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Concentrated Growth Factor (CGF): The Newest Platelet Concentrate and Its Application in Nasal Hyaluronic Acid Injection Complications

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Abstract

Background Several cases of wounds caused by vascular compromise after facial cosmetic injection have been reported in recent years. How to promote wound healing, restore facial appearance, and avoid secondary injury in such patients have remained a clinical challenge. Our study was designed to assess the effect of concentrated growth factor (CGF) for repairing nasal wounds after nasal hyaluronic acid injection.

Methods Six women with nasal wounds after hyaluronic acid injection were enrolled from June 2019 to June 2022. The average time of the first CGF treatment from admission was 2–4 days. CGF gel was prepared from each patient's blood by using a Medifuge™ system. After debridement of the wound, the prepared CGF gel was applied on the wound surface, and the wound dressing was fixed to stabilize the CGF gel. The CGF treatment interval was 3–4 days.

Results The wound began to heal after the first CGF treatment. After 2–3 CGF treatments, the wound was almost completely healed. There was no deflection of the nasal columella, and nasal ventilation function was good. There was no obvious deformity in the appearance of the nose. After follow-up ranging from 2 months to 1 year, the appearance and function of the nose showed satisfactory recovery.

Conclusions CGF has great potential in promoting wound healing and restoring the appearance after complications from nasal hyaluronic acid injection. The preparation of CGF gel is simple, and the clinical application is convenient and safe. In future, more clinical trials are needed to further prove the efficacy and safety of CGF in the treatment of wounds secondary to cosmetic injection.

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 http://www.springer.com/00266.

Keywords Concentrated growth factor · Complication · Hyaluronic acid · Wound healing

Introduction

Cross-linked hyaluronic acid fillers are widely applied in the field of facial rejuvenation given their excellent biocompatibility, non-immunogenicity, and biodegradability [1]. According to the survey of the International Society of Aesthetic Plastic Surgery (ISAPS), a total of 3,558,511 cases of hyaluronic acid injection in women were carried out worldwide in 2020, ranking second only to botulinum toxin. (https://www.isaps.org/medical-professionals/isaps-global-statistics/) Although hyaluronic acid is considered relatively safe (for officially granted products, personnel with professional and formal training, adherence to the indications), there is still a potential risk of serious adverse events, especially with the continuous increase of such procedures in recent years [2].

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Vascular embolism is one of the most crucial and serious complications and tissue necrosis could occur if vascular occlusion is not diagnosed in time and the patient is not treated properly [3, 4]. Ischemic injury may be limited to the dermis, or it could also progress through deeper tissue structures [5]. Ischemic tissue caused by a hyaluronic acid filler vascular event can break down quickly, and wound healing could be delayed if vascular perfusion is revered slowly [5, 6]. Meanwhile, the potential risk of ischemia-reperfusion injury may exist after hyaluronidase injection in the treatment of vascular embolism, which could further aggravate tissue damage [7]. Severe ischemic injuries and formation of secondary wounds may require escalation to secondary care for surgical management [5]. Conventional methods include debridement and gel or wound dressing cover, but in these cases, the wounds tend to heal slowly and are often accompanied by deformity, obvious pigmentation, scar hyperplasia, and contractures, which have a negative impact on patients' lives.

Concentrated growth factor (CGF) is the third-generation platelet concentrate product secondary to platelet-rich plasma (PRP) and platelet-rich fibrin (PRF). CGF was prepared by special differential centrifugation technology to fully activate the alpha-granules in platelets that have higher concentrations of growth factors and $CD34^+$ cells than PRP and PRF [8]. The CGF gel has a complex three-dimensional network structure intertwined with a large amount of fibrin. The arrangement of fibrin in CGF is relatively loose, which allows numerous growth factors (GFs) to be released programmatically with the slow degradation of fibrin scaffolds [9].

In this study, we assessed the efficacy of CGF in repairing secondary skin wounds resulting from complications of nasal hyaluronic acid injection. To the best of our knowledge, this is the first report of the application of CGF in the treatment of secondary wounds after cosmetic injection.

Materials and Methods

General Data

From June 2019 to June 2022, six female patients (mean age: 45.5, range: 28–65 years) with nasal wounds caused by vascular compromise after nasal hyaluronic acid injection were enrolled at the plastic and reconstructive surgery department of the fourth medical center of PLA General Hospital (Table 1). All patients had received hyaluronic acid injections at other hospitals or clinics. The injection site included the nasal tip, alar margins, nasolabial fold, and nasal root. The dosages of the injection at the respective sites were 1.0 mL, 0.6 mL, 0.5 mL, and 0.5 mL. (The injection doses for the remaining two patients were unknown.) The clinical manifestations after vascular embolism were pallor and swelling (n=6), pain (n=6), numbness (n=4), bleeding at the injection site (n=1), skin lesions with "spotted" or "map-like" changes (n=6). No patient showed symptoms of ocular pain, headache, ptosis, and strabismus.

