

Ischemic Stroke Caused by a Hyaluronic Acid Gel Embolism Treated with Tissue Plasminogen Activator

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INTRODUCTION

Previously, Kim et al.¹ reported a case in which the patient experienced a complicated cerebral infarction after receiving a hyaluronic acid gel filler injection. We report on the treatment process in this patient, and then discuss the options for managing an acute ischemic stroke (AIS) following a facial filler injection.

CASE

A 23-year-old man was referred to the emergency department for a sudden ocular pain and vision loss in the right eye that occurred 39 minutes after a perinasal filler injection using hyaluronic acid gel. He denied any medical illness.

His initial blood pressure was 140/90 mmHg, his pulse rate was 74 beats per minute, and his body temperature was 36.5°C. An ophthalmologic examination revealed a lack of a pupillary reflex, a dilated pupil, and complete ophthalmoplegia in the right eye. A fundoscopic examination showed the typical appearance of a central retinal artery occlusion with a cherry red spot on the macula, a markedly pale optic disc, and no pulsation of the retinal arterioles. The National Institutes of Health Stroke Scale score was 12, and it included drowsy mentality, left central type facial palsy, and a left hemiplegia.

All laboratory parameters were within the normal limits. The initial brain computed tomography (CT) findings were normal. Diffusion weighted images showed a high signal intensity in the right frontal, temporal, and parietal lobes. The right ophthalmic artery was not seen at the time-of-flight magnetic resonance angiography. There were no steno-occlusive lesions of the intracranial artery.

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Table 1. Characteristics and clinical data from reports of ischemic stroke which occurred following a filler injection

No	Year	Age	Sex	Diagnosis	Onset to visit time	Filler type	Filler injection site	Ocular pain, diagnosis	Neurologic symptoms	Treatment	Follow-up
1 ²	1998	47	F	Lt. watershed zone infarction	Immediate	Autologous fat	Periorbital	(+), OAO	Stupor, global aphasia, Rt. hemiplegia, deviation of head to the left	(-)	After a few weeks, walk, improved aphasia
2 ⁴	2001	43	M	Embolic MCA infarction	10 minutes	Autologous fat	Lt. nasolabial fold	(+), OAO	Aphasia, Rt. hemiparesis	(-)	After 5 days, recovered
3 ¹¹	2003	39	F	Lt. ICA infarction	1 minute	Autologous fat	Glabella	(-), OAO	Drowsy, global aphasia, Rt. hemiplegia	Steroid	After 4 days, death
4 ¹²	2004	39	M	Bilateral ACA infarction	Immediate	Autologous fat	Lt. glabella, eyelid, temporal	Unknown	Confusion, hypertonia, paraplegia	(-)	After 1 year, mRS 4
5 ¹³	2011	28	F	Lt. MCA infarction	Immediate	Autologous fat	Bitemporal	(-), none	Drowsy, aphasia, Rt. hemiparesis, NIHSS 16	Antiplatelet steroid, oxygen	After 3 weeks, NIHSS 6
6 ¹⁴	2013	52	F	Rt. frontal, parietal, occipital infarction	A few minutes	Hyaluronic acid	Glabella	(+), CRAO	Lt. hemianopsia	Aspirin	After 1 month, Lt. hemianopsia
7 ¹⁵	2013	25	F	Bilateral frontal infarction	A few minutes	Hyaluronic acid	Glabella	(-), CRAO	Lethargy, dizziness, Rt. vision loss, Rt. ophthalmoplegia	Aspirin, steroid	After 2 months, Rt. vision loss, Rt. ophthalmoplegia
8	2013	23	M	Rt. watershed zone infarction	39 minutes	Hyaluronic acid	Rt. nasolabial fold	(+), OAO	Lt. hemiplegia, Lt. spatial neglect	IV-rtPA	After 3 months, mRS 3

F, female; Lt, left; OAO, ophthalmic artery occlusion; Rt, right; M, male; MCA, middle cerebral artery; ICA, internal carotid artery; ACA, anterior cerebral artery; mRS, modified Rankin Scale; NIHSS, National Institutes of Health Stroke Scale; CRAO, central retinal artery occlusion; IV-rtPA, intravenous recombinant tissue plasminogen activator.

An intravenous recombinant tissue plasminogen activator (IV-rtPA) was administered 75 minutes following the stroke onset. Immediately after the IV-rtPA infusion, the neurologic symptoms remained unchanged with the exception of the patient's complaint of a headache. A follow-up brain CT scan did not show any hemorrhagic lesions; however, a follow-up CT scan taken on day 2 showed hemorrhagic transformations in the previous infarcted area, as well as a mild midline shift without any evidence of neurological deterioration. The follow-up CT scan was reperformed 27 hours after the IV-rtPA infusion and more enlarged hemorrhagic transformations and midline shifting were observed; in addition, a decompressive craniectomy was conducted.

Although the patient had undergone a decompressive craniectomy, he could walk and he had a modified Rankin Scale score of 3 after 3 months.

DISCUSSION

Ischemic complications from facial injections of either autologous fat or several other materials have been reported.^{2,3} The injected filler may pass through the ophthalmic and internal carotid arteries, and finally, lodge in the distal middle cerebral artery.^{3,4} Previous studies have demonstrated that blindness and a stroke can occur as a result of the injection of soft tissue fillers in any part of the face.³

Complicated AIS cases that have developed after a filler injection are summarized in Table 1. All the cases had occlusion of the retinal or ophthalmic artery and neurologic symptoms that occurred within 2 hours after the filler injection, but there have been no previous case reports regarding the use of an IV-rtPA.

An IV-rtPA is the only proven medical treatment to reduce the effects of AIS, if it is administered within a 4.5-hour time window.⁵ There are no known standard treatments for an AIS caused by filler injections. An IV-rtPA significantly improved the microvessel perfusion in the ischemic area in rats.⁶ An IV-rtPA can also be beneficial to ischemic stroke patients with small vessel disease,⁷ and it

can be used regardless of major vascular occlusion. On the other hand, thrombus formation can occur around areas with disturbed or slowed blood flow because of the presence of the filler in the artery. Animal studies have been conducted which suggest the benefits of thrombolytic agents in hyaluronic acid embolism.^{8,9} These studies have demonstrated that hyaluronic acid embolism induced the formation of a red thrombus, which is the target of an IV-rtPA. Based on this hypothesis, an IV-rtPA may be an alternative treatment option. Hyaluronidase infusion may be a treatment option for a hyaluronic acid gel embolism,⁸⁻¹⁰ however, there are currently no case reports or studies demonstrating the use of hyaluronidase for AIS following a hyaluronic acid gel injection.

In conclusion, an IV-rtPA may be used in highly selected AIS cases after a filler injection.

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