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CASE REPORT
Cosmetic

Treatment of Facial Artery Embolization Caused by Polycaprolactone-based Dermal Filler with a Regimen Including 5-Fluorouracil

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Summary: Polycaprolactone-based fillers are commonly used in plastic surgery to improve facial aging. However, adverse vascular events following these injections have been reported. An arterial embolism is a rare but serious complication associated with injectable filler procedures. We report a case of arterial embolism in a 35-year-old woman who received a polycaprolactone-based dermal filler at the nasal base and was treated with a regimen containing 5-fluorouracil. We discuss the potential causes of the patient's condition and assess the superiority of our method over conventional approaches. Before treatment, ultrasound detected a decreased flow velocity in the patient's right medial canthus artery with distal hypoperfusion, which improved significantly posttreatment. Long-term follow-up revealed near-disappearance of facial scarring. Our treatment effectively addressed facial artery embolism without any reported adverse reactions. *(Plast Reconstr Surg Glob Open 2024; 12:e6140; doi: 10.1097/GOX.0000000000006140; Published online 6 September 2024.)*

Polycaprolactone (PCL)-based fillers received CE markings in 2009. In 2021, they passed the registration and approval of the National Medical Products Administration and were officially launched in China. This biodegradable collagen-stimulating filler consists of a suspension of 25–50 µm diameter PCL microspheres (30%) in a carboxymethylcellulose (CMC) gel carrier (70%). PCL-based fillers have gained popularity owing to their long-term volumizing effect.[1] They can be used to shape multiple areas, including the alar base, superciliary arch, and posterior temporal region, stimulating collagen regeneration, filling facial deficits, and improving wrinkles.

PCL is widely used in sutures, drug-release systems, implants in various tissues, and tissue engineering. CMC is a nontoxic derivative classified as a "generally recognized as safe" substance by the Food and Drug Administration. Both CMC and PCL have been successfully used in Food and Drug Administration–approved, safe-to-use, resorbable devices.[2]

Each syringe (1 mL) containing filler is premixed with 0.2 mL of 2% lidocaine before use. Supraperiosteal placement is carried out by vertical puncture using 27-G, 1-inch needles, with the amount injected determined by the surface area to be treated (0.2 mL/cm²). For superficial and deep fat placements, a retrograde fanning technique is performed using 25-G, 40-mm cannulas, with each linear thread of 0.1 mL per cm² injected, depending on the surface area.[3]

The safety of PCL-based fillers is supported by their widespread use in routine clinical practice.[2] However, potential side effects include edema, bruising, malar edema, temporary palpable lumps, and discoloration.[3] In recent years, increasing numbers of adverse reactions to PCL-based dermal fillers have been reported. Herein, we report a case of facial artery embolization caused by a PCL-based dermal filler, and describe a new treatment method involving 5-fluorouracil (5-FU) injection.

ILLUSTRATIVE CASE

A 35-year-old woman was injected with PCL-based filler at the nasal base. The patient experienced pain, swelling, and numbness in the right upper lip, with nerve discomfort appearing 20 minutes after the injection. On the following day, the patient visited the clinic. A photograph of the patient's face (Fig. 1A) and B-scan ultrasound

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were arranged before treatment. The results showed significantly reduced blood flow in the right medial canthus artery accompanied by poor distal blood flow. Therefore, we used a novel treatment consisting of five injections of 5-FU. Dexamethasone and low concentrations of 5-FU were injected on all five occasions, with additional heparin-sodium saline injections used for the first three treatments. The patient was administered oral methylprednisolone, mecobalamin, vitamin B1, dexamethasone, and Aescuven Forte. After each treatment, diluted 5-FU compresses were applied for 10 minutes. Following a short course of treatment, circulation improved significantly and discomfort disappeared. The facial artery was marked to understand the course (Fig. 1B). After 3 months of follow-up, the patient's skin condition returned to normal, indicating that our treatment program had a good long-term effect without obvious sequelae (Fig. 1C).

DISCUSSION

Although previous studies have reported that the probability of vascular injury caused by soft tissue fillers is less than 0.05%, such injuries can have serious consequences. Current research suggests that vascular occlusions caused by filler injections may be extravascular or endovascular. Extravascular causes include increased pressure outside the vessel due to excessive injection volume or reactions from edema and inflammatory filler components.[4] Intravascular factors include direct obstruction of arteries by large-molecular-weight fillers and chemical damage to the endothelium from impurities in the filler, which can activate endothelial cells and trigger platelets, coagulation factor XII, and the endogenous coagulation cascade. Release of tissue factors can activate coagulation factor VIII, initiating an exogenous coagulation cascade. As filler causes lumen occlusion, hemodynamic changes occur, leading to embolus formation.[5] According to another study, nonhyaluronic acid fillers require greater pressure for material spreading compared with other fillers ($P < 0.01$). Experienced clinicians typically use pressures significantly lower than those needed for filler propagation and average arterial pressures.[6] Fillers may break down into smaller particles because of blood flow shear stress, blocking tiny blood vessel branches. These mechanisms likely explain the occurrence of arterial branch blockage after injection.[7]