Procedure

Treatment Before Application of the CGF Gel

Some patients received treatments in other hospitals or clinics; these included subcutaneous hyaluronidase injection, infusion of antibiotics and vasodilators, and hyperbaric oxygen therapy. Symptoms such as pain and swelling were relieved, but the numbness and color of skin lesions were not significantly improved. After admission to our hospital, all patients underwent routine preoperative examinations. MRI or CT were used to exclude cases of orbital and intracranial lesions.

According to the condition of skin and soft tissue after admission and the treatment received before admission, patients were treated with percutaneous intra-arterial hyaluronidase and urokinase injection combined with subcutaneous multi-layered hyaluronidase injections; infusion of dexamethasone, alprostadil, dextran 40, and furosemide; as well as local dressing change before application of CGF. The "map-like" skin lesions were limited within several days, but the wound areas did not show marked improvement. The black eschar on the nose of some patients were dry and hard. We repeatedly wiped the scab with hydrogen peroxide, removed the scab, and then filled it with CGF gel after the scab softened.

All patients signed the informed consent for surgery and were informed of the potential risk of a refractory wound, long-term and multiple surgical treatments, nasal alar contracture, deformity, and scar hyperplasia.

Preparation of CGF Gel

A total of 9 mL of blood was extracted from the median cubital vein of the patient and centrifuged. The vacuum negative-pressure tube (without anticoagulant coated on the tube wall, red cap) and centrifugal accelerator were supplied by the manufacturer (Medifuge, Silfraden, Italy) (Fig. 1a). The CGF preparation mode and its operating parameters are as follows: 30 s of acceleration, 2 min at 408 × g, 4 min at 323 × g, 4 min at 408 × g, 3 min at 503 × g, and 36 s deceleration and stop [10].

After the centrifugation procedure, the blood in the centrifuge tube was separated into three layers, namely the platelet-poor plasma layer, CGF layer, and red blood cell

Table 1 Characteristics of nasal wounds after hyaluronic acid injection and CGF therapy of 6 patients

	Wound			Therapy before CGF treatment			CGF treatment	
	Site	Area (cm^2)	Secretion culture	Treatment (including those performed in our hospital or other hospitals)	Days (from hyaluronic acid injection to first CGF treatment)	Results	n	Days (from first CGF Treatment to wound healing)
1	Nasal tip and left nose alar	2.9 × 2.6	Aseptic growth	In other clinics: hyaluronidase (700 units) injection, hyperbaric oxygen therapy In our hospital: hyaluronidase (3000 units) and urokinase (100,000 units) injection, infusion of vasodilators and furosemide, dressing change	8	Symptoms relieved Wound ineffective	2	7
2	Nasal tip and bilateral nose alar	4.5×3.5	*Staphylococcus aureus* and *Staphylococcus epidermidis*	In other clinics: hyaluronidase (500 units) injection and infusion of antibiotics (clarithromycin, unknown dosage) In our hospital: hyaluronidase (3000 units) and urokinase (100,000 units) injection, infusion of vasodilators and furosemide, dressing change	10	Symptoms relieved Wound enlarged	3	12
3	Forehead and nose root	4.5×4.5	Aseptic growth	In other clinics: hyaluronidase (unknown dosage) injection, acupuncture for bleeding In our hospital: hyaluronidase (2250 units) injection, infusion of vasodilators, vacuum sealing drainage	4	Symptoms relieved Wound improvement	2	7
4	Nasal tip and bilateral nose alar	4.0×3.5	*Staphylococcus epidermidis*	In other clinics: hyaluronidase (1000 units) injection, infusion furosemide In our hospital: hyaluronidase (1500 units) and urokinase (100,000 units) injection, infusion of vasodilators and furosemide, dressing change	6	Symptoms relieved Wound ineffective	3	11
5	Right nose alar	2.8 × 2.2	Aseptic growth	In other clinics: hyaluronidase (2000 units) injection, infusion furosemide and antibiotics (cefuroxime sodium, unknown dosage) In our hospital: infusion of vasodilators and furosemide, dressing change	6	Symptoms relieved Wound ineffective	2	6
6	Nasal tip and bilateral nose alar	4.0 × 3.2	*Staphylococcus aureus*	In other clinics: hyaluronidase (600 units) injection, acupuncture for bleeding. In our hospital: hyaluronidase (2500 units) and urokinase (100,000 units) injection, infusion of vasodilators and furosemide, dressing change	9	Ineffective	4	15

layer, respectively, from top to bottom (Fig. 1b). The contents of the tube were quickly poured into a sterile tray (Fig. 1c). The bottom layer was cut off using sterile scissors (starting from 1.5 mm below the connection between

