Irreversible Blindness Following Periocular Autologous Platelet-Rich Plasma Skin Rejuvenation Treatment

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Abstract: **A 49-year-old woman developed acute visual loss in the right eye following bilateral cosmetic platelet-rich plasma injections to rhytids in the glabellar region. External exam showed skin necrosis in the region over the right rhytids and restricted right ocular motility. Dilated fundus exam was significant for ophthalmic artery occlusion. Imaging revealed right eye extraocular muscle ischemia and optic nerve infarction, along with right frontal, parietal, and occipital lobe infarction. Work-up for thromboembolic and vascular etiologies were negative. To our knowledge, this is the first case reported of extensive ischemia following autologous platelet-rich plasma therapy.**

CASE REPORT

The case reported here is in compliance with the Health Insurance Portability and Accountability Act (HIPAA) regulation. An otherwise healthy 49-year-old woman presented to the Yale Eye Center complaining of acute loss of vision in the right eye associated with severe nausea and eye pain. One day prior, the patient underwent an autologous platelet-rich plasma (APRP) injection procedure by an unlicensed practitioner to reduce wrinkles in the glabellar region bilaterally. She reported that blood was taken from her antecubital region by venous puncture and centrifuged to obtain concentrated autologous plasma. Bilateral forehead rhytids injections were performed. The patient was unaware the details of the plasma preparation and the size of needle that was used for injections. She tolerated the first injection on the left side well. However, during the second injection at the nasal end of right eyebrow, she felt the needle penetrate slightly deeper, accompanied by sudden pain and fullness behind her right eye with immediate visual loss over the next few minutes. She then noted transient improvement of vision in nasal field followed by complete loss of vision.

On examination, vision was no light perception in the right eye and 20/20 in the left eye. A pronounced right afferent pupillary defect was present. Motility of the right eye was restricted in supraduction and adduction resulting in a right exotropia and hypotropia in primary gaze. External exam demonstrated a 1 cm area of ecchymosis and induration above the right medial brow. The eyelids were soft and there was no proptosis or resistance to retropulsion. Anterior segment exam was unremarkable in both eyes except moderate conjunctival hyperemia in the right eye. Intraocular pressure was within normal limits bilaterally. Fundus exam of the right eye revealed profound optic disc pallor, diffuse retinal whitening including fovea, marked attenuation of arterioles with abrupt ending of the vessels in midperiphery, and central macular edema. Absence of a cherry red spot suggested diffuse choroidal ischemia. No Hollenhorst plaque was seen. The left fundus exam was unremarkable.

Head and neck CT showed right subacute frontal lobe ischemia without identifiable compromised vessels. MRI/MRA of brain and orbit demonstrated restricted diffusion along the course of the right optic nerve and multiple subacute infarcts involving right frontal, parietal, and occipital lobes (Fig. 1). Asymmetric abnormal FLAIR/T2 signal of the right medial rectus muscle was suggestive of ischemia (Fig. 2). Bone marrow edema within the right frontal bone with irregular enhancement involving the overlying skin was also shown. MRA of the brain and neck was negative for cavernous sinus pathology, or vertebral or carotid artery dissection. CTA of the head and neck and transthoracic echocardiogram identified no embolic origin. Echocardiogram and carotid dopplers were negative.

Laboratory tests revealed mildly elevated erythrocyte sedimentation rate (26 mm/h, normal 0–20), and C-reactive protein (3.8 mg/L, normal 0.1–3.0) with a normal complete blood count test. Further work-up for thrombotic and arteritic processes were all negative, including PT/PTT, INR, Beta2-glycoprotein, homocysteine, protein-C and S, D-dimer, antithrombin III, cardiolipin, jak2, C3, C4, Anti-DNA ab, Lupus anticoagulant, rheumatoid factors, antineutrophil cytoplasmic antibody, and hemoglobin screen.

The patient was diagnosed with acute right ophthalmic artery occlusion and brain infarction as a complication of periorbital APRP injection. Having arrived outside the window of intra-arterial tPA, she was treated with ocular massage, topical timolol 0.5% and brimonidine 0.2%, and oral steroids. The patient declined anterior chamber paracentesis. She was given intravenous antibiotics for possible infectious cause of periorbital swelling and erythema. External and fundus photography 1 week after presentation demonstrated ecchymosis and ischemia of the right glabellar region (Fig. 3) and diffuse retinal whitening and ischemia (Fig. 4). Ocular motility returned to normal by week 2. One year after presentation, the patient's vision remained no light perception in the right eye with residual scarring and hard nodules of the right glabellar region. Patient subsequently underwent scar revision surgery of the right glabella a year later. The pathology of scar tissue showed lipid-based foreign body with giant cell reaction that was consistent with prior injection of foreign material within deep tissues (Fig. 5).

