

## CASE REPORT

# Cutaneous Adverse Reaction to Bio-Alcamid® Implant

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**Abstract.** In the last years new and numerous materials for the correction of defects and wrinkles have been developed. One of these materials is Bio-Alcamid®, a non reabsorbable gel polymer constituted by meshes of poly-alkyl-imide, without known adverse effects. We report a 34-year-old woman that had Bio-Alcamid® implants for acne scars and several months after presented nodular lesions together with a painful inflammatory nodule. The nodule was drained and culture of the purulent material yielded *Streptococcus viridans*. A cytology and a cellular block of that material showed a granulomatous inflammatory reaction together with a foreign body. The different types of reactions to implants and their pathogenic mechanism are discussed. It is important to know these possible reactions to filler materials given their increasing use and the potential medico-legal consequences.

**Key words:** Bio-Alcamid®, filler substances, foreign body granuloma.

## REACCIÓN CUTÁNEA TRAS IMPLANTE CON BIO-ALCAMID®

**Resumen.** En los últimos años se ha producido la aparición de nuevos y numerosos materiales para la corrección de defectos y arrugas. Uno de estos materiales es el Bio-Alcamid®, un gel polimérico gelatinoso no reabsorbible constituido por redes del grupo alquilimida, del cual no hay descritos efectos adversos. Presentamos una mujer de 34 años que recibió inyecciones de Bio-Alcamid® por cicatrices post-acné presentando varios meses después lesiones nodulares, junto con un nódulo inflamatorio muy doloroso. Fue drenado extrayéndose gran cantidad de material purulento y cultivándose un *Streptococcus* grupo *viridans*. Se realizó una citología y un bloque celular de ese material donde se objetivó una reacción inflamatoria granulomatosa junto con un material extraño.

Se discuten los diversos tipos de reacciones a implantes y su mecanismo patogénico. Es importante el conocimiento de estas posibles reacciones a los materiales de relleno por el incremento debido a un mayor uso y por las consecuencias médicas y legales.

**Palabras claves:** Bio-Alcamid®, sustancias de relleno, granuloma a cuerpo extraño.

## Introduction

In 1899 Gersuny published an article on the use of liquid silicone as a filler injected into the scrotum of a patient in order to reconstruct a testicle after an orchiectomy for tuberculosis.<sup>1</sup> Since then there has been a steady increase in the use of implants and filler substances to correct defects

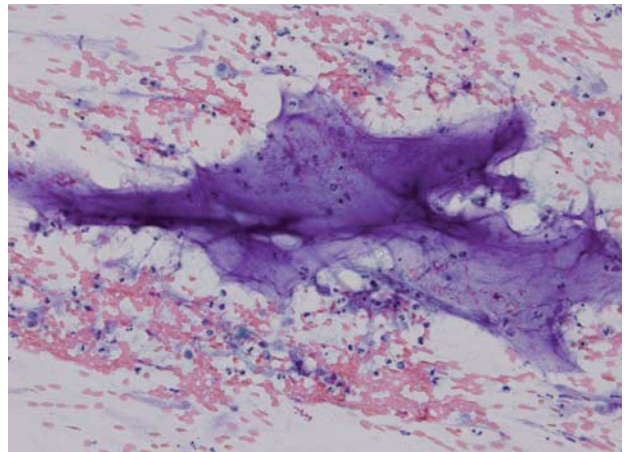
and wrinkles. According to the American Society of Aesthetic Plastic Surgery, 8.3 million cosmetic procedures were performed in 2003 and 12 million in 2004, representing a year-on-year increase of 44%. Furthermore, this increase is mainly accounted for by nonsurgical procedures. Thus, surgical procedures accounted for half of all procedures in 1997, a third in 2004, and 18% in 2004. Looked at another way, since 1997 the number of nonsurgical procedures has increased by 764%.<sup>2</sup>

The high demand for cosmetic interventions has led to the development of many new filler substances, and although improvement is evident, the ideal product has yet to be developed. This ideal product should be easy to inject, nonallergic, inert, incapable of migrating, and biologically compatible with the host tissue. Filler substances can be

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**Table 1.** Classification of Filler Substances According to Duration

<i>Nonpermanent</i>	<i>Semipermanent</i>	<i>Permanent</i>
Collagen (Zyderm)	Polylactic acid (New-Fill)	Silicones
Hyaluronic acid derivatives (Restylane)	Calcic hydroxyapatite (Radiance)	Hydroxy-ethyl-methacrylate (Dermalive)
	Dextran (Reviderm)	Polymethylmethacrylate (Artecoll)
		Polyvinylhydroxide (Evolution)
		Polyacrylamide (Aquamid, Bio-Formacryl)
		Polyalkylamide (Bio-Alcamid)

**Figure 1.** Painful nodule at the corner of the mouth, more palpable than visible.**Figure 2.** Smear showing foreign matter and inflammatory infiltrate (Papanicolaou magnified  $\times 200$ ).