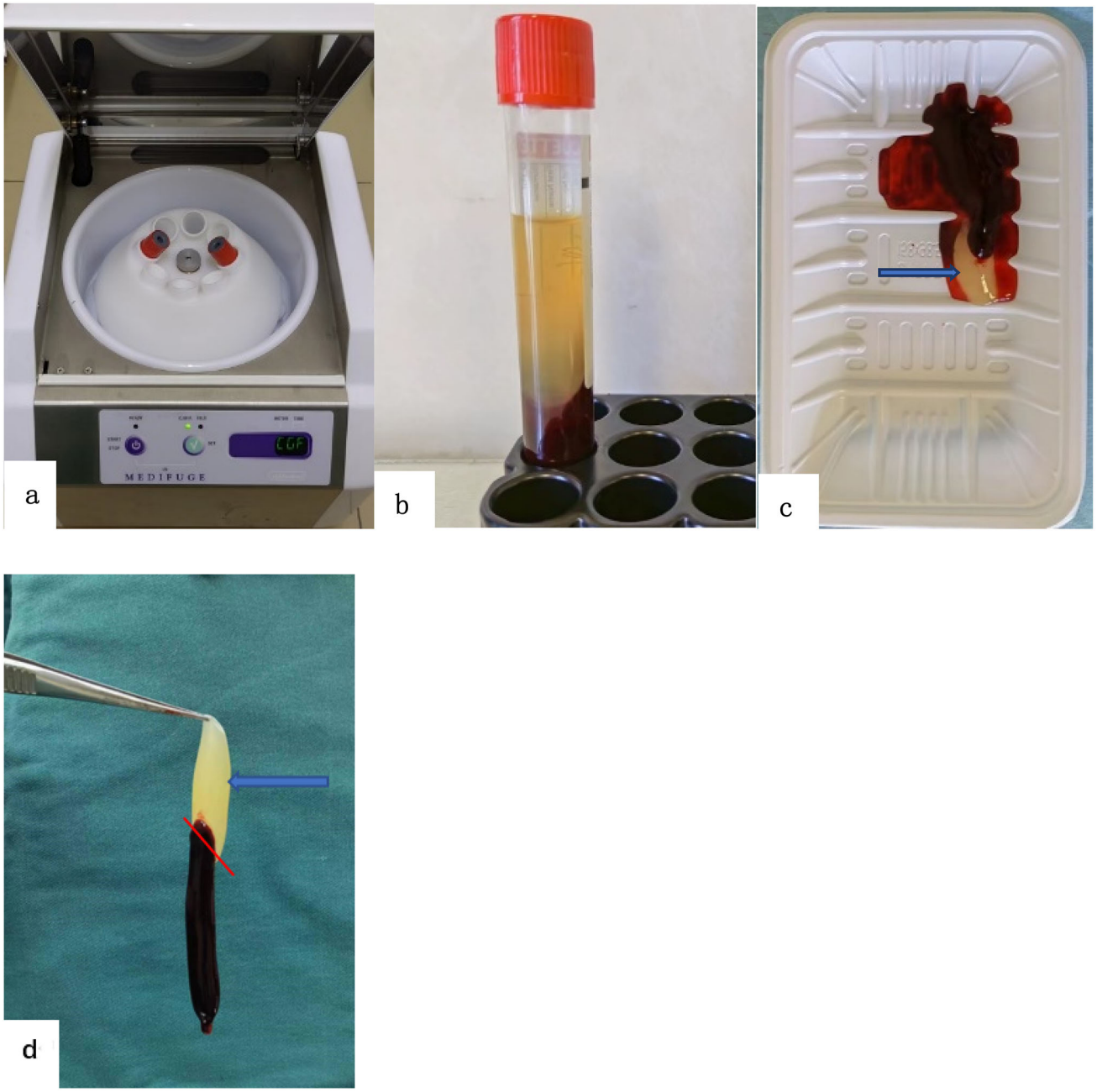

Fig. 1 Preparation of the CGF gel. **a**: Medifuge centrifuge for extraction of CGF from patient blood sample. **b**: Red-cap tube prepared to obtain gel phase CGF after centrifugation. **c**, **d**: The arrow indicates the gel phase CGF. The red line shows where the cut is made (Color figure online)

the middle layer and the bottom layer) to obtain the CGF clot (Fig. 1d) [11]. Then, the CGF portion was cut into small blocks.

Wound Management and Application of CGF Gel

The patient was placed in the supine position, and the face was routinely disinfected and draped. A total of 2 mL of 1% lidocaine hydrochloride injection was used for infraorbital nerve block anesthesia in the infraorbital foramen, and 4 mL of lidocaine hydrochloride injection was used for local infiltration anesthesia. The necrotic tissues, black scabs, and secretions on the nose surface were removed. The secretion of the wound was collected and cultured. Saline and NeutroPhase Wound Cleanser (NovaBay Pharmaceuticals, USA) was used to wash the wound repeatedly. The edge of the wound was properly trimmed until it bled slightly, and the CGF gel blocks were evenly applied to cover the surface of the wound. Vaseline gauze and aseptic gauze were fixed on the nasal surface to

stabilize the CGF gel. An appropriate nasal supporter was placed in the nasal cavity to avoid nose alar contracture and deformity.

Postoperative Treatment

The patients were required to keep the dressing in place after the operation. CGF treatment was repeated every 3–4 days according to the condition of each patient's wound. Before each treatment, the patients were photographed to assess the condition of the wound. The times of CGF treatment, the wound healing period, and the patient's self-evaluation and satisfaction with the treatment were recorded.

