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Case Report

Watch out for scars- Vascular complication due to hyaluronic acid dermal filler

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Abstract The frequency of cosmetic application and the possibility of complications are increasing day by day all over the world. It can be said that the most important complication that can be seen after cross-linked hyaluronic acid filler applications is vascular complications, because there may be results such as tissue loss and vision loss. A forty six year old female patient was consulted from the plastic surgery clinic with complaints of purple discoloration and pain on her forehead. In the anamnesis, it was learned that the patient's wrinkle in the frontal region was filled with filler 4 days ago. A bluish-purple area in a reticular pattern that does not disappear with pressing was observed, starting from the glabellar area and progressing towards the frontal hairline. Vascular complication due filler material and ischemia was considered in the patient and treatment was started immediately. Totally 300 U of hyaluronidase was injected intra and subdermally. It was recommended to mix of topical betamethasone valerate and fusidic acid three times a day and apply topically to the complained area, and apply hot compress 4 times a day for 4 minutes. The patient was referred for hyperbaric oxygen therapy for an average of 2-2.5 hours per day for 2 consecutive days. On the 7th day after the first hyaluronidase administration, the patient's physical examination revealed no signs of significant ischemia and vascular occlusion. Our aim in sharing this case was to state that although the risk of vascular complications in filler applications is related to the amount of filling, there is a risk of vascular complications even in very-very small filling applications. In addition, if there is a previous surgical, traumatic or burn scar tissue in an area, we think it would be beneficial to think twice before applying.

Key words
Vascular complications; Hyaluronidase; Filler complications; Vascular occlusion.

Introduction

The frequency of cosmetic application and the possibility of complications are increasing day by day all over the world. It can be said that the most important complication that can be seen after cross-linked hyaluronic acid filler applications is vascular complications, because there may be results such as tissue necrosis, related tissue atrophy, tissue loss and vision loss. For example, blindness may develop due to retinal artery embolization in nasal radix and glabellar applications. Studies show that the retina can tolerate hypoxic damage for approximately 60-100 minutes before the damage becomes permanent.[1,2] But more recent studies show that vascular occlusion can cause retinal infarction even within 12-15 minutes.[3]

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Case report

A forty six year old female patient was consulted from the plastic surgery clinic with complaints of purple discoloration and pain on her forehead. In the history, it was learned that the patient's wrinkle in the frontal region was filled with filler 4 days ago and 4 days later, the

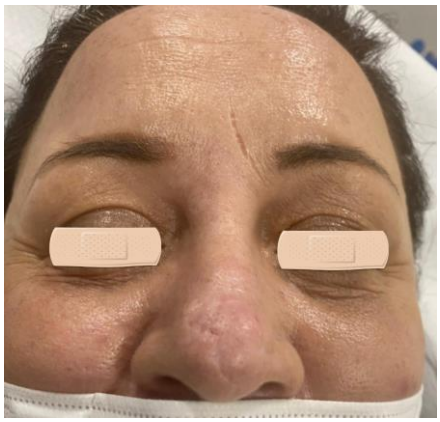

Figure 1 The condition of the patient before the application.

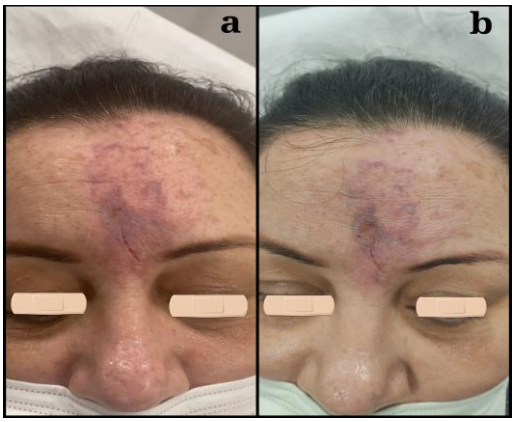

Figure 2 The condition of the patient just before and after the second hyaluronidase application.

patient reached her doctor by phone and stated that she had a purple discoloration on her forehead and a pain. In further questioning it was learned that, 1.5 years ago the mole from the nose was excised and the pathology result was reported as basal cell carcinoma, but the patient did not remember when and how the forehead wrinkle formed. Cross linked hyaluronic acid filler was applied intradermally into scar on nasal area and wrinkle on glabellar area with 27 G needle 4 days ago. A total of 0.09 ml. of filler was applied in the glabellar area.

On physical examination, there was an atrophic scar in the nasal tip and supratip region, and a wrinckle line approximately 2 cm in length in the left half of the glabellar area, that does not improve with stretching **(Figure 1)**.

A bluish-purple area in a reticular pattern that does not disappear with pressing was observed, starting from the glabellar area and progressing upwards with the left paramedian and middle frontal region and towards the frontal hairline. There were several millimetric vesicular lesions in the glabellar area. Some areas of the ecchymotic lesion was lighter-grayish in color. There was no obvious coldness. There was a slight temperature increase in the area. There was no significant increase in pain on deep palpation of the upper-inner part of the orbital rim and deep palpation of the primary application site. Capillary refill time could not be reliably evaluated because the skin had an ecchymotic appearance. Vascular complication due filler material and ischemia was considered in the patient and treatment was started immediately.