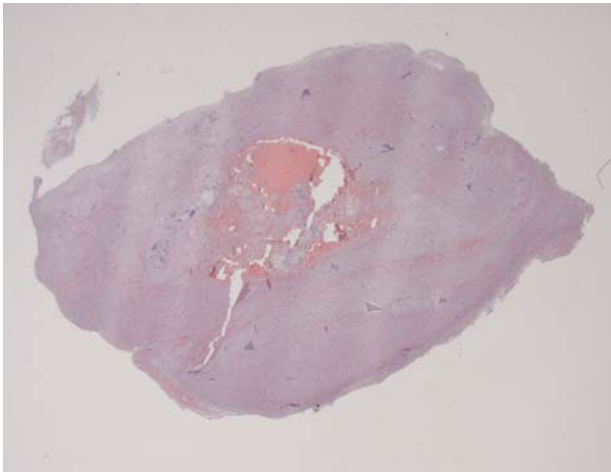
classified in accordance with duration and biodegradability as resorbable (nonpermanent), semipermanent, and permanent (Table 1).

More recent products are inert and the incidence of side effects is low. Nonetheless, all filler products are capable of producing an allergic reaction. Given the increasing use of filler products, it is important to learn more about allergic reactions to permanent products as they are difficult to manage and even to diagnose. The case described below refers to an allergic reaction to a permanent filler.

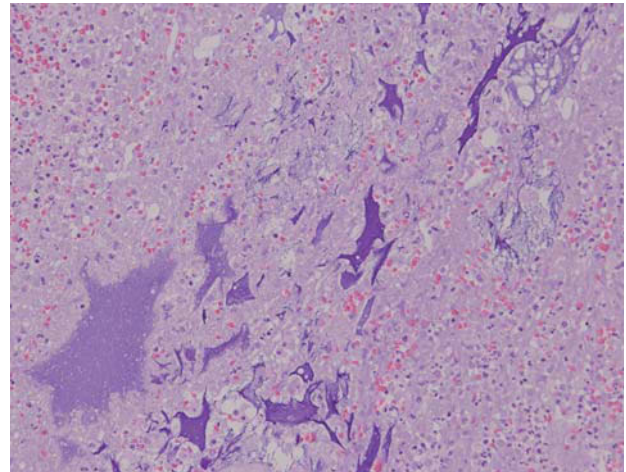
## Case Description

A 34-year-old woman, with no allergies or medical background of relevance, received injections of Bio-Alcamid in both cheeks in March 2003 as treatment for post-acne scarring. From July 2004, the patient began to develop a series of nodular, painful lesions of varying sizes, one of which began to suppurate a cheesy substance. The patient also developed a mild fever. Treatment with clarithromycin and intramuscular methylprednisolone produced an

improvement. In October 2004 the patient came to our surgery as a consequence of the nodular lesions (Figure 1). A biopsy was taken using an intraoral approach to avoid scarring. The biopsy, however, was not deep enough to show significant abnormalities, and the patient refused to have it repeated. In June 2005, the patient visited the emergency department with a very painful inflamed nodule at the left corner of her mouth and mild fever. The nodule, once drained of a large quantity of purulent material, reduced considerably in size and consequently became much less painful. The patient was prescribed 875 mg/8 h of amoxicillin-clavulanic acid. The inflammation persisted and the nodule was drained again 3 days later. Progress thereafter was satisfactory. A culture of the drained substance yielded *Streptococcus viridans*. A cytological study revealed an inflammatory granulomatous reaction and foreign matter (Figure 2). The remaining material was centrifuged, and the residue was processed and stained with hematoxylin-eosin to obtain a cell block. An intense inflammatory reaction was observed in the cell block, with numerous leucocytes, red cells, epithelioid cells, and giant cells, as well as foreign matter (Figures 3 and 4).



**Figure 3.** Cell block, polygonal in shape with well-defined borders, showing an inflammatory reaction, red cells, and foreign matter (hematoxylin-eosin × 10).



**Figure 4.** Close-up view showing filler substance (hematoxylin-eosin × 200).

The patient’s nodular lesions persist, and she is currently awaiting a court appearance in a suit she is taking because of the reaction.

## Discussion

Faced with a patient with a reaction to a filler substance we can ask two questions. The first question is: is the implanted substance what the patient says it is (in this case Bio-Alcamid)? The second question is: why has a reaction occurred?