Vascular embolization caused by injections are treated using hot compression, massage, nitroglycerin patches, local aspiration, hyperbaric oxygen, and minimally invasive surgery. Our regimen included oral methylcobalamin and vitamin B1 owing to their neurotrophic effects, considering that arterial embolism can cause local nerve damage. Oral Aescuven Forte was prescribed to reduce swelling on the affected side of the face and to alleviate itching and pain. Sodium heparin halted progression of thrombosis resulting from partial vascular embolism caused by fillers and prevented further enlargement of the embolus. Dexamethasone and methylprednisolone were used due to their antiinflammatory, antiallergic, and metabolic properties. The use of 5-FU in our regimen was a relatively innovative addition. As a patient's thin skin is prone to infection, 5-FU helps prevent it by inhibiting thymidine synthase required for DNA and RNA synthesis in bacteria.[8] Second, 5-FU helps combat scar formation, possibly due to fibroblast activity suppression and antifibrotic action through antimetabolite activity.[9] This effect helps maintain the aesthetic appearance of the patient's face. Third, 5-FU has antiinflammatory and antiallergic properties that overlap with the effects of steroid hormones. Its use reduces the amount of steroids required, as well as the risk of tissue atrophy and telangiectasia associated with this treatment.

Compared with the usual treatment protocols, hyperbaric oxygen therapy is required in the face of an embolism, which increases the patient's cost. Compared with antiinfective drugs involved in the conventional regimen, such as macrolides and tetracyclines, 5-FU prevents infections while counteracting scarring and reducing steroid use. In our case, oral medications were used according to the instructions, and the interval between our local

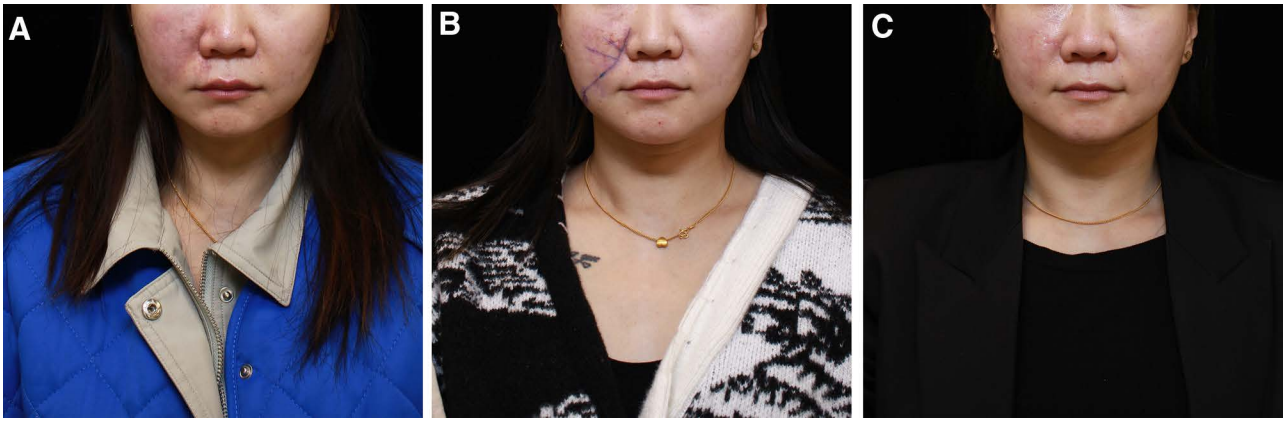

Fig. 1. Photographs of the patient before and after treament. A, A photograph of the patient at presentation. B, A photograph of short-term treatment effect; the approximate course of the facial artery has been labeled. C, A 3-month postoperative photograph of the patient showing her face almost back to normal.

injections of 5-FU and dexamethasone was approximately 1 month, based on departmental experience and recommendations for treating dermal filler-induced inflammatory nodules/granuloma.[2]

However, some limitations of our treatment program should also be noted. We recognize that 5-FU can cause serious side effects, including redness, pain, pigmentation, ulceration, burning sensation, and skin peeling. It is often combined with triamcinolone acetonide to reduce side effects. However, dexamethasone and methylprednisolone were considered more favorable for the patient under embolic conditions; therefore, we did not use triamcinolone acetonide. This may have increased the probability of adverse reactions to 5-FU. Additionally, because 5-FU inhibits myeloid cell proliferation, careful monitoring of complete blood counts is necessary for future therapeutic practice.[10] Although 5-FU causes immunosuppression, it can inhibit bacterial DNA and RNA synthesis by inhibiting thymidine synthase, which is required for DNA synthesis,[8] especially in methicillin-resistant *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Escherichia coli*, and *Vibrio harveyi*, thereby strongly inhibiting autoinducer-2 production and preventing pathogen infection.[11] The increased risk of infection due to immunosuppression conflicts with the direct bactericidal action against infection. Therefore, low concentrations of 5-FU and diluted 5-FU wet compresses were adopted to achieve antiinfection effects while ensuring patient immunity. Nevertheless, this method has certain risks that require further investigation.

CONCLUSIONS

Injecting PCL-based fillers can lead to serious consequences such as arterial embolisms. The risks associated with using these fillers cannot be ignored. We offer a therapeutic regimen, including 5-FU, a novel approach for treating vascular embolism, which requires further study.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

PATIENT CONSENT

The patient provided written consent for the use of her image.

ETHICAL APPROVAL

The study was approved by the ethics committee of Peking Union Medical College.

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