DISCUSSION

Autologous platelet-rich plasma is obtained by centrifuging autologous blood until the plasma platelet level exceeds that of normal blood. Autologous platelet-rich plasma is commonly used in the setting of ulcers, burns, wounds, hair loss, and facial rejuvenation by way of angiogenesis and collagen synthesis through upregulation of growth factors and cytokines contained in platelet alpha granules.[1–4] Recently, physicians and cosmetologists across the country have been exploring its use as cosmetic filler for skin augmentation.

There are varieties of APRP based on their preparation process and resultant components. For instance, Leukocyte-rich PRP contains more white blood cells than traditional PRP isolated by dual speed centrifugation. Platelet-rich fibrin matrix has a lower concentration of platelets than traditional PRP by including plasma and proteins in a larger volume. These variables can make difference in the ingredients of oxygen-free

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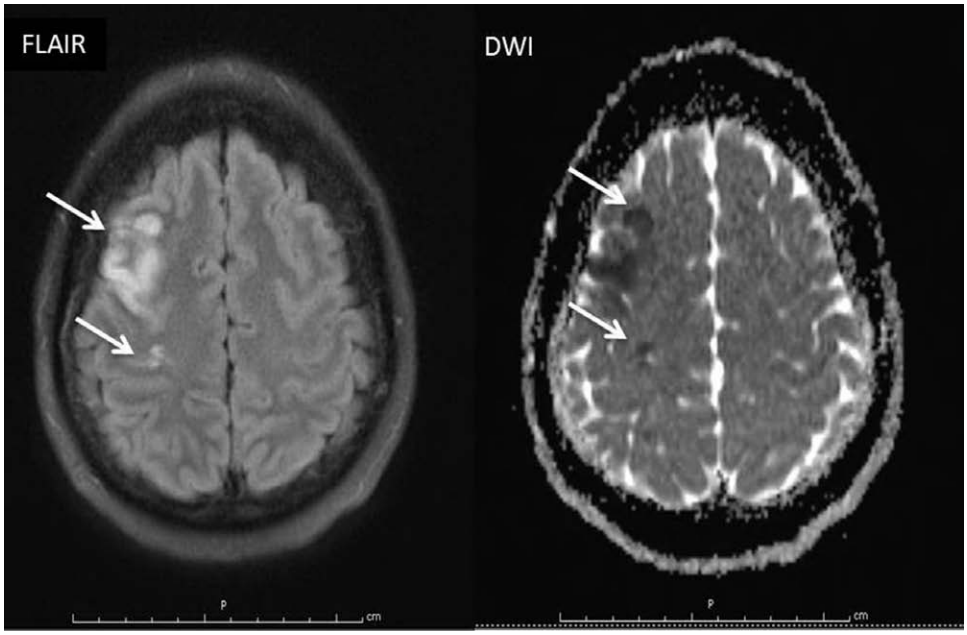

FIG. 1. MRI brain: FLAIR image and DWI demonstrate ischemia of right frontal and parietal lobes (*arrows*). DWI, diffusion weighted image.