Results

The average time of the first CGF treatment from admission was 2–4 days. The wound began to heal after the first CGF treatment and the granulation tissue of the residual wound was fresh and ruddy. Symptoms such as numbness and tenderness were significantly improved. After CGF treatment, the bacterial culture of wound secretion indicated aseptic growth. After about 2–3 times of CGF treatment, the wound was almost healed. One patient asked to leave the hospital in advance for personal reasons, but the wound had healed significantly. The patients had no obvious contractures in the nasal alar margins and no significant changes in the contour of the nose, and the function of nasal ventilation was good. The micro-plasma radiofrequency technology combined with glucocorticoid or nanofat injection was used to further treat slight scarring and pigmentation in two patients after wound healing. After follow-ups ranging from 2 months to 1 year, the appearance and function of the nose had recovered satisfactorily, and there was no recurrence.

Representative Cases

Case 1

A 28-year-old woman underwent bilateral nasolabial fold hyaluronic acid injection (total 1.0 mL) at a local cosmetic institution. Immediately after the injection, the left nasal basal skin became painful. The skin around the injection site showed a "map-like" change with injection site skin blanching. On the 2nd and 3rd days after injection, 300 and 400 units of hyaluronidase were injected at the local site, respectively. Hyperbaric oxygen therapy was performed on the 4th day. Although the pain reduced, the skin and soft tissue necrosis did not show significant improvement.

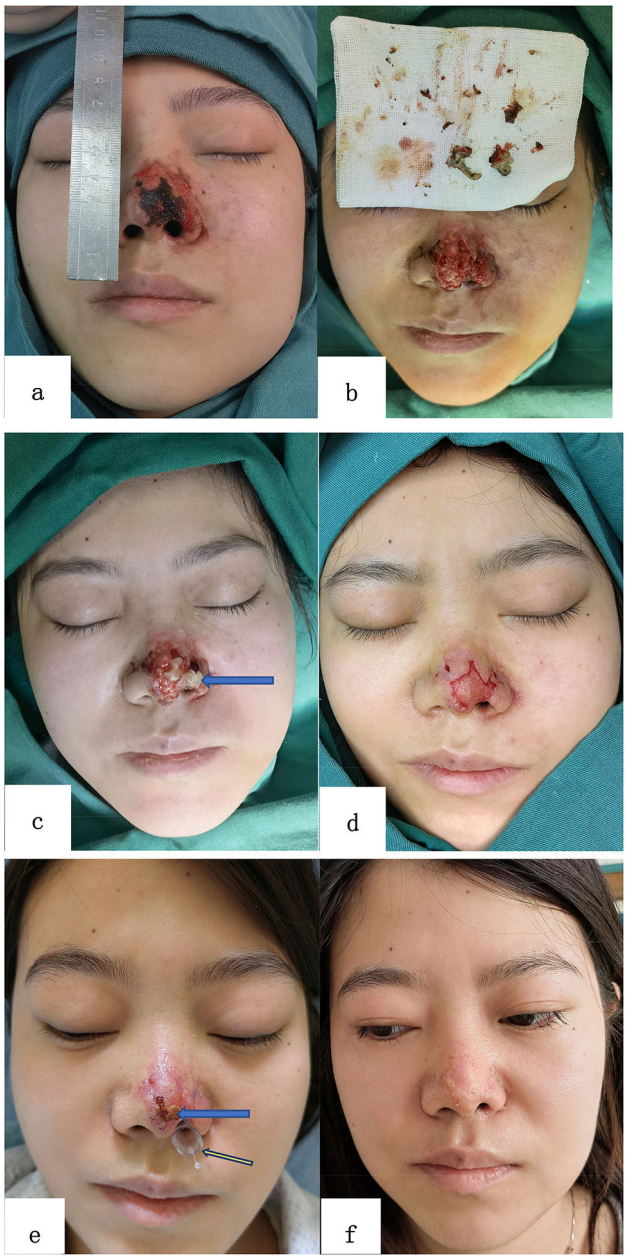

Fig. 2 Representative patient (case 1) undergoing application of CGF therapy. **a**: Preoperative. **b**: Nasal debridement of necrotic skin and soft tissue. **c**: The CGF gel is applied to cover the wound. The blue arrow indicates the CGF gel. **d**: After the first CGF treatment. **e**: After the second CGF treatment. The blue arrow indicates the residue from absorption of the CGF gel. The yellow arrow indicates the nasal supporter. **f**: 4 months after the second CGF treatment (Color figure online)

After admission, a 2.9 cm × 2.6 cm black and dry scab on the nose was observed, with skin ulceration on the nose tip and left nose alar margin (Fig. 2a). After finishing the relevant examinations, percutaneous intra-arterial hyaluronidase (2250 units) with urokinase (100,000 units) was injected into the left facial artery and the left dorsal nasal

artery. A topical subcutaneous hyaluronidase injection (750 units) was also administered. The black eschar on the nose was dry and hard. We wiped the scab with hydrogen peroxide repeatedly until the scab softened.

CGF treatment was initiated on the 4th day after admission. A total of 9 mL of autologous venous blood was collected, and a Medifuge centrifuge tube (red cap) was used to prepare the CGF gel. The wounds on the face and nose were disinfected. The black scabs on the surface of the wounds were removed, and the wound edge was scratched until it slightly bled (Fig. 2b). The wound was washed with NeutroPhase Wound Cleanser and normal saline. Nasal cartilage was not observed. After disinfection and cleaning, the CGF gel was evenly applied to cover the fresh wound surface (Fig. 2c). Vaseline gauze and aseptic gauze were fixed on the nasal surface to stabilize the CGF gel. A nasal supporter was placed in the left nasal cavity to avoid nose alar contracture and deformity (Fig. 2e).

