OBSERVATION

Delayed Inflammatory Reaction to Bio-Alcamid Polyacrylamide Gel Used for Soft-Tissue Augmentation

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Background: Given the recent boom of the cosmetic industry, there is a wealth of new products available to patients and physicians, including soft-tissue fillers. Bio-Alcamid polyacrylamide gel (Polymekon, Milan, Italy) is a filler that has potential to cause adverse reactions.

Observations: Two patients who had previously been treated with Bio-Alcamid outside of the United States presented with different manifestations of inflammatory responses to the product. These reactions were challenging to treat.

Conclusions: Despite claims of safety, Bio-Alcamid and possibly other soft-tissue fillers available worldwide have the potential to cause adverse reactions. Physicians should be aware of the various presentations and treatment options for these reactions.


Volume replacement using soft-tissue fillers has become useful in treating the aging face as well as human immunodeficiency virus (HIV)- and highly active antiretroviral therapy (HAART)-associated lipodystrophy. A lucrative and high-demand market has resulted in multiple products that are available to physicians and patients. The most popular fillers in the United States for age-related volume loss and HIV lipodystrophy include hyaluronic acids fillers (Restylane and Perlane; Medicis Aesthetics, Scottsdale, Arizona, and Juvederm Ultra and Juvederm Ultra Plus; Allergan, Santa Barbara, California), calcium hydroxyapatite (Radiesse; BioForm Medical Inc, San Mateo, Calif), and poly-L-lactic acid (Sculptra; Dermik, Bridgewater, New Jersey). Newer products, such as porcine collagen (Evolve; OrthoNeutrogena, Los Angeles, California), have become available within and outside the United States. Some of these products may have potential adverse effects.

Polyacrylamide gels, including Aquamid (Ferrosan NS, Copenhagen, Denmark) and Bio-Alcamid (Polymekon, Milan, Italy), are non-US Food and Drug Administration (FDA)-approved fillers used for soft-tissue augmentation worldwide. Aquamid is a 5% polyacrylamide polymer with 97.5% water. Bio-Alcamid is composed of a base of 2.5% to 5% cross-linked polyacrylamide and 95% to 97.5% water. Polyalkylamide is a polymer within the polyacrylamide family. In the past, the manufacturer's Web site has referred to the product's composition as polyacrylamide. Recently, the information on the Web site has been updated to state that the gel is composed of polyalkylamide.

We describe 2 cases of inflammatory reactions occurring at least 1 year after injection of a polyacrylamide gel (Bio-Alcamid). In both cases, alternative diagnoses were originally considered. It is important for physicians to be aware of new and less commonly used cosmetic treatments, including those used primarily outside of the United States.

REPORT OF CASES

CASE 1

A 66-year-old woman was seen for a 12-hour history of facial edema and pain that occurred 2 days after infraorbital and mental nerve blocks and injection of cross-linked hyaluronic acid (Juvederm Ultra...
Plus) to the marionette folds and lips. The patient had no chronic medical problems and denied a history of bleeding diathesis. She previously had injections of a polyacrylamide 4% gel (Bio-Alcamid) into the chin twice in Israel, the first injection 2 years prior and the second injection within the past year.

On examination, the patient had considerable edema with induration of the right cheek, mandible, and superior aspect of the neck. A moderate amount of edema was noted on the patient’s left cheek and neck (Figure 1). The cutaneous and mucosal surfaces were extremely tender to palpation. Differential diagnosis included hematoma, infection, and inflammatory reaction.

Under local anesthesia, an 18-gauge needle was used to aspirate approximately 7 mL of blood. The needle was redirected toward the mental crease, and 2 mL of blood mixed with a yellow, viscous-appearing substance was then extracted. After aspiration, the edema was notably decreased. The patient was discharged to her home and prescribed 2 weeks of treatment with clarithromycin, 500 mg, twice daily. A bacterial and acid-fast mycobacterial culture of the material was negative for organisms.