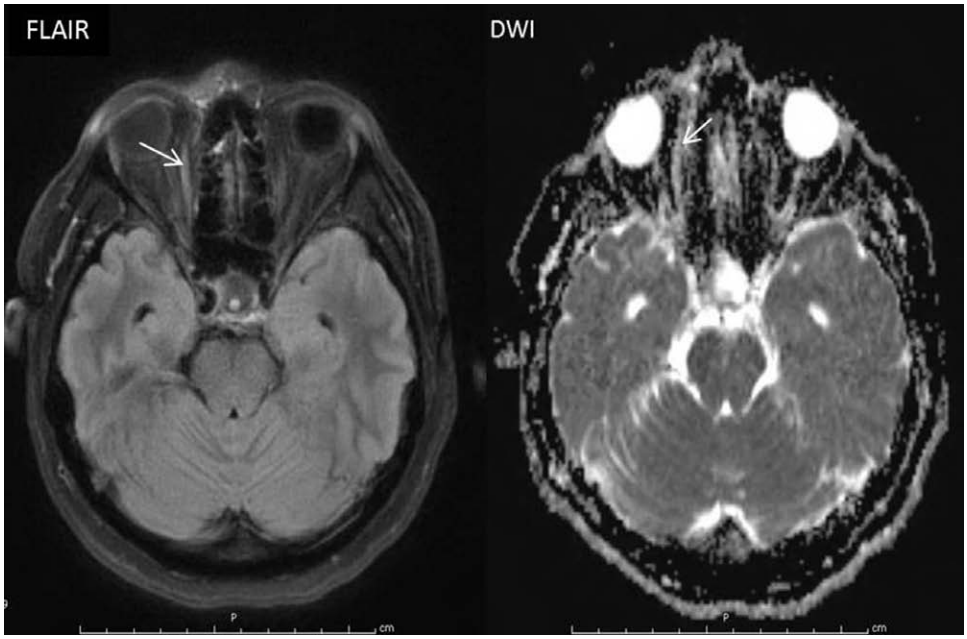

FIG. 2. MRI head and orbit: FLAIR and DWI images demonstrate right medial rectus ischemia. DWI, diffusion weighted image.

radicals and lysosomal enzymes, as well as growth factor concentrations, release, and binding abilities. Some practitioners deliberately modify these products before injection, including mixing the PRP with fillers.[4] The patient declined to disclose the contact information of the practitioner who performed the injection. Therefore, it was unclear if this APRP product was made properly or altered before the injection.

Autologous platelet-rich plasma therapy is relatively contraindicated in patients who is under chronic antiaggregant therapy.[5] Cautions should be taken if the patient has nonsteroidal anti-inflammatory drug usage 7 to 10 days before the procedure, an active infection, systemic use of corticosteroids within 2 weeks before injection, and conditions putting the patient in a hypercoagulative state, such as smoking and oral contraceptive use. Past medical history and medication reconciliation should be carefully obtained before APRP treatment. This patient was a nonsmoker and was not taking any medications before the injection.

Visual complications from various periocular synthetic cosmetic fillers have been previously reported.[6–9] Recently, US Food and Drug Administration issued a safety alert on the risks of visual loss and stroke secondary to the unintentional soft tissue filler injection into facial blood vessels.[10] Autologous platelet-rich plasma is not often used as a physical filler. The effects are usually the result of growth factors and other material contained or

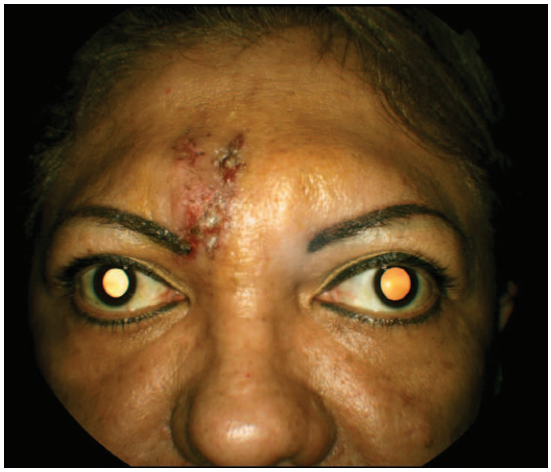

FIG. 3. Ecchymosis and ischemia of right glabellar region 1 week after injection of APRP to rhytids. APRP, autologous platelet-rich plasma.

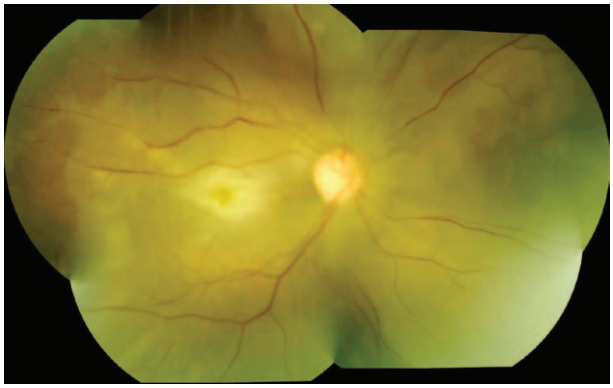

FIG. 4. Color fundus photo of right eye taken 1 week after vision loss following PRP, demonstrating diffuse retinal whitening and ischemia. PRP, platelet-rich plasma.

