

Periorbital Lipogranuloma after Facial Autologous Fat Injection and Its Treatment Outcomes

Jun Young Park, Namju Kim

Department of Ophthalmology, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Korea

Purpose: To investigate periorbital lipogranuloma cases that developed after autologous fat injection and to determine various treatment outcomes from these cases.

Methods: This retrospective study involved 27 patients who presented with periocular mass (final diagnosis of lipogranuloma) and had history of facial autologous fat injection. The collected data included information on patient sex, age, clinical presentation, number and site of fat injections, interval between injections, duration from injection to symptom onset, fat harvesting site, use of cryopreservation, and treatment outcome.

Results: The most common presenting symptom was palpable mass (92.6%), followed by blepharoptosis and eyelid edema. The mean time from injection to symptom onset was 13.6 ± 29.2 months (range, 2 to 153 months). Patients were managed by intralesional triamcinolone injection (six patients) and surgical excision (three patients); 18 patients were followed without treatment. Among the six patients who underwent intralesional triamcinolone injection, five showed complete resolution, and one showed partial resolution. Among the 18 patients who were followed without management, three showed spontaneous resolution over a 5-month follow-up period.

Conclusions: Lipogranuloma can develop in the eyelid after autologous fat injection into the face. Both surgical excision and intralesional triamcinolone injection yield relatively good outcomes. Simple observation can be a good option because spontaneous resolution can occur in a subset of patients.

Key Words: Autologous fat injection, Periorbital lipogranuloma

Facial autologous fat injection is a commonly used cosmetic procedure for facial augmentation and recontouring [1]. Autologous fat as a soft tissue filler has many advantages including that it is abundant, inexpensive, easy to

harvest, and autogenic and thereby does not result in the severe side effects or potential risks that come with allogenic fillers [2]. Autologous fat injection has therefore been thought to be a safe technique, with relatively minor complications such as chronic edema and calcification [3]. However, several recent studies have reported cases of periorbital lipogranuloma after facial autologous fat injection [4,5]. Clinicians have also encountered patients with periorbital lipogranuloma after facial autologous fat injection at outpatient clinics. However, to the best of our knowledge, there have been only case or series reports

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Corresponding Author: Namju Kim, MD. Department of Ophthalmology, Seoul National University Bundang Hospital, Seoul National University College of Medicine, #82 Gumi-ro, 173 beon-gil, Bundang-gu, Seongnam 13620, Korea. Tel: 82-31-787-7379, Fax: 82-31-787-4057, E-mail: resourceful@hanmail.net

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with a small sample size, and the largest report includes only nine cases. Here, we present findings on 27 patients who developed periorbital lipogranuloma after autologous fat injection for facial augmentation.

Materials and Methods

Twenty-seven patients presenting with periocular masses (final diagnosis of lipogranuloma) between December 2010 and May 2015 and who underwent facial autologous fat injection were recruited, and their medical records were reviewed for this study. Collected data included information on patient sex, age, clinical presentation, margin reflex distance, exophthalmometric value, number and site of autologous fat injections, interval between injections, duration from injection to symptom onset, fat harvesting site, use of cryopreservation, radiological findings, pathological reports, and treatment outcome. Margin reflex distance was defined as the distance between the center of the pupillary light reflex and the upper eyelid margin with the eye in primary position. Exophthalmometric values were investigated using Hertel exophthalmometry (Carl Zeiss, Jena, Germany). Results were analyzed using the *t*-test (SPSS ver. 15.0; SPSS Inc., Chicago, IL, USA); a *p*-value less than 0.05 was considered significant for all statistical tests. The research conducted in this study met the tenets of the Declaration of Helsinki and was approved by the institutional review board of Seoul National University Bundang Hospital before data collection.

