moderate firmness, but no pain, itching, or purulent discharge was present. Ultrasound examination revealed scattered irregular hypoechoic areas in the subcutaneous soft tissue located approximately 2 millimeters from the skin surface. We performed drug injection therapy only on the visible area. Followed up for 26 months, the symptoms improved and did not relapse after drug injection therapy (Fig. 7).

Case 2

A 29-year-old female underwent exogenous growth factor filler injections throughout her face at a private aesthetic

Table 2 Detailed descriptions of complications by anatomic location

Site of injection	Number	Symptoms
Whole face	7	Facial flushing, redness, and sensitivity
		Significant facial tissue hyperplasia 3–6 months later that affected facial movement.
Forehead	11	Sensitivity, itching
		Disseminated abnormal hyperplasia at the surface. Of the 11 cases, 7 presented with ulcerations and purulent discharge.
Eyebrow ridge	6	Redness, itching
		A visible lump between the eyebrows and the nasal dorsum, that was firm on palpation.
Tear troughs	9	Redness, itching
		Nodules and stripes clearly detected at the tear trough after 6 months
Cheeks	11	Facial flushing, sensitivity, itching. Hard lumps on the surface and motion with facial movement
Nasolabial folds	9	Sensitivity, itching,
		Lumps that moved with facial movement and a foreign body sensation from inside the mouth
Chin	12	Redness, itching, pain
		Stiff lumps and continued hyperplasia

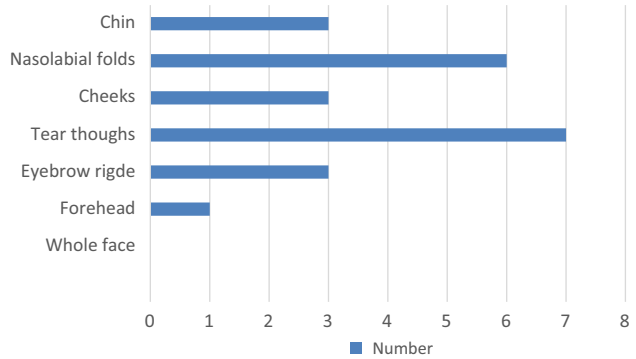


Fig. 4 The injection sites of the 23 patients who reported an improved outcome following injection treatment alone

Table 3 Results of 28 patients who were managed with injections alone

Satisfaction	Number	Percentage (%)
Improved	23	82.14
Resolved	3	10.72
Not improved	2	7.14

Table 4 Results of 37 patients who underwent surgery after failing injection therapy

Satisfaction	Number	Percentage (%)
Improved	30	81.08
Resolved	4	10.82
Not improved	3	8.10

Table 5 Post-treatment satisfaction of 65 patients

Satisfaction	Number	Percentage (%)
Improved	53	81.54
Resolved	7	10.77
Not improved	5	7.69

institution. Six months after treatment the patient complained of hot flashes and itching after exposure to alternating heat and cold. She later noted subcutaneous tissue hypertrophy and abnormal hyperplasia that exceeded the scope of her normal facial shape, affecting her facial function and activity. A hard lump could be clearly palpated, seriously affecting her cheek. An ultrasound performed upon referral to our department showed scattered irregular hypoechoic areas in the subcutaneous soft tissues of the patients entire face without obvious borders that were 7 mm from the skin of her cheek and 3 mm from the skin of her forehead. The patient underwent injection treatment followed by full-face suction treatment. Operative pathology was significant for a giant cell reaction and an intermuscular lipoma. The patient's postoperative appearance was significantly improved, her facial activity and function returned to normal, and no significant relapse was observed at 32-month follow-up (Fig. 8).