The above treatment was repeated 3 days after the first CGF treatment for a total of 2 times. After the first treatment, the wound area decreased significantly (Fig. 2d). The residual wound was fresh and there was no obvious secretion. After the second treatment, the nasal wound almost healed (Fig. 2e). The tenderness and numbness were relieved compared to before. A 4-month follow-up after discharge showed that the nasal wound healed well and there was no recurrence (Fig. 2d).

Case 2

A 65-year-old woman underwent a nasal hyaluronic acid injection (0.6 mL) at a local cosmetic institution. Bleeding occurred at the injection site at the tip of the nose about 2 h after injection. The nose tip showed persistent swelling and was painful.

After admission, a region of skin and soft tissue necrosis measuring 4.5 cm × 3.5 cm with yellow purulent secretions was observed on the nose (Fig. 3). The routine examination and treatment were the same as in Case 1. Nasal wound culture was positive for *Staphylococcus aureus* and *S. epidermidis*. CGF treatment and debridement were initiated on the 3rd day after admission and were repeated every 3–4 days. After 2 treatments, the secretion culture of the wound showed aseptic growth, and the wound was basically healed. A total of 3 CGF treatments were performed. The patient wished to be discharged from the hospital in advance owing to personal reasons. By this time, however, the patient's nasal wound had healed significantly, and the surgical area was clean at the time of discharge.

Discussion

This study mainly explored the efficacy of CGF in the treatment of six cases of nasal skin and soft tissue necrosis caused by vascular compromise after nasal hyaluronic acid injection.

Rhinoplasty is one of the most common procedures in the field of plastic surgery, and nasal hyaluronic acid injection is the most popular operation in rhinoplasty [12, 13]. However, a surging number of reports on postoperative complications of cosmetic injection have drawn the attention of clinicians in recent years [3]. Among them, skin and soft tissue necrosis and blindness caused by vascular embolism are the most serious complications. Blackening of tissues and increased map-like changes of ischemic areas occur due to hemorrhagic skin necrosis, which is a manifestation of thrombotic occlusion. The extent of skin and soft tissue necrosis mainly depends on the degree of vascular occlusion, time of vascular recanalization, establishment of collateral circulation, integrity of blood vessels, general basic conditions, and the presence of infection [5, 14].

Current studies on vascular compromise after cosmetic injection mainly focus on the mechanism of vascular embolization and vascular recanalization treatment. Few studies on the treatment of secondary wound after complications of cosmetic injection have been reported. It usually indicates the wound has been in the inflammatory stage for some time if the depth of the necrosis into the underlying structures [5]. Then, treatment to promote wound healing may be required after recanalization.

Hyaluronidase is very effective in dissolving hyaluronic acid and has been proven effective in preventing tissue necrosis [15]. However, soft tissue may continue to break down in the late stage of tissue damage even when hyaluronidase is applied, as the damage has already been caused [5]. Previous studies have also shown that hyaluronidase injection does not completely eliminate large necrosis, although it limits the necrotic area [16]. In addition, once vascular supply is re-established, oxygen supplementation promotes enzymatic reactions that produce mediators such as reactive oxygen species (ROS) including superoxide and hydrogen peroxide. These harmful free radicals can damage endothelial cells, causing vasoconstriction and intravascular thrombosis, further aggravating tissue damage [7]. In a model of aging skin of nude mice, Sun et al. provided evidence that CGF can enhance the content of superoxide dismutase (SOD) and reduce glutathione (GSH), an enzyme that can protect biological membranes from ROS damage and maintain normal cell function, in serum and skin of mice; significantly reduce the level of malondialdehyde (the final product of free