Results

Twenty-seven patients with periorbital lipogranuloma were recruited and enrolled in this study (Table 1). All but one patient (case 2) were female, with a mean age of 40.2 years (range, 23 to 63 years). Presenting symptoms were palpable mass in 25 patients (92.6%), eyelid edema in nine patients (33.3%), and eyelid erythema in three patients (11.1%). Facial autologous fat injection was performed by a plastic surgeon in 23 cases (85.2%) and by a dermatologist in two cases (7.4%). The site of injection was the forehead in 19 patients (69.2%), the whole face including the forehead in six patients (23.1%), and the upper eyelid in two patients (7.7%). The number of injections was two in 23

patients, three in one patient, and one in three patients. All patients who received two or more injections were treated with cryopreserved fat at the second or third injection. The mean interval between first and second autologous fat injections was 2.65 ± 1.07 months (range, 1 to 5 months), and the mean time from the final injection to symptom onset was 13.6 ± 29.2 months (range, 2 to 153 months). The site of fat harvesting was the thigh in 18 cases (66.7%), abdomen in six cases (22.2%), and buttocks in one case (3.7%). Blepharoptosis, defined as a difference in margin reflex distance >1 mm, was observed in 11 cases (40.7%). Exophthalmos, defined as an exophthalmometric value >1 mm, was found in four cases (15.4%). Sixteen patients underwent radiologic imaging (orbital computed tomography [CT] in eight, orbital magnetic resonance imaging [MRI] in eight, both in two). Orbital CT images showed a focal ill-defined soft tissue enhancing lesion. Orbital MRI images showed ill-defined heterogeneous enhanced soft tissue swelling with fat-containing lesion with or without rim enhancement.

Surgical excision was performed in three patients to remove the mass and to identify pathological abnormalities. Histopathological examination revealed variable-sized fat tissue with foreign body reaction and fat necrosis, features characteristic of lipogranuloma. One month after surgery, the masses and eyelid swelling had disappeared. Intraleisional triamcinolone injection (Triam, 40 mg/mL, 0.1 mL) was performed in six other patients; five of whom showed complete resolution, and one showed partial resolution. Among the five patients with complete resolution, one experienced recurrence 2 months after resolution. There were no significant side effects except mild bruising. Eighteen patients refused any management; among them, three patients (cases 15, 22, and 24) showed spontaneous resolution over 5 months of follow-up. Cases with spontaneous resolution presented with only one mass and no other symptoms. They also had trends toward relatively shorter intervals between injections (1.33 ± 1.52 vs. 2.65 ± 1.07 months, $p = 0.335$) and shorter times from injection to symptoms (6.65 ± 4.73 vs. 13.6 ± 29.2 months, $p = 0.144$), though these differences were not statistically significant.

Case reports

1) Case 1

A 29-year-old woman presented with a 3-month history

Table 1. Demographics and clinical characteristics

Age (yr) / sex	Clinical presentation					Autologous fat injection history					Surgery / intraslesional triamcinolone injection	History of DL operation		
	Clinical symptom	Site of lesion	No. of lesions	Aspects of lesion	Difference in MRD between the eyes (mm)	Difference in exophthalmometry between the eyes (mm)	No. of injections	Interval between injections (mon)	Time to symptoms* (mon)	Sites of autologous fat harvest			Sites of injections	Cryopreservation
1 47/F	Mass	LUL	1	Lateral round mass	1	0	2	1	3	Abdomen	Forehead	Yes	Excisional biopsy	No
2 36/M	Mass	RUL	1	Central ovoid mass	0.5	0	1	0	33	Abdomen	Upper eyelid	No	Excisional biopsy	Yes
3 28/F	Mass	RUL	1	Lateral round mass	0	0	2	2	9	Thigh	Upper eyelid	Yes	Excisional biopsy	Yes
4 30/F	Mass, edema	RUL	1	Soft amorphous mass	2	0	2	4	9	Thigh	Forehead	Yes	Triam inj	No
5 41/F	Mass, erythema	RUL	1	Central ovoid mass	1	0	2	2	18	Thigh	Whole face	Yes	Triam inj	No
6 29/F	Mass, edema	RUL, superomedial orbit	1	Soft amorphous mass	2	0	2	2	16	Buttocks	Forehead	Yes	Triam inj	Yes
7 48/F	Mass	LUL	1	Central ovoid mass	2	1	2	3	5	Thigh	Forehead, cheek	Yes	Triam inj	Yes
8 49/F	Mass, erythema	BUL	2	Central ovoid mass	0.5	0	2	3	7	Thigh	Forehead, cheek	Yes	Triam inj	Yes
9 59/F	Mass, edema	RUL, RLL	2	Central ovoid mass	0	1	2	3	11	Thigh	Forehead, cheek	Yes	Triam inj	No
10 48/F	Mass, edema	RLL	1	Ovoid semi-movable mass	0	0	2	NA	12	NA	Whole face	NA	No	No
11 23/F	Mass	RLL	1	Central round mass	0	0	2	3	20	Abdomen	Forehead	Yes	No	No
12 28/F	Mass, edema, pain	LUL, superomedial orbit	1	Central hard mass	0.5	0	2	2	9	Abdomen	Forehead	Yes	No	Yes
13 41/F	Mass, edema, pain	RUL, RLL	2	Medial and lateral round mass	2	1	2	3	11	Thigh	Whole face	Yes	No	No
14 53/F	Mass	LUL	1	Lateral ovoid mass	1.5	0.5	2	2	5	Abdomen	Forehead, cheek	Yes	No	No