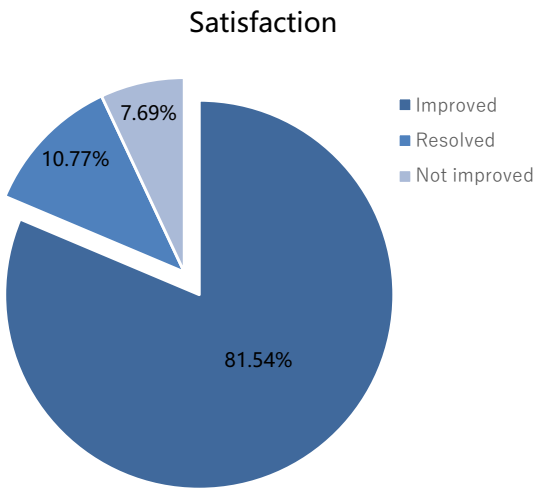


Fig. 5 Satisfaction of 65 patients

Discussion

Exogenous growth factors are a large group of regulatory proteins that attach to cell surface receptors and serve as chemical messengers. Exogenous growth factors that are commonly used clinically include fibroblast growth factor (bFGF) [4], vascular endothelial growth factor (VEGF) [5]and epidermal growth factor (EGF) [6]. A series of *in vivo* and *in vitro* experiments have shown that exogenous growth factors mediate inter- and intracellular signaling pathways that control cell growth, proliferation and differentiation, thereby promoting vascular and tissue regeneration [2, 7].

Fabi [8] previously noted the promising clinical applications of topical and injectable growth factors. Topical exogenous growth factor is currently the only form of this