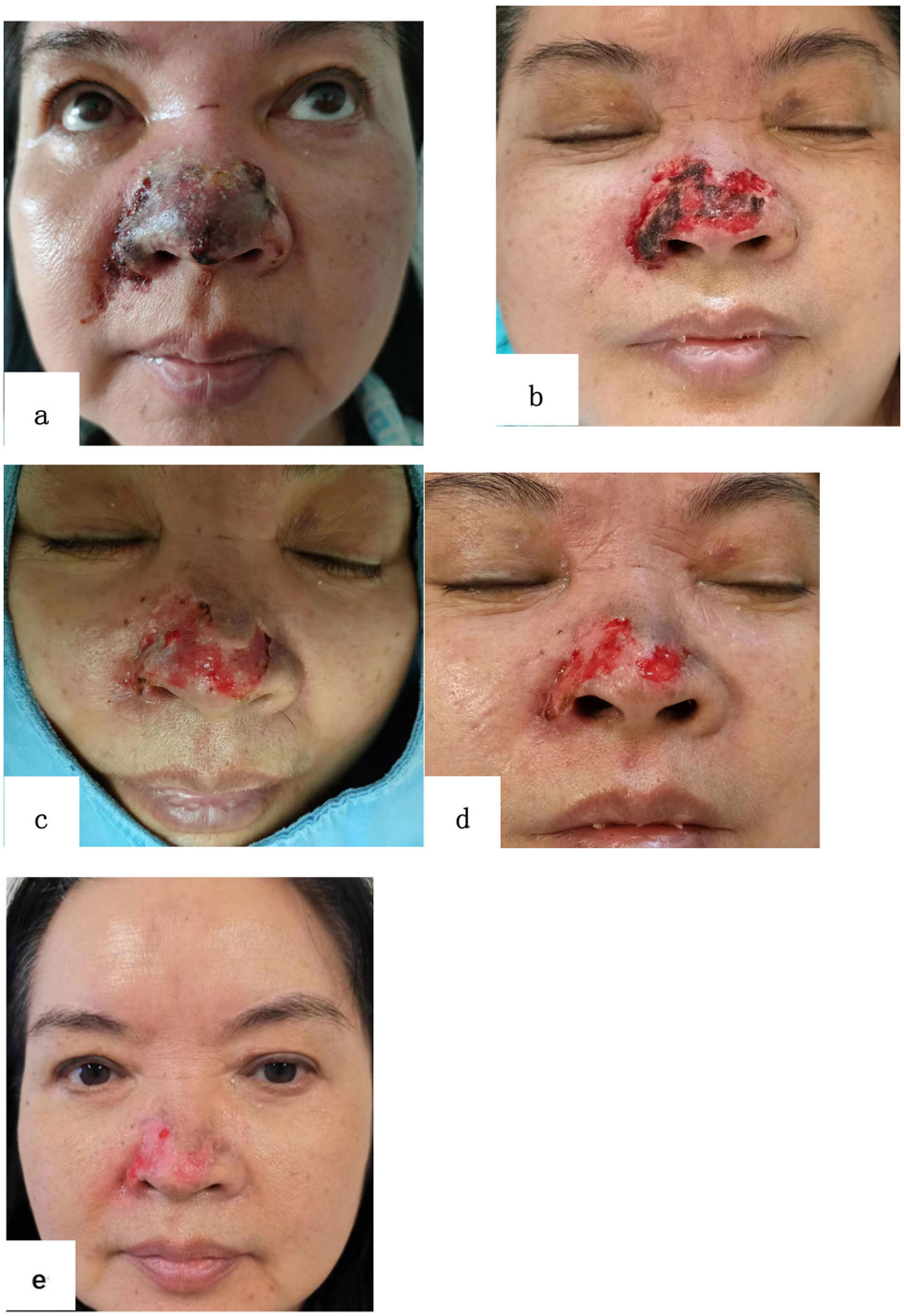

Fig. 3 Representative patient (case 2) undergoing application of CGF therapy. **a**: Preoperative. **b**: Nasal debridement of necrotic skin and soft tissue. **c**: After the first CGF treatment. **d**: After the second CGF treatment. **e**: After the third CGF treatment

radicals); and improve the content of collagen and elastin in skin [17]. Zhang et al. also indicated that CGF can protect human dermal fibroblasts (HDFs) against ultraviolet radiation; CGF mediated this effect by inhibiting the production of ROS and reducing oxidative damage in cells and an inhibiting the P38 mitogen-activated protein kinase/activated protein-1 (P38MAPK/AP-1) signaling pathway, thus preventing the degradation of dermal fibers [10].

The nose possesses a three-dimensional structure that shapes the aesthetic center of the face, and any imbalances in the nose structure are immediately evident. Debriding necrotic tissue in the nose, preventing infection in the wound area, and accelerating the healing process, while at the same time reducing excessive hyperplasia of scar and contracture deformity in the nasal alar margins are the major challenges for clinicians. Based on this, we applied

the CGF gel to repair the nose wound caused by hyaluronic acid injection, with good results.

Wound healing is actually a dynamic and coordinated repair process involving the interplay of multiple factors. Platelet concentrate products can provide a variety of bioactive cells, fibrin, cytokines, and growth factors, including PDGF (platelet-derived growth factor), TGF-β1 (transforming growth factor-β1), EGF (epidermal growth factor), bFGF (basic fibroblast growth factor), and VEGF (vascular endothelial growth factor) that are responsible for promoting angiogenesis and repairing tissue cells [18] . In addition, CGF also contains fibronectin, which can be used for the construction of three-dimensional structures on which it functions, accommodating platelets and leukocytes, and providing scaffolds for biological activities such as cell proliferation and migration [18, 19]. After platelet activation, chemokines and histamine are released, which can directly induce platelet aggregation and play an anti-infection role through an indirect chemotactic effect on leukocytes [20]. Another distinctive feature of CGF is that it contains a large number of CD34+ cells. CD34, regarded as a stem cell marker and endothelial marker, can enhance the proliferation and migration ability of vascular endothelial cells, which play an essential role in endothelial repair and vascular reconstruction [21].