The first question is relevant because a patient is often not sure or cannot remember what substance was injected,

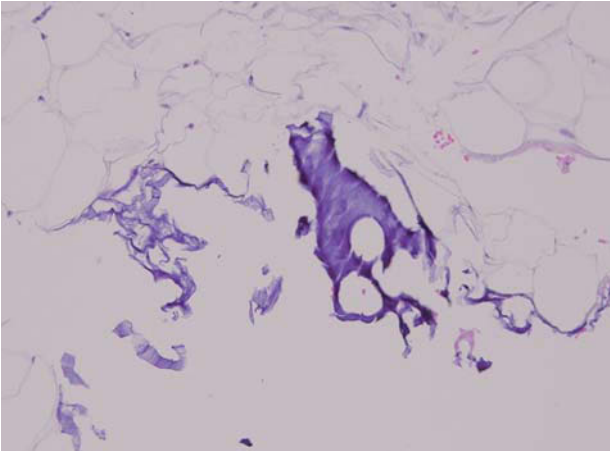
and cases have even been reported in which a histologic study demonstrated the use of a different substance to what the patient believed was used—often fraudulently, as has been the case, for example, with liquid silicone.<sup>3,4</sup> It is important, therefore, to be aware of adverse effects to filler substances, given the medical and legal consequences and given the likely increase in reactions arising from a more widespread use of fillers.

Several histologic patterns correlating with a range of substances have been described. Consequently, the findings of histopathologic studies differ according to the type of microimplant.<sup>4,6</sup>

In histological terms, 2 broad granulomatous reactions can be distinguished (Table 2):

**Table 2.** Histology of Reactions to Cosmetic Implants

Type	Implant	Histologic Finding
Classic foreign body granuloma	Artecoll	Numerous rounded cystic spaces of similar size and of a nonbirefringent material. Histiocytes surrounded by giant cells.
	Dermalive	Translucent polygonal pink irregular particles of varying sizes. Asteroid bodies.
	New-fill	Multiple birefringent irregularly sized and needle-shaped particles. Fibrosis.
	Aquamid	Violaceous macrophages and giant cells with microvesicles.
	Bioplastique	Small irregularly sized and shaped cystic spaces with serrated nonbirefringent translucent bodies.
	Bio-Alcamid	Polymorphous granulomatous infiltrate with giant cells. Violaceous material with a granular appearance.
Cystic-macrophagic granuloma	Liquid silicone	Different sized extracellular cysts. Foamy macrophages. Empty spaces.



**Figure 5.** Detail of a Bio-Alcamid implant in an ex vivo skin sample (hematoxylin-eosin  $\times 200$ ).

1. The classic foreign body granuloma (with giant cells and inflammatory infiltrate around the foreign body), for which various reaction patterns exist, depending on the substance injected.
2. The cystic-macrophagic granuloma (with extracellular cysts and foamy macrophages), responding to an injection of liquid silicone.

Bio-Alcamid—a nonresorbable gel polymer consisting of networks of alkylimide (an acryl derivative) groups and water (3% and 97%, respectively)—is designed to correct soft tissue defects. The substance should be implanted in the hypodermis and not in muscles or mucosa. Once injected, Bio-Alcamid becomes enclosed within a collagen capsule, which isolates it from the host tissue by acting as an endogenous prosthesis. A range of studies have demonstrated that Bio-Alcamid is not mutagenic, toxic or sensitizing, and that it shows no tendency to migrate.<sup>7,8</sup> According to the manufacturer, it does not trigger granulomatous reactions,<sup>9</sup> and few cases of reactions to Bio-Alcamid have been described in the literature.<sup>10,11</sup> Only one case includes a histologic description,<sup>11</sup> however, so its histopathological pattern is unknown. That said, it is quite probable that—as happens with many implants—reactions are simply not notified. With the patient's prior consent and with a view to assessing staining characteristics (Figure 5), we implanted Bio-Alcamid in a sample of skin ex vivo, given that the sample would not produce the kind of response mechanisms that often determine the histologic pattern. The staining pattern and structure of the material were very similar to those obtained for the patient, thereby confirming that the implant was, in fact, Bio-Alcamid.

The host's particular immune response greatly affects the production mechanism, which is why a reaction may

not occur until months or even years after the implant, particularly when the implant is permanent. Another theory as to mechanism (steadily gaining ground) is infection—whether at the moment of the injection, as a consequence of reactivation, or even several months after implantation—by latent microorganisms with a low pathogenic potential.<sup>6,12</sup> A culture demonstrated the presence of *Streptococcus viridans*, which probably caused the inflamed and painful nodule in our patient. Although *Streptococcus viridans* is found in the buccal mucosa of healthy individuals, several studies have demonstrated its pathogenic potential.<sup>13</sup> This bacterium may have reached the site of infection at the moment of the injection or during the first diagnostic biopsy taken using an intraoral approach.

It is important to remember that although these reactions can occur when an expert performs the procedure, they are more frequent when the procedure is performed by inexperienced individuals using inappropriate techniques.<sup>14</sup> In the case of our patient, the procedure was not performed by a physician, and the indication was not entirely clear given the small volume of post-acne scars; furthermore, the technique used was faulty, as the product was administered very superficially (as demonstrated by the fact that we could not access the material when we performed a biopsy using an intraoral approach).

In conclusion, we have described a new case of a reaction to a filler substance (which was very probably Bio-Alcamid). We wish to draw attention not only to the importance of filler injections being given by suitably qualified professionals, but also to the importance of notifying adverse reactions, given the medical and legal consequences.

#### Conflicts of Interest

The authors declare no conflicts of interest.

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