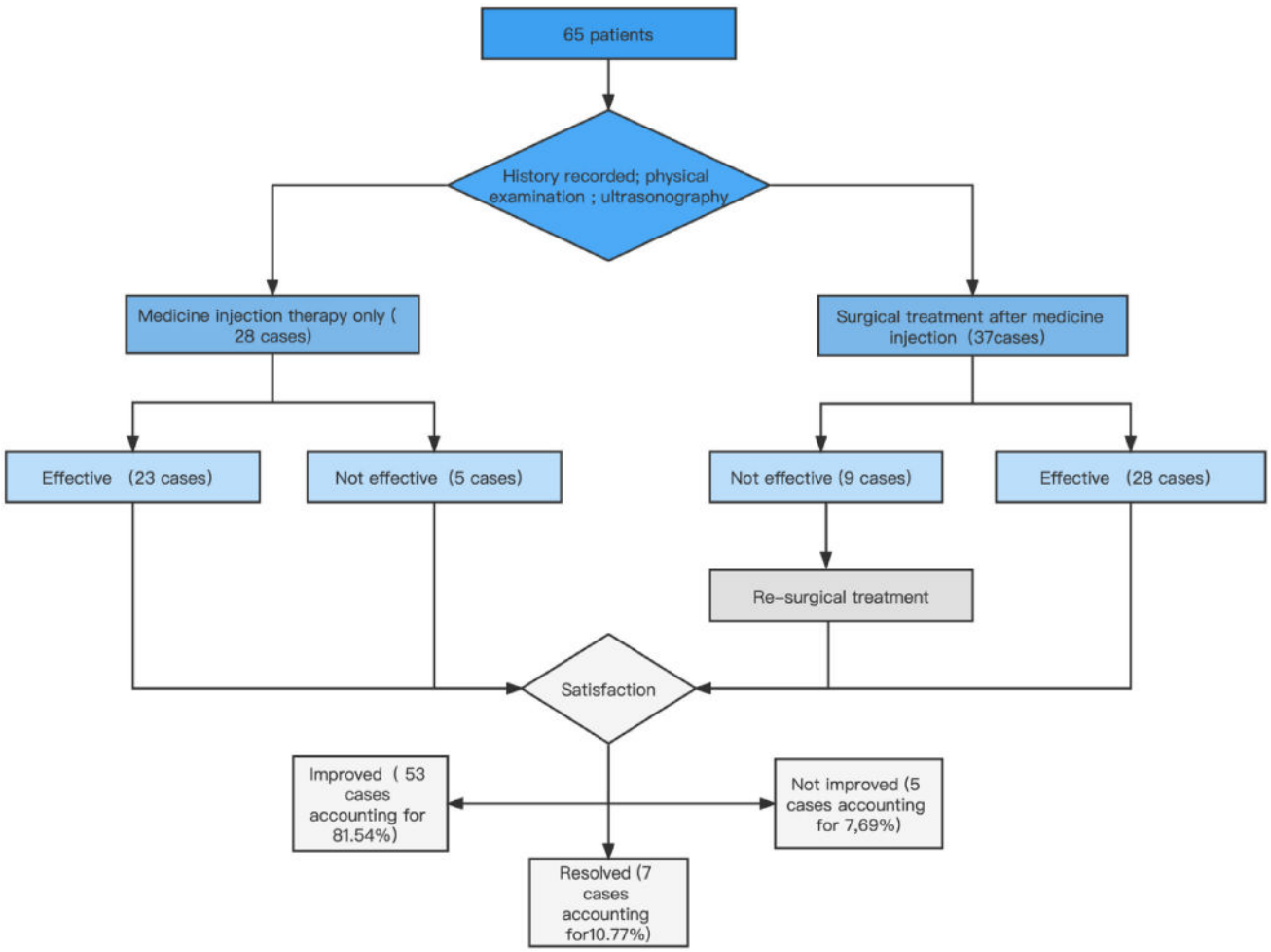


Fig. 6 Treatment process for 65 patients

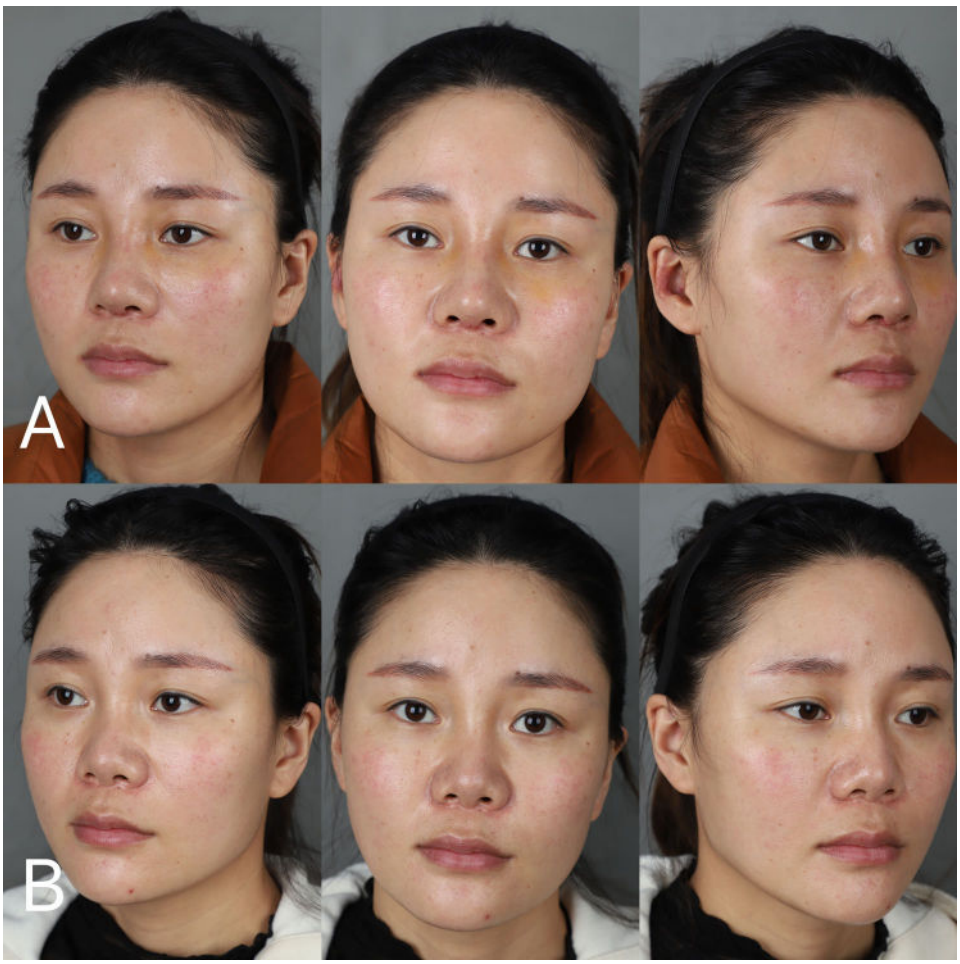


Fig. 7 Patient 1 followed up for 26 months. After drug injection therapy, the symptoms improved and did not relapse. **A** 6 months after growth factor injection and **B** after injection therapy alone

modality currently approved by the US Food and Drug Administration (FDA), and the topical exogenous growth factors that are widely used in clinical practice have demonstrated excellent wound healing and epidermal regeneration properties. Platelet rich plasma (PRP) has also been approved by the FDA as an injectable growth factor based on limited foreign reports. The FDA has otherwise noted that the safety, efficacy, tolerability and stability of exogenous growth factor formulations have not been proven [8]. There is additional concern that exogenous growth factors can induce the malignant transformation of lesions and cellular atypia because some malignant cells have receptors for certain exogenous growth factors, which may thereby increase their proliferation [9]. Thus, although injectable exogenous growth factors have significant clinical potential, their safety and tolerability remain to be fully understood.

Some cosmetic institutions have bypassed these regulatory limitations to capture the economic benefits of injectable growth factor. Unfortunately, complications such as skin hypersensitivity and abnormal hyperplasia at the injection site have been commonly reported in both domestic and international works [2]. However, few articles have documented the details of these complications, nor their anatomic distribution. The amount of sample size of the present work permitted this summary for the first time.

All patients in this report presented with facial lesions that were either distributed throughout the face (10.77%) or localized to the frontotemporal region (16.92%), eyebrow ridge (9.23%), tear troughs (13.85%), cheeks (16.92%), nasolabial folds (13.85%) or chin (18.46%). Complications manifested as varying degrees of facial flushing (29 cases), sensitivity (43 cases), itching (23 cases), tissue hyperplasia (32 cases), hard lumps (17 cases), nodules and stripes (13 cases), ulcerations (10cases) and/or purulent discharge (12 cases).

The second highest complication rate (16.92%) was in frontotemporal region. Since this region requires a larger volume of filler and has a higher absorption rate, multiple treatments are often needed to achieve satisfactory results. There are some incorrect theories that the use of exogenous growth factor mixed with adipose or hyaluronic acid fillers can minimize filler absorption rate and stimulate tissue