The concentration of basic fibroblast growth factor (bFGF) in CGF was significantly higher than that in activated PRP and PRF [18]. bFGF plays an important role in the clinical management of hypertrophic scar and scarless wound healing by effectively inhibiting the terminal differentiation of myofibroblasts. The reduction of myofibroblasts may also inhibit the transformation of endothelial/epithelial cells into mesenchymal cells, while reactivation of dermal fibroblasts into α-SMA-positive myofibroblasts is the most important pathophysiological cause for the formation of hypertrophic scars [22]. Application of bFGF may promote fibroblast proliferation and DNA synthesis through phosphorylation of ERK/Akt, meanwhile resulting in the synthesis of cellular matrix metalloproteinase-1 and degradation of collagen, avoiding excessive deposition of extracellular matrix and preventing scar hyperplasia [23].

During the process of wound repair after cosmetic injection, patients often complain of symptoms such as numbness, suggesting the development of ischemic neurological injury after local vascular embolization. The blood blockage of the peripheral nerve constitutes an important pathophysiological mechanism in nerve injury, and the severity and duration of ischemia are the key factors leading to the ultimate injury. Qin et al. explored how CGF could promote nerve repair. They found that the CGF membrane could enhance the repair of injured sciatic nerve in rats, and *in vitro* experiments further verified that CGF could promote the migration of Schwann cells (SCs) and secretion of neurotrophic factors such as nerve growth factor (NGF) and glial cell line derived neurotrophic factor (GDNF), partly through the integrin β1-mediated activation of the FAK pathway [24, 25].

CGF has been widely used in orthopedics, stomatology, and many other fields. Extensive research has also been carried out on plastic surgery, particularly on facial rejuvenation, but few studies on postoperative complications after cosmetic surgery have yet been reported. The preparation of CGF completely mimics the natural coagulation process without adding any artificial catalysts, and most importantly, CGF is derived from autologous blood. CGF treatment is very safe, reduces secondary tissue damage, and has an outstanding cost-benefit ratio. To prepare the CGF gel, the patient's autologous venous blood is extracted, placed into a special centrifuge tube, and centrifuged in accordance with the setting mode to eventually obtain the CGF layer. The preparation of CGF does not require a very complicated or expensive equipment. By using the principle of differential centrifugation, researchers can easily extract CGF from patients' blood.

Our study has some limitations. For example, the number of cases in this study was limited, and long-term follow-up data were also insufficient. In addition, as the assessment of wound healing and scar formation is mainly based on subjective judgment of clinicians, there may be some bias in interpreting the results. In future studies, more patients need to be enrolled to conduct high-quality randomized controlled trials and collect tissue biopsies to further verify the efficacy of CGF for postoperative complications after cosmetic injection.

Conclusion

CGF can significantly promote wound healing, improve nasal appearance, prevent nasal deformity by promoting angiogenesis, prevent infection, nourish nerves, and inhibit scar hyperplasia after complications from nasal hyaluronic acid injection. The clinical preparation of CGF gel is simple, and the clinical practice is convenient. The patients were satisfied with the treatment efficacy. In the future, more large-scale and high-quality randomized controlled trials are needed to further prove the effectiveness and safety of CGF in the treatment of various wounds, gather consensus, and optimize clinical management.

Funding None.

Declarations

Conflict of interest All authors disclosed no relevant relationships

Ethical Approval This study was approved by the ethics committee of the Fourth Medical Center of PLA General Hospital. All procedures performed in our study were in accordance with the ethical standards of the institutional and/or national research committee.

Patient Consent Patients provided written consent for the use of their images.

