Letter to the Editor

Late Onset Complications Secondary to Polyacrylamide Hydrogel-Based Filler for Rehabilitation of HIV-Related Facial Lipoatropy

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In 2015 we reported our experience of a 5-year follow-up study regarding the utilization of polyacrylamide hydrogel-based filler for rehabilitation of HIV-related facial lipoatropy.[1] The outcomes of this study confirmed the safety and efficacy of this noninvasive treatment as already stated in an earlier report of 18-month follow-up period for that study population.[2]

In the 5-year follow-up, patients were randomly assigned to 1 of 2 study groups: A or B. In Group A, 18 patients (12 men, 6 women) were enrolled and were treated by injection of a variable amount of product in the first session, ranging from 8 to 24 mL, and further touch-ups were performed when needed. In Group B, 13 patients (9 men, 4 women) were enrolled and were injected with 2 mL of product per session; this treatment was repeated at 8-week intervals until full correction was observed.[1]

In the 31 treated patients, there was no occurrence of local infection, foreign body reaction, or product migration during the whole follow-up period; in 9 cases, small, nonvisible, palpable nodules where recorded. These nodules appeared within the first 36 months of follow-up and lasted throughout the previous 5-year study.[1] In the last 6 months, approximately 10 years after the injections, 3 patients returned with some complications.

Case 1

A 46-year-old Caucasian male patient received highly active retroviral therapy (HAART) 8 years earlier, presenting a class 3 James[3] facial lipoatrophy scale, was referred to Maxillo-Facial Unit of the Second University of Naples (called University of Campania "Luigi Vanvitelli" since 2015) in 2008 for rehabilitation of HIV-related facial lipoatropy. Before being referred to us, this patient already received blood serum evaluation and was considered suitable for the treatment by physicians of the infective disease hospital "Cotugno" in Naples. The patient received a first treatment (the treatment protocol was previously described)[1] of 12 mL of filler injection and a touch-up performed 8 weeks later of an additional 2 mL filler. The patient was followed up for 5 years and no adverse events were recorded. In March 2018, he returned, complaining about the hardening of the cheeks secondary to filler injections noted as a progressive worsening in the last 2 years (Figure 1).

Case 2

A 44-year-old Caucasian male patient, presenting a class 2 James[3] facial lipoatrophy scale and in the HAART regimen for 6 years previous, referred to our department in 2008 for rehabilitation of HIV-related facial lipoatropy. This patient was sent to our department by the infective disease Hospital

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Figure 1. This 55-year-old Caucasian male patient presented with bilateral hardening of the cheeks 9 years after polyacrylamide hydrogel injections. Shown here are the (A) frontal, (B) three-quarters right, and (C) three-quarter left views.

"Cotugno" in Naples. The patient belongs to Group B of the previously published study[1] and received a total amount of 9 mL of filler injected; the injections were performed once every 8 weeks and the amount per each session was up to 2 mL. The patient was monitored for 5 years and did not show any adverse events up to 1 year ago; 8 years after the injections, he noted a progressive swelling bilaterally in the cheeks, and stated this adverse event to be stable since 6 months. The patient was not visited. In April 2018 he sent photographs via e-mail showing his clinical situation (Figure 2) and asked for an oral drug to solve the problem. We replied to the e-mail explaining that oral drugs cannot definitively solve the problem. We invited him to return to the hospital to evaluate how to proceed to solve this adverse event; however, the patient refused the invitation.

Case 3

A 37-year-old Caucasian male patient in the HAART regimen for the 4 years previous, presenting a class 3 James[3] facial lipoatrophy scale, was referred to our department in 2008 for rehabilitation of HIV-related facial lipoatropy. This patient was sent to our department by the infective disease Hospital "Cotugno" in Naples. The patient belongs to Group B of the previous published study and received a total amount of 12 mL of filler injected. Within the first 12 months, the patient detected nonvisible palpable nodules bilaterally (which persisted through the 5 years of follow-up), although the facial feature corrections were considered satisfactory by the patient. The patient returned to our hospital in February 2018 with a large abscess in the left cheek presenting a bruising and thinned skin area next to the left oral commissure and was hospitalized (Figure 3A). During the anamnesis, the patient reported several swelling events in last 3 years, not always on the left side but also on the right, which recovered with oral antibiotic therapy. However, this time the swelling did not recover after therapy and became larger than usual. Endovenous antibiotic therapy was given to the patient (Ceftriaxon ev, 2 g/day), but after 3 days, a