0.5 ml (75 Units) hyaluronidase was immediately applied to the patient's primary filler application area and the entire ecchymotic area intra and subdermally, and the patient was followed up with hot compress for 10 minutes. At the end of 10 minutes, effacement was observed in the reticular ecchymotic areas close to the patient's frontal hairline. Another 1 ml. (150 U) hyaluronidase was applied to the same areas in the same way and a hot compress was applied to the area again. After 10 minutes of observation, ecchymotic-looking reticular areas except the right half of the lesions on glabellar area, were improved and returned to normal skin color, and vesicular lesions completely regressed. Another 0.5 ml (75 U) hyaluronidase was applied to the patient supraperiosteally just above the orbital rim in the primary filler application area and hot compress was continued. After the third application, ecchymotic color change continued only in the area 2-3 cm superomedial to the medial end of the right eyebrow, and the middle was paler. On

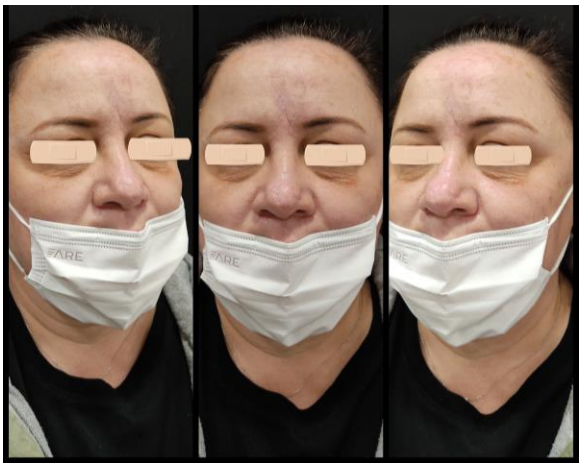

Figure 3 The condition of the patient in the 1st week of treatment.

examination with a magnifying glass, the pale and grayish colored area in the middle of the area was atrophic **(Figure 2)**.

The patient was prescribed nitroglycerin ointment and a mixture of topical betamethasone valerate and fusidic acid, and it was recommended to mix both creams three times a day and apply topically to the complained area, and to continue applying hot compress 4 times a day for 4 minutes. The patient was referred for hyperbaric oxygen therapy by contacting the center that applied hyperbaric oxygen therapy outside the hospital, and received hyperbaric oxygen therapy for an average of 2-2.5 hours per day for 2 consecutive days, the first of which was the day of hyaluronidase administration. The patient was called for daily follow up. The application of nitroglycerin ointment was stopped after she stated that the nitroglycerin ointment gave her a headache in the second day control. The remaining ecchymotic appearance gradually improved and on the 3rd day of the treatment, a slightly eroded area of approximately 7x8 mm was observed in the atrophic-looking pale area in the middle of the ecchymotic area.

Thereupon, triticum vulgare aqueous extract and centella asiatica extract were prescribed topically to the patient 3 times a day and added to the treatment. In the ongoing follow-ups, the ecchymotic area was completely healed, while the eroded area in the center was completely epithelialized on the 3rd day after its formation. On the 7th day after the first hyaluronidase administration, the patient's physical examination revealed no signs of significant ischemia and vascular occlusion **(Figure 3)**. All topical treatments were discontinued.

Discussion

Circulatory collapse and infarction can occur for two different reasons: intravascular application of the filling or external compression of the vascular structures. It is generally thought that vascular complications occur as a result of intravascular administration. In intravascular application, the filling material may directly occlude the vascular lumen, and platelet aggregation around the filling material may increase the obstruction. As a result, a hypoxic environment is formed in the tissues, which causes a decrease in the sensitivity of the vascular structures to NO, resulting in vasospasm and further increasing tissue hypoxia. In the second scenario, the filling material exerts external pressure on the vessel and ischemia occurs in peripheral tissues due to this. As explained above, ischemia reduces the sensitivity of vascular structures to NO, and the vasospasm that occurs due to this further increases the hypoxic state. As a result of all these, inflammatory changes are triggered in the tissue and edema occurs. Edema also exacerbates hypoxia by increasing vascular compression. All these processes trigger and intensify each other.[4]

In order to reduce the possibility of complications in filling applications, 3D anatomy should be well known by the practitioner.