(Continuing)

Table 1. Continued

Age (yr) / sex	Clinical presentation				Autologous fat injection history						Surgery / intrasional triamcinolone injection	History of DL operation	
	Site of lesion	No. of lesions	Aspects of lesion	Difference in MRD between the eyes (mm)	Difference in exophthalmometry between the eyes (mm)	No. of injections	Interval between injections (mon)	Time to symptoms* (mon)	Sites of autologous fat harvest	Sites of injections			Cryopreservation
15 52/F Mass, erythema	LUL	2	Medial and lateral central mass	0	0	2	3	5	Thigh	Whole face	Yes	No	No
16 46/F Mass	LUL, superomedial orbit	1	Medial hard non-movable mass	0	0	2	3	153	NA	Forehead	NA	No	No
17 63/F Mass	RUL	1	Lateral ovoid mass	1	0	2	3	7	Abdomen	Forehead	Yes	No	No
18 31/F Mass	LUL	1	Lateral round soft mass	0.5	0	3	5, 3	10	Thigh	Forehead, cheek	Yes	No	Yes
19 38/F Edema	RUL	1	Lateral round mass	2	0	2	2	10	Thigh	Forehead	Yes	No	No
20 39/F Mass	RUL	1	Central round mass	1	0	2	3	10	Thigh	Whole face	Yes	No	No
21 34/F Mass	BUL	2	Medial and lateral round mass	0	0	2	1	6	Thigh	Forehead	Yes	No	No
22 27/F Mass	RUL	2	Medial and lateral ovoid mass	0	0.5	2	1	3	Thigh	Whole face	Yes	No	No
23 47/F Mass	RUL, superomedial orbit	1	Superomedial orbital mass	0.5	1	1	0	11	Thigh	Forehead	Yes	No	No
24 31/F Mass	RUL	1	Central fixed mass	1.5	0	1	0	12	Thigh	Forehead, cheek	No	No	Yes
25 48/F Mass	RUL	1	Lateral round mass	0	0	2	2	10	Thigh	Upper eyelid	Yes	No	No
26 37/F Edema	RUL	1	Lateral ovoid mass	0	0.5	2	5	3	Thigh	Forehead, cheek	Yes	No	No
27 32/F Mass	BUL	2	Central ovoid mass	0	1	2	3	14	Thigh	Forehead	Yes	No	No

MRD = margin reflex distance; DL = double lid; LUL = left upper lid; RUL = right upper lid; Triam inj = triamcinolone injection; BUL = both upper lids; RLL = right lower lid; NA = not available.

*Time to symptom onset from first injection.

of palpable mass in her right upper eyelid (Fig. 1A). She had received autologous fat injection twice on her forehead at a local plastic surgery clinic 1 year prior. The fat was harvested from her thighs, injected, and the remained was cryopreserved until used for the second injection. The interval between the first and second injections was 2 months. The mass was a 5-mm-sized round fixed mass just below the superior orbital rim margin. Orbit MRI scan showed a fat-containing lesion with peripheral enhancement and adjacent skin enhancement in the right upper eyelid area (Fig. 1B). The mass was excised through eyelid crease incision: after the skin and orbicularis muscle were incised and dissected along the preseptal plane, the 8-mm-sized round mass was exposed superficial to orbital fat. Histological examination revealed foreign body reaction–induced lipogranuloma with fat necrosis (Fig. 1C and 1D). The mass and swelling completely disappeared 1 week after the surgery.