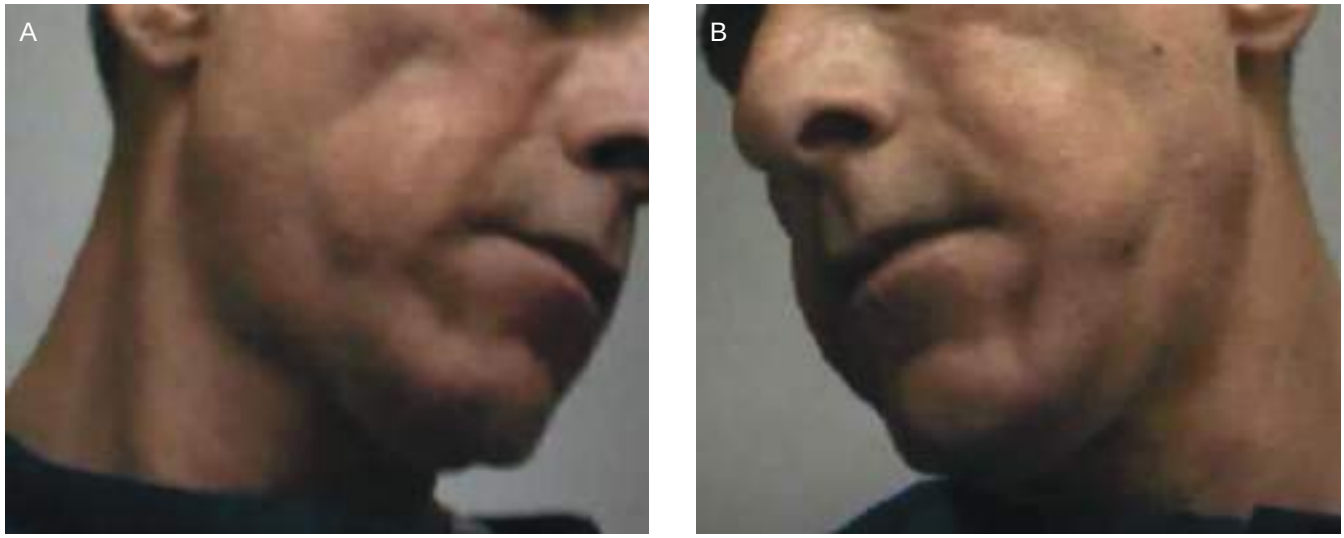

Figure 2. This 53-year-old Caucasian male patient presented with bilateral persistent swelling developed 9 years after polyacrylamide hydrogel injections. Shown here are the (A) three-quarters right and (B) three-quarters left views. The photographs were self-taken by the patient and sent via email. The patient declined to visit in person.

fistula developed from the area next to the left oral commissure where bruising and thinning of the skin was present. The patient was sent to the OR, and approximately 50 mL of purulent and inflammatory material was drained. Antibiotic washes were performed. Secondary to abscess drainage, a 2-cm area of soft tissue deficit developed (Figure 3B). After daily curettage and advanced dressing, it healed by secondary intervention within 1 month with retracting scar tissue (Figure 3C).

DISCUSSION

Polyacrylamide hydrogel is a hydrogel made up of a minor backbone of 2.5% cross-linked polyacrylamide and 97.5% nonpyrogenic water. It attained European Union certification in 2001 and has been in clinical use in Europe for cosmetic purposes since 2000 under the brand name Aquamid (Contura International, Soeborg, Denmark).[4] Several long-term studies regarding utilization of this hydrogel-based filler have been published in the fields of both cosmetic and reconstructive procedures for the rehabilitation of HIV-related facial lipoatrophy.[1,2,5-7] In a prospective multicenter study of 251 patients treated with polyacrylamide hydrogel injections for facial soft tissue augmentation, Wolter and Pallua noted a total of 104 adverse events in 73 patients (29 percent); 53 (51%) were considered treatment related and occurred in 40 patients (15.9%).[5] Gel induration was the most recorded adverse event and occurred in 9 patients. Itching, hematoma, pain, discoloration, edema, and infection were also recorded throughout the study; 2 of the adverse events were classified as serious and both were infections. However, aesthetic outcome was rated as "very good" or "good" by 96.5% of patients and by 96.0% of investigators at final available follow-up. Authors concluded that for patients who desire facial soft-tissue augmentation, Aquamid is an excellent alternative to surgery.[5] Previous studies also showed favorable results from treating facial lipoatrophy with polyacrylamide hydrogel in significantly immunocompromised patients; De Santis et al reported a successful experience at 2 and 5 years in the management of HIV-related facial lipoatrophy in a very high-risk group in terms of susceptibility to infection.[6,7] Also in our previous 5-year follow-up study, 27 patients demonstrated satisfactory and safe results (4 patients discontinued after the initial 18-month study); there was no occurrence of local infection, foreign body reaction, or product migration during the follow-up period.[1] We emphasize the role of the asepsis when injecting polyacrylamide hydrogel to avoid the side effect of greatest concern: infection. We introduce a specific treatment process performed chlorhexidine preparation, including double cleansing of the area to be treated; moreover, patients were given intravenous antibiotic therapy during the procedure and oral antibiotic therapy afterward for 5 days. They were instructed to avoid shaving and perfume or cologne in the treated areas to prevent contamination of the injection sites.[1]

At 9 years after the injections, we recorded 3 cases of adverse events. The first was considered very serious (case no. 3) and required surgical intervention. In the other 2 cases, the complications were not resolved. Moreover, patient number 2 did not return for a visit but sent to us an e-mail selfie photos attached (Figure 2, A and B) showing his clinical situation. One patient belonged to group A and

