Hyaluronic acid (HA)-based dermal fillers are most commonly used in the field of aesthetic medicine. HA is very popular due to its high biocompatibility and favorable outcome. In cases of adverse reactions of the skin to filler injection, local edema or erythema may appear, which disappear within a few days. Severe complications, such as skin necrosis and even cerebral infarction, are rare. Beleznay et al. described the incidence of vascular complications up to 3 in 1000. Most of the vascular complications of HA fillers that have been reported are associated with skin necrosis. To our best knowledge, a thrombosis of a frontal vein as a late-onset adverse reaction after HA filler injection has not been reported yet.

**CASE REPORT**

A 35-year-old woman received an HA filler injection in the forehead area. About 3 months later, swelling occurred above her right eyebrow with the simultaneous appearance of headache and light flashes in her right eye (Fig. 1). Concerning the patient’s medical history, she was not suffering from any diseases, nor was she taking any medication regularly. Except for a septrhinoplasty revision several years ago, she has had no previous surgery. As the patient was not aware of any connection between her condition and the HA filler injection, she did not initially mention it in the emergency room. In an interdisciplinary setting, the diagnosis was conducted by neurologists, angiologists, vascular surgeons, dermatologists, and ENT specialists. In the department of neurology, no focal neurological deficit was seen. The color duplex sonographic examination by the angiologist showed thrombosis of the right frontal vein, with a diameter of about 2 cm (Fig. 2), whereas the ophthalmic vein and the jugular vein were regularly perfused. The MRI scan showed no complication of a sinus vein thrombosis. Further neurological deficits were excluded and the CT-scan (skull) was inconspicuous. There was no incidence of coagulopathy in the blood tests. The etiology of the thrombosis of the frontal vein remained at first unclear. Therapy with low molecular weight heparin (60 mg subcutaneous 1-0-1) was applied and later changed to apixaban (5 mg 1-0-1). The patient still reported a persistent severe forehead pain. Until the appearance of the current symptoms, she had not recognized any peculiarities on her forehead after the filler injection 3 months ago. Under the anticoagulation for more than 4 weeks, the thrombosis was still visible and
caused stable symptoms. Therefore, the thrombosed part of the vein was resected under local anesthesia in a joint operation, and the vein was ligated in the direct proximity of the thrombosis (Fig. 3). In the follow-up, she had no symptoms and there was no swelling on the forehead anymore. Small scars remained but that did not disturb the patient. Anticoagulation therapy ceased directly after surgery. The histological result showed the thrombosis within the vein with a chronic inflammation reaction to foreign material that is strongly evident for HA (stained with Alcian blue) (Fig. 4).

**DISCUSSION**

In our case, the thrombosis of the frontal vein led to recurrent pain and to distinct swelling of the forehead. We applied low molecular weight heparin (because of its anticoagulative and anti-inflammatory effects) for the treatment of the thrombosis. These effects, however, are not fully understood. After several weeks of anticoagulation in the reported case, the symptoms persisted. The most feared risk is that the thrombosis could progress into the deep venous system, thus leading to the life-threatening complication of a sinus vein thrombosis. Ultimately, surgery is recommended to remove the thrombosis. To reduce the risks, injections of fillers should be performed by experienced physicians to detect complications early enough to induce an appropriate therapy. The application of fillers by experienced physicians ensures a high standard of patient safety.
The patient in this case, unfortunately, did not initially mention the filler injection, thus causing a delay in diagnosis and treatment. This reveals the importance of a detailed history and physical examination, including asking relevant questions about injectables received. We should consider a thrombosis in young patients with unexplained swelling of the face as a differential diagnosis. Patients should be actively asked if they have had filler injections in the past.

A surprising aspect is the appearance of the thrombosis 3 months after the filler injection. As far as we know, no case has been published yet describing a late-onset reaction several months after a filler injection. Cassiano et al.7 described a delayed skin necrosis of the forehead following HA filler injection 2 days after injection, and Bravo et al.8 reported the same several hours after an HA filler injection. Histological results of our patient confirm a chronic inflammatory reaction of the tissue to HA. It has already been shown that vascular-related complications can be caused by intravascular injection or external compression.7 We assume that HA was encapsulated, and HA had no contact with the immune system or the patient had clinically silent complications within the first months after the HA filler injection. As HA was still found in the connective tissue, complications such as a thrombosis could reoccur. It is essential that both the patient and the treating physicians know of this in case symptoms recur, even several months after injection.

**SUMMARY**

Vascular complication as a reaction to HA-based filler is a rare but possible complication of any filler injection. A detailed history and physical examination by asking specific history of injectables and an interdisciplinary approach would help in the diagnosis at an early stage. The first choice in the therapy of a thrombosis in a frontal vein is the application of low molecular weight heparin. In the case of treatment-resistant thrombosis, as in the present case, resection of the thrombosed vein may be necessary.

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