2) Case 2

A 31-year-old woman was referred to Seoul National University Bundang Hospital with a 3-week history of swelling and palpable mass in her right upper eyelid (Fig. 2A). Seven months prior to her referral, she had autologous fat harvested from her thigh and injected into her forehead

by a plastic surgeon, followed by a second injection 2 months later with cryopreserved fat. On physical examination, her right eye was 2 mm ptotic and also 2 mm proptotic. There was an approximately 5-mm-sized palpable mass in the superomedial periorbital area. Orbital MRI showed multiple bubble-shaped enhancing lesions compatible with lipogranulomas in both upper eyelids (Fig. 2B). The patient received intralesional triamcinolone (4 mg/0.1 mL) injections on her right eye, at the deep medial orbit and central eyelid. At a 1-week follow-up after receiving these injections, the swelling had decreased, and the ptosis had improved to an margin reflex distance difference of 1 mm. Three months after injection, the mass had completely disappeared, and the ptosis was completely resolved.

Discussion

This study analyzed 27 cases of periorbital lipogranuloma following autologous fat injection into the face. Presenting symptoms were palpable mass, eyelid edema, eyelid erythema, blepharoptosis, and exophthalmos. The mean

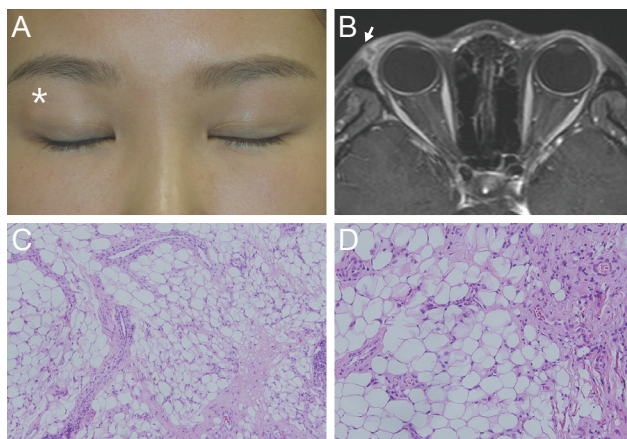


Fig. 1. (A) A 29-year-old woman presenting with a 3-month history of palpable mass in the right upper eyelid (asterisk) that developed 10 months after an injection of cryopreserved autologous fat into her face. (B) A T1-weighted axial magnetic resonance image shows a fat-containing lesion with peripheral enhancement (arrow) and adjacent skin enhancement in the right upper eyelid. (C,D) Typical findings of granulomatous foreign body reaction with diffusely infiltrated chronic granulomatous inflammatory cells with fat necrosis and fibrosis (hematoxylin and eosin stain, $\times 100$, $\times 400$).

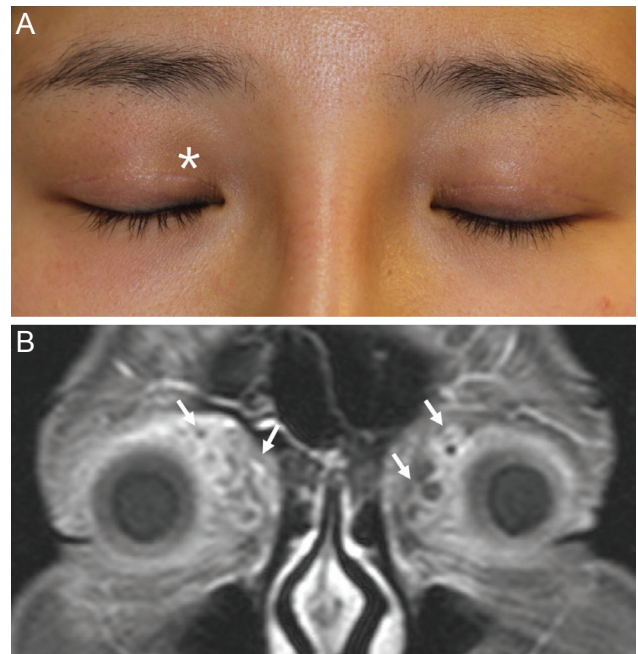


Fig. 2. (A) A 31-year-old woman presenting with a 3-week history of palpable mass in the right upper eyelid (asterisk) that developed 7 months after an injection of cryopreserved autologous fat into her forehead. (B) A T2-weighted coronal image reveals multiple lesions (arrows) of heterogeneous high signal intensity in both upper eyelids.