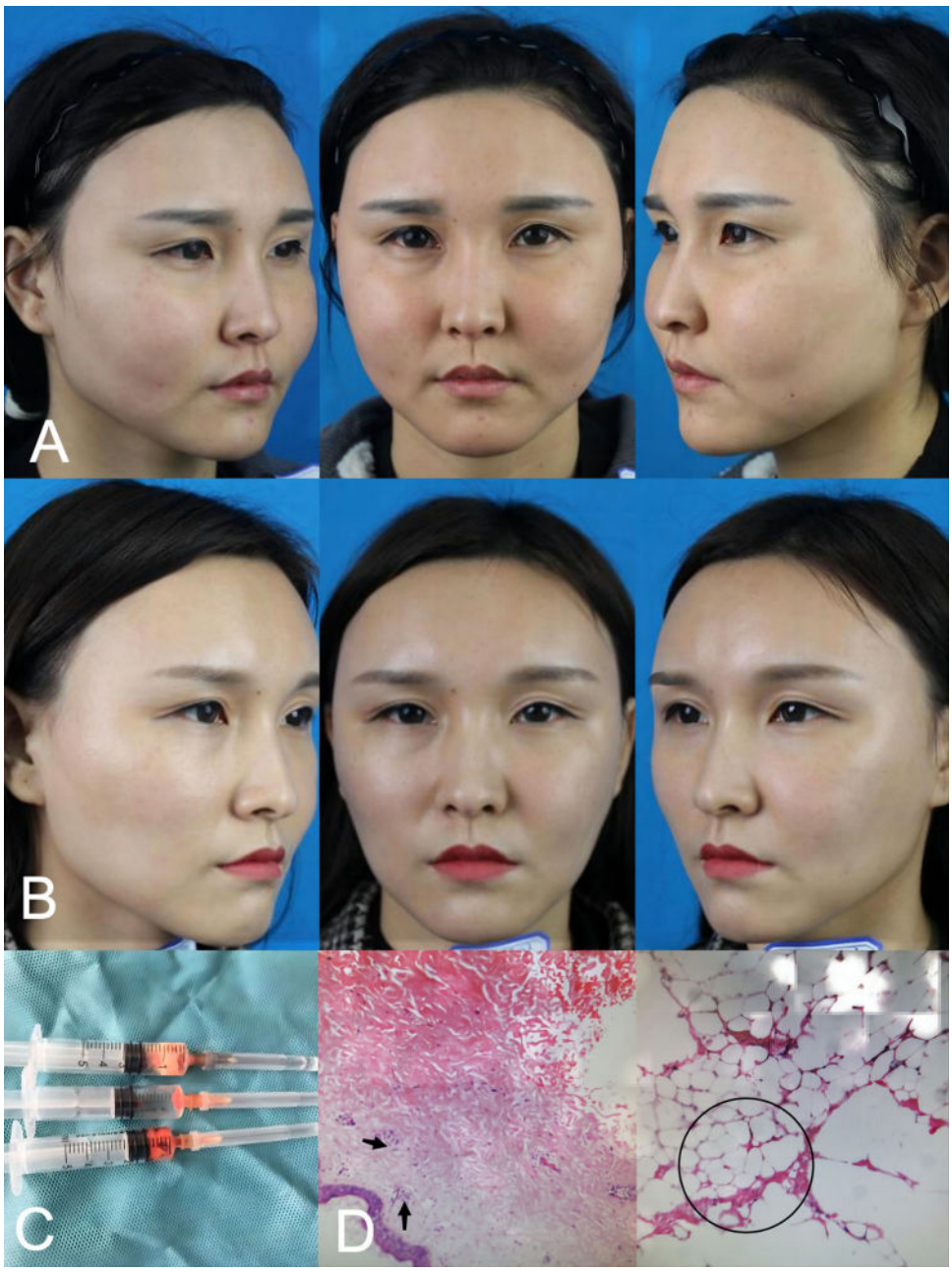


Fig. 8 Patent 2 Follow-up time was extended to 32 months, and during this period, there was no recurrence. **A** 6 months after the growth factor injection and **B** after sequential treatment protocols **C** intraoperative tissue removal **D** Pathological results, a giant cell reaction (Arrows show) and an intramuscular lipoma (the circle shows)

regeneration. However, our clinical experience suggests that while the addition of exogenous growth factor does have a positive impact on the pre-filling period, it results in disordered tissue proliferation during the later period. Chin injections (18.46%) had the highest complication rate. This may be because of the increased facial activity in this area and the limited efficacy of conventional injections, driving some to add exogenous growth factor. Other anatomic regions accounted for a relatively small percentage of total complications, which we believe is because traditional fillers yielded better results in these areas.

Few articles have documented the details of complications following an exogenous growth factor injection. Liao [3] described such complications superficially, noting briefly that lumps could form after an exogenous growth factor injection. Our study reported redness, itching and skin sensitivity as the initial symptoms of a complication following exogenous growth factor injection. We believe that these symptoms appeared in the skin because of early neovascularization following the growth factor injection. Tissue hyperplasia was the main reason for patients to consult a clinic and was most likely to affect their facial appearance and function. We therefore specifically sought

to understand the reasons for hyperplasia after exogenous growth factor injection and propose the following etiologies: (1) exogenous growth factors interact synergistically to cause the multiple types of tissue cells to differentiate and proliferate. The synthetic matrix eventually leads to the formation of fibrous and granulation tissue. Concurrent mesenchymal proliferation and neovascularization also occur; (2) exogenous growth factor increases the extent of cellular proliferation by disseminating to the adjacent cells. This eventually results in an immune response and inflammatory reaction that leads to uncontrolled hyperplasia of the surrounding tissues; (3) exogenous growth factors increase tissue blood circulation, resulting in tissue proliferation.