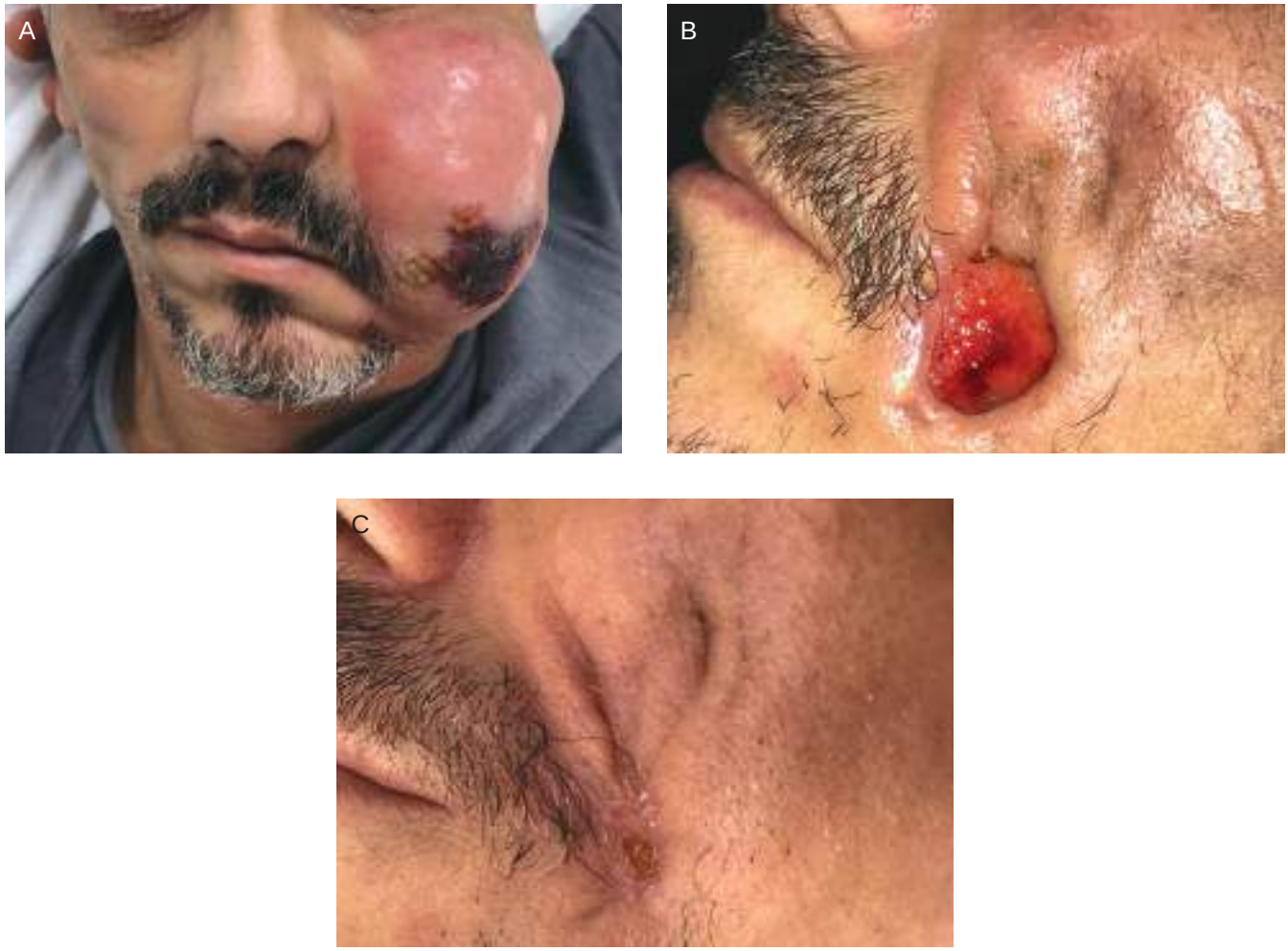

Figure 3. This 46-year-old male patient presented with bruising and a thinned skin area next to the left oral commissure. (A) A large abscess developed in the left cheek. He was injected 9 years earlier with polyacrylamide hydrogel. (B) The soft tissue deficit developed after the drainage of the abscess. (C) The area healed after 1 month of curettage and advanced dressing showing retracting scar tissue.

received 14 mL of product (12 mL in a session and 2 mL in a further touch-up), and the other 2 patients belonged to group B and respectively received the injections of 9 and 12 mL of filler. However, we had no clinical data regarding the other 24 patients we monitored for 5 years in the previous study; this is a big limitation regarding an objective evaluation of this filler safety and regarding the predictability of the treatment.

CONCLUSION

Based on the published literature, polyacrylamide hydrogel-based filler is described as safe and predictable for facial cosmetic purposes and also for rehabilitation of HIV-related facial lipoatrophy. However, it is mandatory to discuss with the patient before the treatment and clearly explain how dramatic complications related to product infection can appear also after a long time from the implantation.

Disclosures

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