Two weeks later, the patient presented with edema of the right chin, and 5 mL of a viscous, blood-tinged fluid was aspirated. Bacterial culture of this material was negative for organisms. The patient’s symptoms are thought to be an inflammatory response secondary to disruption of the previously injected Bio-Alcamid by Juvederm injection.

CASE 2

A 52-year-old woman was seen for a tender nodule in the right subalar triangle approximately 1 year after injection of Bio-Alcamid in Lebanon (Figure 2). The patient reported that the Bio-Alcamid had been injected near the corners of her mouth and along the nasolabial folds. The patient complained of localized pain in addition to the appearance of the nodule, but she was otherwise well and denied systemic symptoms.

On examination, the patient had a tender, fluctuant 1.5-cm nodule in the right subalar triangle. An 18-gauge needle was used to puncture the nodule, and a whitish-gray material was expressed and sent for culture testing. The lesion was also injected with 0.4 mL of triamcinolone suspension (2.5 mg/mL). The patient was discharged and given a prescription for amoxicillin–clavulanate potassium, 500 mg twice daily for 7 days. The patient returned 3 weeks later reporting little to no improvement of the nodule, as well as new nodules. A culture specimen from the previous visit showed no growth of bacteria or acid-fast mycobacteria. On examination, she had 5 tender nodules, ranging in size from 1 to 2 cm. The presumptive diagnosis of an inflammatory response to Bio-Alcamid was made. An 18-gauge needle was used to puncture the nodules, and again a whitish-gray material was drained from each nodule. The patient was given a prescription for amoxicillin–clavulanate potassium, 500 mg twice daily for 7 days. Over the next 2 years, the patient returned for approximately 10 visits for drainage of new nodules. Multiple courses of antibiotics, including amoxicillin–clavulanate potassium, minocycline hydrochloride, 100 mg twice daily, and cephelexin hydrochloride, 500 mg twice daily, did not alter the clinical course. Each nodule would reduce after drainage and then recur over a period of 2 to 3 weeks.

COMMENT

We report recurrent inflammatory reactions after injection of Bio-Alcamid gel: 1 patient had acute edema after presumed disruption of Bio-Alcamid by injection of a hyaluronic gel, and 1 patient had multiple, persistent inflammatory nodules. Both patients experienced their adverse events more than 1 year after injection of Bio-Alcamid. In both cases, reaction to Bio-Alcamid was a diagnosis of exclusion.

Bio-Alcamid is a hydrogel that has been used in Europe since 2001 as a permanent filler substance for age-related volume loss and for HIV-related and HAART medication lipoatrophy. It is not currently approved by the FDA for use in the United States. Bio-Alcamid is approved in Canada only for the treatment of HIV- and HAART-associated facial lipoatrophy. It is nonbiodegradable and hydrophilic. After injection it becomes an “endoprosthesis” owing to fibroblast activity around the substance, which forms a thin fibrous capsule. The thin capsule contrasts with thicker capsules found surrounding silicone, which is a hydrophobic permanent filler. It has been speculated that the thin capsule formed...
around Bio-Alcamid may be flimsy in subcutaneous and mammary tissue, which could result in capsular rupture with force, muscle activity, or vigorous massage, especially in patients with a thin subcutaneous layer. An incomplete or absence of capsule in or near muscle has also been reported. The pumping action of the muscles may therefore result in gel migration, especially years after injection.

Although the permanent nature of Bio-Alcamid is often considered an advantage, there are numerous reports of adverse events. Complications related to Bio-Alcamid therapy can be early and late occurring and include infection, product migration, and sterile inflammatory abscesses. Late-occurring reactions can occur months to years after injection. In 1 report of 25 patients with late-occurring adverse effects caused by polyalkylimide fillers, the mean latency period between injection and symptoms was 13.4 months. The etiology is usually related to disruption of the fibrocellular layer surrounding the product following invasive procedures such as injection of additional filler material (as in case 1), blepharoplasty, and dental work. After these procedures, there may be pain and edema, as occurred in both of our patients. Serologic findings most commonly show elevated acute phase reactants, but increased angiotensin-converting enzyme (ACE) (with normal calcium levels), lactate dehydrogenase (LDH), positive antinuclear antibody, and abnormal electrophoresis abnormalities may be found. Our patients declined biopsy; however, based on clinical presentation and course, these cases most likely represent late-occurring inflammatory reactions. Published cases have reported nonspecific foreign-body granulomas on histopathologic examination.