Although there are numerous reports of complications following exogenous growth factor injection, few articles discuss how to manage these complications. Liao [3] summarized the management of lump formation after exogenous growth factor injection, recommending surgical excision. In contrast, the present work recommends a trial of intralesional injections, with surgical treatment reserved for recalcitrant or refractory cases. Our article proposes this sequential treatment protocol and describes the comprehensive results of that strategy.

A total of 65 patients participated in this study. Relatively small lumps without inflammation or severe complication were treated conservatively via injections. This strategy is much less invasive than surgery from the patient's perspective, making it highly preferred as an initial treatment. In terms of disease progression, vascular proliferation and infiltration occurs before disordered proliferation, suggesting that local lesions are more sensitive to injectable therapy. Further, as these lesions are also relatively localized, injectable steroids can enhance collagen breakdown and suppress the immune response, thereby causing the tissue to atrophy. It can therefore simultaneously reduce scarring. Of the 28 patients that we treated with injections alone, 23 had satisfactory results (total effective rate of 82.14%).

We have previously studied the ideal drug type, combination and concentration for the treatment of complications following exogenous growth factor injection. This led to the two medications (corticosteroids and antitumor drugs) used in the present work. Xu et al. [10] confirmed that corticosteroids inhibit mitogenesis, collagen synthesis and the proliferation and biosynthesis of fibroblasts and keratinocytes. With respect to corticosteroid choice, we compared triamcinolone acetonide and compound betamethasone. Triamcinolone acetonide dissolves slower and deposits locally compared with betamethasone, which may predispose to white calcification spots local to the injection site. Other potential side effects may include telangiectasis, atrophy, steroid acne, pigment changes, necrosis, ulcerations and systemic side effects [11]. In contrast, compound betamethasone is a new type of compound preparation that has a high solubility, fast absorption rate and few adverse effects. Our previous clinical experience noted that such adverse effects were more common with corticosteroids alone. This agreed with previously published literature, which has shown that corticosteroids combined with antitumor drugs are much more beneficial than corticosteroids alone [12, 13].

We selected two antitumor drugs (bleomycin and 5-FU) as combination therapy. Antitumor drugs block DNA and RNA synthesis, have anti-angiogenic properties and inhibit fibroblast growth and reproduction to reduce collagen deposition [14, 15]. Both drugs were used in our preliminary clinical practice, but bleomycin was associated with more complications compared with 5-FU, including hyperpigmentation, skin erythema, pain and ulcerations [16]. We therefore selected 5-FU. This is in agreement with international guidelines, which recommend 5-FU injections for uncontrolled hyperplastic lumps [17]. Work by Khalid FA [18] further supports the clinical potential of intralesional 5-FU. Our clinical experience is that the combination of the two drugs is effective at decreasing neovascularization, reducing the inflammatory response and inhibiting tissue proliferation.

In the study, we treated hyperplasia with compound betamethasone 1mL + 5-FU 0.1mL. We have previously tried 0.5–2.5 grade concentrations (0.5 gradient at each interval) of compound betamethasone and 0.05-0.15 grade concentrations (0.05 gradient at each interval) of 5-FU. Compound betamethasone 1mL + 5-FU 0.1mL had the best result, while 0.5–2.5mL compound betamethasone and 0.05–0.15mL 5-FU are safe concentration ranges.

If after multiple attempts at injection therapy a desired effect is not achieved, surgical treatment can be considered. This was required for 37 patients in the present work, yielding a total effective rate of 81.08%.