time from injection to symptom onset was 13.6 ± 29.2 months (range, 2 to 153 months). The diagnosis of periorbital lipogranuloma is based on characteristic clinical manifestations with history of autologous fat injection into the face and radiologic tests including CT and MRI if necessary. Due to its retrospective nature at a tertiary referral center, the study included only patients who had clinically demonstrable lesions; however, there are likely a larger number of patients with subclinical lipogranuloma among those who undergo facial autologous fat injection.

Two different mechanisms have been proposed for the etiology of lipogranuloma. One is an exogenous mechanism through foreign body reactions to lipid or oil-like substances, which result from the inability of the body to metabolize exogenous lipids in the tissue interstitium. The other mechanism is endogenous degeneration of lipids secondary to allergic reactions and/or trauma [6]. In our study, 24 of 27 patients (88.9%) underwent two or more autologous fat injections, and all but two with unverifiable data had used cryopreserved fat in the second injection. The mean duration of fat cryopreservation was 2.65 ± 1.07 months (range, 1 to 5 months). A previous study on fat cryopreservation showed that the viability of adipocytes declines rapidly after frozen storage at both -15°C and -70°C for 1 day and decreases gradually over 8 weeks, at which time only approximately 5% of the fat cells are viable [7]. Thus, it is possible that most cryopreserved fat used in secondary or tertiary injections contains non-viable adipocytes and oil-like substances, which could cause lipogranuloma through foreign body reactions. However, in our study, three patients underwent autologous fat injection only once and so were unrelated to cryopreservation. Therefore, the mechanism of lipogranuloma of these cases might not involve foreign body reactions but rather endogenous degeneration of lipids secondary to allergic reactions and/or trauma.

The characteristic predisposition of the upper eyelid to lipogranuloma can be explained by the galea in the superficial musculo-aponeurotic system. Injected fat tissue can migrate through the galea aponeurosis and the retroorbicularis fascia due to gravity, facial muscle movement, and postoperative massage of the injection sites [8]. In this study, orbital CT and MRI scans demonstrated that the most common location of periorbital lipogranuloma was the preseptal area (13 cases), followed by the preaponeurotic orbital area (five cases). All patients with preaponeurotic

lipogranuloma had a history of upper eyelid blepharoplasty; considering inevitable septal defect following blepharoplasty, the location of the lipogranuloma might be relevant to whether or not the orbital septum was intact.

Three patients who underwent mass excision reported resolved mass and swelling. Among the six patients who received intralesional triamcinolone injection, five showed complete resolution, and one showed partial resolution. There have been no reports on the effect of triamcinolone injection on lipogranuloma. We managed the lipogranulomas of six patients with intralesional triamcinolone injection, and the results were excellent. These findings suggest that intralesional triamcinolone injection is a good treatment option for patients who do not want to undergo an invasive surgical procedure.

Three patients in this study showed spontaneous resolution, all of whom had only one mass lesion with no other symptoms. These patients had shorter injection intervals (mean, 1.33 months) and shorter symptom onset (mean, 6.65 months) compared to other patients, though these differences were not statistically significant due to the small number of cases. However, these findings suggest that patients with lipogranuloma presenting with one mass lesion and no other symptoms can be managed by regular follow-up without invasive management, anticipating spontaneous resolution.

The limitations of our study are its retrospective nature and the possible selection bias toward patients more sensitive to symptoms or with good compliance. Pathological diagnosis was performed in only three cases, and systemic corticosteroid therapy was not used as a treatment option for any patients. Therefore, well-controlled prospective studies are warranted to investigate the actual incidence of lipogranuloma, natural history, and treatment outcomes according to type of management.

We present 27 patients who developed periorbital lipogranuloma after autologous fat injection. In conclusion, lipogranuloma can develop in the eyelid following autologous fat injection, and clinicians should be conscious of this possible complication.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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