References

1. Sciabica S, Tafuro G, Semenzato A, Traini D, Silva DM, Reis L et al (2021) Design, synthesis, characterization, and in vitro evaluation of a new Cross-Linked hyaluronic acid for pharmaceutical and cosmetic applications. Pharmaceutics. https://doi.org/10.3390/pharmaceutics13101672
2. van Loghem J, Funt D, Pavicic T, Goldie K, Yutskovskaya Y, Fabi S et al (2020) Managing intravascular complications following treatment with calcium hydroxylapatite: an expert consensus. J Cosmet Dermatol 19:2845–2858. https://doi.org/10.1111/jocd.13353
3. Urdiales-Galvez F, Delgado NE, Figueiredo V, Lajo-Plaza JV, Mira M, Ortiz-Marti F et al (2017) Preventing the complications associated with the use of dermal fillers in facial aesthetic procedures: an expert group consensus report. Aesthetic Plast Surg 41:667–677. https://doi.org/10.1007/s00266-017-0798-y
4. Xu X, Zhou G, Fu Q, Zhang L, Yu Y, Dong Y et al (2021) Efficacy of intra-arterial thrombolytic therapy for vision loss resulting from hyaluronic acid filler embolization. J Cosmet Dermatol 20:3205–3212. https://doi.org/10.1111/jocd.14111
5. Farmer A, Murray G, Croasdell B, Davies E, Convery C, Walker L (2021) Facial vascular events and tissue ischemia: a guide to understanding and optimizing wound care. J Clin Aesthet Dermatol 14:S39-48
6. Ors S (2020) The effect of hyaluronidase on depth of necrosis in hyaluronic acid Filling-Related skin complications. Aesthetic Plast Surg 44:1778–1785. https://doi.org/10.1007/s00266-020-01759-2
7. Al-Qattan M, Al-Kattan W (2004) Skin wound healing, ischemia-reperfusion injury and nerve regeneration: similarities in the sequential events and molecular basis. Can J Plast Surg 12:131–133. https://doi.org/10.1177/229255030401200307
8. Rodella LF, Favero G, Boninsegna R, Buffoli B, Labanca M, Scari G et al (2011) Growth factors, CD34 positive cells, and fibrin network analysis in concentrated growth factors fraction. Microsc Res Tech 74:772–777. https://doi.org/10.1002/jemt.20968
9. Xu F, Qiao L, Zhao Y, Chen W, Hong S, Pan J et al (2019) The potential application of concentrated growth factor in pulp regeneration: an in vitro and in vivo study. Stem Cell Res Ther 10:134. https://doi.org/10.1186/s13287-019-1247-4
10. Zhang M, Zhang T, Tang Y, Ren G, Zhang Y, Ren X (2020) Concentrated growth factor inhibits UVA-induced photoaging in human dermal fibroblasts via the MAPK/AP-1 pathway. Biosci Rep. https://doi.org/10.1042/BSR20193566
11. Zhao QM, Gao J, Huang XX, Chen XP, Wang X (2020) Concentrated growth factors extracted from blood plasma used to repair nasal septal mucosal defect after rhinoplasty. Aesthetic Plast Surg 44:511–516. https://doi.org/10.1007/s00266-019-01474-7
12. Carella S, Ruggeri G, La Russa R, Volonnino G, Frati P, Onesti MG (2022) Clinical management of complications following filler injection. Aesthetic Plast Surg 46:886–894. https://doi.org/10.1007/s00266-021-02650-4
13. Moon HJ (2018) Injection rhinoplasty using filler. Facial Plast Surg Clin North Am 26:323–330. https://doi.org/10.1016/j.fsc.2018.03.006
14. Murray G, Convery C, Walker L, Davies E (2021) Guideline for the management of hyaluronic acid filler-induced vascular occlusion. J Clin Aesthet Dermatol 14:E61–E69
15. DeLorenzi C (2017) New high dose pulsed hyaluronidase protocol for hyaluronic acid filler vascular adverse events. Aesthet Surg J 37:814–825. https://doi.org/10.1093/asj/sjw251
16. Wibowo A, Kapoor KM, Philipp-Dormston WG (2019) Reversal of post-filler vision loss and skin ischaemia with High-Dose pulsed hyaluronidase injections. Aesthetic Plast Surg 43:1337–1344. https://doi.org/10.1007/s00266-019-01421-6
17. Sun W, Li T, Yao H, Kang L, Dong F (2021) Effects of concentrated growth factor and nanofat on aging skin of nude mice induced by D-galactose. Physiol Res 70:425–35. https://doi.org/10.33549/physiolres.934640
18. Kim TH, Kim SH, Sandor GK, Kim YD (2014) Comparison of platelet-rich plasma (PRP), platelet-rich fibrin (PRF), and concentrated growth factor (CGF) in rabbit-skull defect healing. Arch Oral Biol 59:550–558. https://doi.org/10.1016/j.archoralbio.2014.02.004
19. Sadeghi-Ataabadi M, Mostafavi-Pour Z, Vojdani Z, Sani M, Latifi M, Talaei-Khozani T (2017) Fabrication and characterization of platelet-rich plasma scaffolds for tissue engineering applications. Mater Sci Eng C Mater Biol Appl 71:372–380. https://doi.org/10.1016/j.msec.2016.10.001
20. Edelblute CM, Donate AL, Hargrave BY, Heller LC (2015) Human platelet gel supernatant inactivates opportunistic wound pathogens on skin. Platelets 26:13–16. https://doi.org/10.3109/09537104.2013.863859
21. Tabatabaei F, Aghamohammadi Z, Tayebi L (2020) In vitro and in vivo effects of concentrated growth factor on cells and tissues. J Biomed Mater Res a 108:1338–1350. https://doi.org/10.1002/jbm.a.36906
22. Tiede S, Ernst N, Bayat A, Paus R, Tronnier V, Zechel C (2009) Basic fibroblast growth factor: a potential new therapeutic tool for the treatment of hypertrophic and keloid scars. Ann Anat 191:33–44. https://doi.org/10.1016/j.aanat.2008.10.001
23. Akita S, Akino K, Hirano A (2013) Basic fibroblast growth factor in scarless wound healing. Adv Wound Care (New Rochelle) 2:44–49. https://doi.org/10.1089/wound.2011.0324
24. Qin J, Wang L, Zheng L, Zhou X, Zhang Y, Yang T et al (2016) Concentrated growth factor promotes Schwann cell migration partly through the integrin beta1-mediated activation of the focal adhesion kinase pathway. Int J Mol Med 37:1363–1370. https://doi.org/10.3892/ijmm.2016.2520
25. Qin J, Wang L, Sun Y, Sun X, Wen C, Shahmoradi M et al (2016) Concentrated growth factor increases Schwann cell proliferation and neurotrophic factor secretion and promotes functional nerve recovery in vivo. Int J Mol Med 37:493–500. https://doi.org/10.3892/ijmm.2015.2438