

# Exudative-Granulomatous Reaction to Hyaluronic Acid (Hylaform®)

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We are the first to report on a case where, an exudative reaction occurred and then turned granulomatous and lasted for 6 weeks after the injection of hyaluronic acid for the treatment of perioral wrinkles. In the intracutaneous test, the granulomas were reproducible and histologically verifiable.

## Patients and Methods:

A formation of an exudative reaction that increasingly turned granulomatous occurred on a 53-year-old female patient 2 days after the injection of Hylaform®. The maximum of the eczema reaction was reached after approx. 4 to 6 days and was healed after a further 4-5 days.

From the third day on, papular skin changes, which had completely regressed again after 6 weeks, could be felt.

The patient had undergone the same treatment at a cosmetician s approx. 18 months before. This was tolerated without complications then.

The epicutaneous test with the European standard series, ointment bases, plastic-resin-adhesive series from the Hermal company, as well as, with Hylaform® was read after 24, 48 and 72 hours.

A scratch and intracutaneous test with Hylaform® was carried out with readings after 20 minutes, 6, 24, 48, 72 hours and 6 days.

A biopsy was taken from the place of the intracutaneous test on the left volar forearm after 30 days.

The ingredients of Hylaform® were unfortunately not made available to us from the manufacturer, despite repeated requests.

## Results:

In the epicutaneous test, no type IV sensitization was provable. The intracutaneous test showed a

crescendo reaction, beginning after 24 hours and increasing until the sixth day. From the third day on a granuloma, which was no longer provable after 6 weeks, could be felt.

Histological findings: Foreign body granuloma with proof of basophil materials that is similar to mucin and probably corresponds to the test substance Hylaform®.

## **Discussion:**

Hylaform® is a viscoelastic gel that is increasingly being used for patients who have become sensitive to bovine collagen or wish an immediate treatment without prior skin testing (as it is prescribed with collagen).

After the injection of Hylaform®, a distinct exudative-granulomatous reaction, which could be reproduced in the intracutaneous test and which found its histological correlate, occurred on our patient. The sensitization probably resulted from the same substance injected underneath the wrinkles 18 months before. Similar reactions during the treatment with collagen (Zyderm®/Zyplast®) have been described (1, 2). In these cases, immunological processes were assumed, however no clear relation to an allergic reaction (according to Coombs and Gell) could be found. Barr et al spoke rather of histological changes, as they appear with granuloma annulare, necrobiosis lipoidica diabetorum and rheumatic nodules. The histological correlate is also similar to the changes resulting from insect bites. However, the authors did not want to entirely exclude an allergic component.

Local side effects after collagen injections such as redness and eczema along the canals caused by the injections appeared in 1.3% from approx. 7000 patients in a study by Castrow et al (3). In most cases, these disappeared within the first 4-6 months, some however remaining visible even after 1 year.

Such side effects during the treatment of wrinkles with hyaluronic acid have not been described up to now. Although, undesired concomitant reactions were observed after intraarticular injection for the treatment of osteoarthritis of the knee by Puttick et al (4). Here pain, redness and swelling, which continued for about 3 weeks, appeared within 24 hours.

Whether immunological or allergic processes are in the foreground of injections of hyaluronic acid, this cannot be explained. The reproducibility of the reaction in the intracutaneous test points to an allergic reaction; the formation of granulomas and the histological result point more to an immunological pathogenesis. The complete regression within 6 weeks is remarkable for it occurs in a considerably shorter period of time than with collagen. Granulomatous reactions have also been increasingly observed by the university clinics in Frankfurt and Regensburg. In summary, this case report indicates that a thorough explanation including all side effects for the patient and an intracutaneous test with later readings are recommendable before an intended reinjection of hyaluronic acid in the treatment of wrinkles. It should be demanded that Hylaform® be only injected by doctors. It is essential to change the leaflet in the package and include the necessary information.

*(For references please contact authors)*

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