Areas such as the nose, glabella, columella, frontal region are risky areas in terms of vascular complications, and it is recommended to use a small amount of filler, especially with a smaller particle size, softer structure and as little as possible, with light pressure, very slowly and by asking the patient whether there is pain or not. It is recommended to perform a capillary refill examination before the application and even to record it as a video for comparison after the application. There are studies showing that the risk of vascular complications is lower in USG-guided applications.[5]

In a review of cases with vascular complications, Beleznay *et al*. reported that only 33.3% of the cases reported that the application was done with a cannula or a needle, and that 10 out of 16 cases needle and 6 cannula were used. They showed that the 27 G cannula can pierce the vessels like a needle when applied with the same force.[6] More recent studies also point out that the safety of cannula use has been somewhat exaggerated. In the study of Zhou *et al*., consisting of 9 blindness, 1 blindness and stroke, and 18 patients with vascular complications, a total of 28 patients with extensive necrosis, it was shown that 22-27 G cannulas were used in 25 of these patients.[7] They stated that the use of cannulas smaller than 25 G should be avoided in filling applications.

There are studies showing that aspiration before the application of cross-linked hyaluronic acid fillers is 53% and 33-63% reliable.[8,9] Reliability of aspiration was found to be associated with needle radius, length, and negative pressure application time. In a systematic review published by Kapoor *et al*; the elastic modulus (G') and cohesiveness of the filler found a relationship with the inner lumen width of the needle, but not with the needle length and negative pressure time.[10] As a result, negative aspiration does not indicate that the application will be completely safe. In addition, it has no place in fillings applied in the form of linear retraction, as in our case, since a negative aspiration in one area does not mean that it will be negative in other areas as well.

Ischemic symptoms due to vascular circulatory disorder after administration usually begin to become clinically evident immediately after administration or within a few hours after administration.[3] Sometimes it can occur after a few days. Possible causes of this situation are as follows: embolism to narrower vessels more distal than the application site, enlargement in volume due to the hygroscopic structure of hyaluronic acid and causing intravascular occlusion or external pressure, platelet aggregation around hyaluronic acid and occlusion of the vessel.

In our case, a total of 0.09 cc Teosyal RHAII cross-linked hyaluronic acid filler was applied intradermally to the glabellar area. Our aim in sharing this case was to state that although the risk of vascular complications in filler applications is related to the amount of filling, there is a risk of vascular complications even in very-very small filling applications. In addition, if there is a previous surgical, traumatic or burn scar tissue in an area, we think it would be beneficial to think twice before applying. Because after such situations, fibrosis in the tissue significantly reduces the expansion capacity of the tissue and increases the possibility of vascular complications. We think that after traumas such as surgery or incision, the vascular anatomy of the area deteriorates and some collateral connections are lost, which may increase the risk of vascular complications. We think that since trauma/ incision and fibrosis may impair the lymphatic drainage of the area, it may cause more edema in the application area and/ or continue for a longer time, which will increase the compression on the vascular

structures and cause an increased risk of vascular complications.

Although it is sometimes recommended to apply pressure to the main vascular structures of the application area during the application, as it may cause narrowing of the vessel diameter and prevent or reduce the retrograde flow of the intravascular applied filling, there is no clear information on this subject.

Examination with USG doppler and/or testing of tissue extensibility with saline before the application may allow a decrease in the probability of vascular complications.

The administration of anesthetics containing adrenaline for anaesthesia is not recommended because it may mask discolorations during application and thus prevent the chance of early detection and early intervention of intravascular application.

It is recommended to observe the patient in the clinic for 30 minutes after applying to areas with vascular risk and to test the capillary refill time bilaterally during this period. When tissue infarction develops, as in our case, the area may begin to turn gray.[11] Vesicular or pustular lesions in the area usually begin to appear on the 3rd day after application.[5]

Since hyaluronidase can diffuse into the vein even after extravascular administration, intravascular administration is not essential.[5,12] Schelke *et al*. showed that even lower doses of hyaluronidase, such as 35-60 U, applied intravascularly using ultrasound or high-frequency ultrasound, can dissolve intravascular hyaluronic acid. Since there is a risk of anaphylaxis after hyaluronidase administration, adrenaline should be available.

Spindle *et al*. showed that thrombus formation accompanies the event after intravascular hyaluronic acid administration, and therefore, the process of thrombolysis should be considered in the treatment.[14]

Topical use of nitroglycerin in the very early period may not increase perfusion, even worsen, and cause ischemia, as it will dilate the vessels and cause the product to progress to smaller arterioles or capillaries more distally.[15]

There are opinions in favor of not using corticosteroids, as they may delay the healing process and worsen the possible infection picture. Since infection was not considered in our case, topical steroids were used.

After the vascular obstruction is treated, a chain of damage due to reperfusion begins in the tissue, and superoxide, hydrogen peroxide and other oxygen free radicals play a role in these events.[16] Therefore, the intervention to vascular occlusion is time sensitive, as the prolongation of hypoxia and ischemia brings with it more reperfusion injury.

Informing the patient in terms of possible vascular complications before the application, obtaining verbal and written consent, checking the capillary filling times, taking photographs at the appropriate angle, in the appropriate background, in the appropriate light, stating that the patient should be careful about conditions such as pain that does not gradually decrease and discoloration in the application area or that gradually increases in intensity. In case of encountering these situations, it is necessary to determine a form of communication that can always be reached and to think twice when applying to scar areas.

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