Patients who develop inflammatory swelling or nodules, ulcerations or purulent discharge should undergo an immediate debridement. Surgical debridement can effectively remove infected lesions and necrotic tissue, thereby protecting the surrounding normal tissues from being invaded and avoiding a systemic infection. A suction was performed prior to excision to minimize soft tissue damage. Postoperative injections can be performed postoperatively to effectively reduce the risk of recurrence and scarring. Tissue defects or depressions required coverage with a fascial flap of the surrounding tissue.

The advantage of our sequential treatment strategy is that lesions can be controlled with timely injection therapy. This effectively reduces the scope of surgery and mitigates the extent of soft tissue damage due to the growth factor injection reaction. With respect to surgical treatment,

suction as first line therapy can effectively minimize the surgical incision. Excision with postoperative injection therapy is recommended only for those whose condition could not be improved with suction alone. The postoperative injections are key to reducing recurrence and scarring. We prefer concealed incisions when an excision is performed. The above strategy can minimize scarring to the maximum extent possible and reduce the impact of the complication and its treatment on long-term facial appearance.

Among who are were treated via injection only in the present work (Figure 3), the sites that achieved the best results were the tear troughs (30.43%) and nasolabial folds (26.08%). When treating facial complications, we found that areas that required smaller doses of injection therapy, such as the tear troughs and nasolabial folds, yielded better efficacy. In contrast, large injection treatments such as the entire face and frontotemporal area were less effective and often required multiple surgeries. If patients require urgent improvement, surgery should be pursued as initial management as injection treatment is time-consuming. In this article, 37 patients required surgical treatment after evaluation. Postoperative satisfaction was reported to improve in 30 cases (81.08%), complete relief of symptoms in 4 cases (10.82%), and no improvement in 3 cases (8.10%). The reason for dissatisfaction in these three cases is that, first of all, the injection area in the three cases was relatively large and the injection layer was rather deep, and the repeated recurrence after surgery, which contributed to the difficulty of achieving satisfactory results for the patients.

The pathological examination revealed the presence of giant cell reaction and intermuscular lipoma. We presume that these findings are commonly associated with infection and foreign body granulomatous reactions caused by the injection of growth factors. Terziroli Beretta-Piccoli B [19] states that giant cell reaction, which is characterized by a hyperproliferative disorder, is a reaction of the body to chronic infection. On the other hand, the foreign body giant cell reaction refers to a granulomatous inflammation, a histological pattern that occurs following cellular injury. In addition, intermuscular lipomas, which are benign, have been suggested to develop as a result of trauma or chronic infection [20]. In this particular study [21], the authors propose that the development of intramuscular lipomas is induced by local injection of growth factors and exhibits characteristics resembling adipocyte hyperplasia. Besides, previous research [22] has shown that basic fibroblast growth factor (bFGF) promotes the proliferation of human adipose-derived stem cells and regulates adipogenesis. Therefore, it is possible that the observed reactive adipocyte proliferation in the reported cases is associated with the stimulation caused by the injection of growth factors.

Exogenous growth factor has significant therapeutic potential in the areas of traumatic healing and tissue regeneration. However, the unregulated use of exogenous growth factor can lead to irreversible damage if complications occur. It is still unclear if growth factor injection complications can be prevented or treated in a more effective way. This article summarizes our current clinical evaluation and management of these complications, which may serve as a reference for clinical practice. Clinicians are encouraged to provide their own suggestions and clinical treatment experience to develop ideas for a more efficient treatment protocol. However, a limitation of this manuscript is that pathologic outcomes were not statistically or objectively analyzed, which could be a focused of future studies. Indeed, regulatory authorities should monitor illegal centers and impose restrictive laws. Moreover, the public should be aware that these cosmetic procedures are performed under professional medical observation and by specialist doctors.

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Declarations

Conflict of interest The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethical Approval This study was approved by the Ethics Committee of the Xijing Hospital; Air Force Medical University (Approval number: KY20170212).

Informed Consent Patient provided informed consent to participate in this study.

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