Complications have been treated with antibiotics, drainage, oral or intrallesional steroids, nonsteroidal anti-inflammatory drugs (NSAIDs), hydroxychloroquine sulfate, and removal of the product, with varying results. Patients may have recurrent symptoms, as occurred in our patients.

Negative findings from cultures grown from aspirated material from inflammatory reactions are the norm. One case of a patient with a positive culture test for Staphylococcus viridians has been reported. In most cases, patients are given antibiotics while the culture results are pending. Patients with an inflammatory response to Bio-Alcamid usually improve with a combination of antibiotics, drainage, and steroid injections, but improvement is usually not achieved with antibiotics alone. It is possible that puncture of the capsule may introduce bacteria that are not detectable in culture but may stimulate chronic inflammation. Therefore, the implant of temporary or permanent fillers may serve as a growth medium for biofilm formation. Polyalkylimide fillers may theoretically decrease protein adhesion and macrophage function and therefore decrease the ability of the host to respond to bacterial infection. The impaired immune response results in smoldering inflammation. It has recently been shown that Staphylococcus aureus forms a bacterial biofilm on hydrophilic substances, whereas Escherichia coli prefers hydrophobic substances. The introduction of a Staphylococcus species through skin and implant puncture could explain biofilm formation. Once a bacterial biofilm is established, elimination of the bacteria stimulating the inflammation is extremely difficult. Removal of all of the filler material plus long-term, broad spectrum antibiotics that are able to penetrate the implant capsule are advocated.

Distinguishing inflammation due to a bacterial biofilm from a low-grade hypersensitivity reaction is difficult. Most filler substances have been reported to have immunogenicity, including hyaluronic acid (HA). A study of delayed immune-mediated effects from HA and HA combined with polymethylmethacrylate included 25 cases of patients with symptoms starting 1 to 60 months after injection. The adverse effects were inflammatory nodules, cutaneous leukocytoclastic vasculitis, sarcoid-like reactions, and labial granulomas, and serum abnormalities were present in all of those tested. Although rare, hypersensitivity should always be considered in the differential diagnosis of a patient presenting with an inflammatory reaction after receiving an injection of any filler. Intradermal skin testing with a filler substance before treatment may be helpful in susceptible individuals.

Aquamid has similar qualities to Bio-Alcamid. It is not FDA approved for use in the United States but is used in Europe for soft-tissue augmentation. A recent report of 10 cases of delayed immune-mediated adverse effects showed a similar latency period from injection to symptoms (10 months), similar clinical manifestations (inflammatory nodules and pseudoabscesses), laboratory abnormalities (elevated acute phase reactants, ACE, LDH), and response to treatment (mixture of remission after drainage, NSAIDs, and intrallesional steroids and recurrent inflammatory episodes).

With the explosion of new substances coming to market for soft-tissue augmentation, it is essential that physicians be aware of both short- and long-term effects of new materials. Globalization of the cosmetic surgery market presents unique challenges to physicians. It is important for cosmetic physicians to be aware of potential presentations and complications of products that are not routinely used in local practice. Industry must also recognize the potential complications and problems with products, and disclose reported complications in their literature. For example, Pur Medical Corp (Toronto, Ontario), the Canadian distributor of Bio-Alcamid, suggests on their Web site that the product is suitable to combine with other fillers, biocompatible, has little reaction with human tissue, and does not migrate. Our cases illustrate that this may not be accurate. As novel soft-tissue fillers are used clinically, it is likely that we will discover new and unforeseen complications, which we must disclose to patients.

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REFERENCES