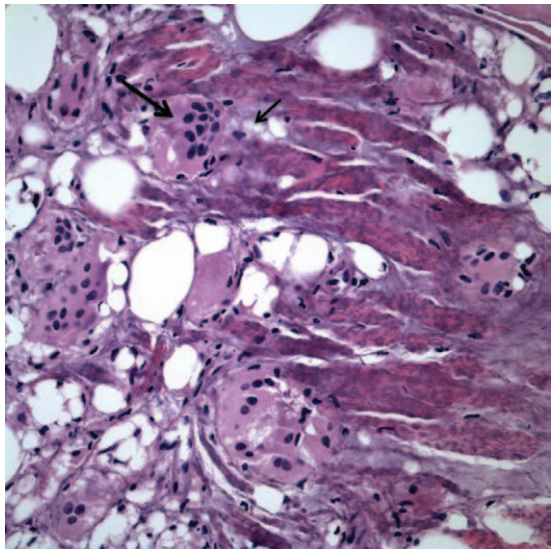

FIG. 5. H&E stain of the right glabella scar tissue (×400). The *bold arrow* shows the giant cell reaction for foreign bodies (*thin arrow*) within deep muscle layers.

secreted by platelets rather than the physical filling effects. To our knowledge, there have been no reports of vision loss associated with APRP when used as a filler. Carle et al.[6] described 3 patients who presented with sudden loss of vision after injection of 3 different dermal fillers (hyaluronic acid, autologous fat, and bovine collagen mixed with polymethylmethacrylate microspheres) into the forehead area. They hypothesized that retrograde flow of fillers through arteries resulted in ocular ischemia. Studies have demonstrated retrograde embolic travel through the retinal, ophthalmic, and often internal carotid arterial systems.[11,12] The authors believe that a similar mechanism was responsible for vision loss in the patient. In a series of 44 patients, concurrent ocular and brain infarctions occurred in 27% and final visual acuity was NLP in 61% of subjects. Visual prognosis was worst with autologous fat.[7] In a 2012 systematic review of 29 articles describing 32 patients with visual loss following cosmetic injections, the nasolabial (n = 7) and scalp (n = 3) areas were the most common injection sites, followed by the forehead, glabella, cheek, and temples. All patients but 3 (18%) remained NLP.[8]

These reports highlight the importance of intimate understanding of facial vascular anatomy during cosmetic injections. The patient's case of ophthalmic artery occlusion following APRP exemplifies the visual loss that can inadvertently occur with both traditional and novel cosmetic materials. Full awareness of injection plane to be intradermally rather than subdermally may help reduce or eliminate vascular compromise. Aspirating before injection, applying topical vasoconstrictors, and using smaller needles (30 to 32 G) with slow technique and judicious use of pressure are recommended precautionary measures.[8,11,13–15] Early recognition is important and immediate and aggressive treatment is mandate should vascular complications occur.[14,15]

The authors hypothesize that the technique used in administering the APRP may have contributed to the visual complications. The site of injection was close to superior orbital artery and superior trochlear artery, presumably causing inadvertent injection of APRP into the artery. Pressure from the syringe likely resulted in retrograde flow of the platelet clot, from the superior orbital or trochlear artery to proximal branches, resulting in occlusion of the ophthalmic artery and other regions of the right middle cerebral artery, which caused diffuse ischemia. Ischemic area of the glabella in this patient seemed rather superficial for an arterial embolization, indicating possible concurrent vein occlusion. The limited ocular motility can be explained by the acute ischemic injury to the extraocular muscles, which was confirmed by imaging. The authors infer that the syringe was not drawn back upon before injection to assess for intravascular needle placement and this may have led to inadvertent intra-arterial injection. The presumed etiology is further supported by negative systemic work-up and normal echocardiogram, MRA, and CTA imaging.

Skin nodularity at the site of injection is sometimes more problematic with improper use of physical fillers. It is not a usually seen effect after APRP injection. However, poor centrifugation technique of APRP or improper mixing of fillers can form delayed onset inflammatory or noninflammatory nodules of the tissues.[15] The pathological exam of the glabella scar in this patient confirmed the presence of foreign bodies within the deep tissues.

The findings in this case emphasize the importance of adequate training in new procedures. The authors recommend that caution be taken when injecting fillers in the glabellar region due to the rich vascular supply in this region and to prevent skin necrosis or devastating visual complications. Furthermore, the authors suggest that periocular injections be performed by licensed practitioners who are familiar with orbital anatomy and the rich anastomosis of facial arteries. Qualified practitioners are highly trained and are more capable to deal with complications

that may arise. While extraocular in nature, filler injections can cause devastating visual consequences and awareness and proper counseling of patients is important.

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