

**Case Report**

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**Hybrid cooperative complexes of high- and low-molecular weight hyaluronic acid injections in a patient with a history of pulmonary sarcoidosis****Rossi Elena<sup>1\*</sup>; Spadafora Marco<sup>1</sup>; Caramaschi Stefania<sup>2</sup>; Villarica-Hayano Windie<sup>3</sup>; Trakatelli Myrto<sup>4</sup>**<sup>1</sup>Department of Dermatology, Head and Neck Skin Cancer Service, Modena and Reggio Emilia University, Modena, Italy.<sup>2</sup>Department of Diagnostic, Clinic and Public Health Medicine, University of Modena and Reggio Emilia, Modena, Italy.<sup>3</sup>The Skin Inc Dermatology and laser Center, Manila, Philippines.<sup>4</sup>Second Department of Dermatology, Aristotle University Medical School, Papageorgiou General Hospital, Thessaloniki, Greece.**\*Corresponding Authors: Elena Rossi**

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**Keywords:** sarcoidosis; hyaluronic acid; filler; skin remodeling; skin laxity.**Introduction**

Injectable soft tissue filler procedures are a popular choice for the rejuvenation of the aging face. Thermal cross-linking of high- and low-molecular weight Hyaluronic Acid (HA) yields stable cooperative hybrid HA complexes with higher resistance to enzymatic degradation without the need for chemical agents [1]. Such formulations, such as IBSA Pharmaceuticals' Profilllo, have proven effective and safe both *in vitro* and in a multitude of patients with differing underlying conditions [2].

Sarcoidosis is a multisystemic disease of unknown etiology characterized by the formation of immune granulomas in several organs, primarily in the lung and lymphatic system [3]. The skin is the second most common organ affected in sarcoidosis (25-30% of cases), either as local sarcoïdal granuloma forma-

tion, or as reactive nonspecific inflammation [3]. Tattoos, scars and cutaneous filling procedures have been reported as a potential triggers, and cases have been published reporting granulomatous inflammation in association with almost any kind of filler commercially available [4,5].

**Case report**

A 53-year-old female Caucasian patient was evaluated in Modena (Italy) for initiation of HA treatment for facial skin rejuvenation. The patient's medical history was notable only for mediastinic non-Hodgkin lymphoma diagnosed in 2010, treated surgically and with chemotherapy with complete resolution. At the time of initial evaluation, the patient denied any comorbidities and the use of prescription or illicit drugs. Beginning in 2015, over the course of 5 years the patient was treated with

2-4 sittings a year of HA injections. The HA in question was ultrapur grade, in a formulation of thermally-stabilized, cooperative hybrid HA complexes (Prophilo; IBSA). Injections were performed following IBSA's specifically developed Bio Aesthetic Point (BAP) technique for the bioremodeling of the malar and submalar areas, consisting of 0.2 mL boluses delivered with a 29G needle in the superficial layer of 5 symmetric anatomically receptive areas (total 64 mg of HA in 2 mL):

- at the zygomatic protrusion;
- at the nasal base;
- anterior to the tragus;
- lateral to the midline on the chin;
- and superior to the mandibular angle.



**Figure 1:** Pre-treatment (2015) and progress photographs from 2016 to 2020.

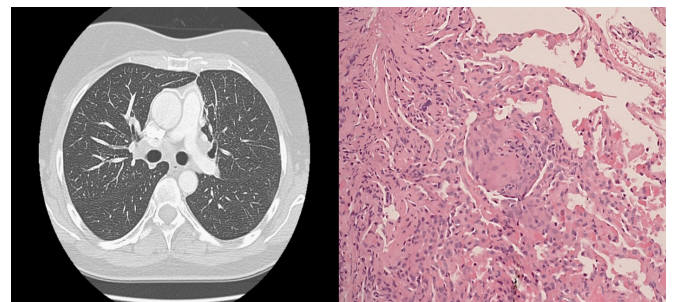
## Discussion

To the best of our knowledge, and after review of published clinical experience, this seems to be the first reported case of a patient with a history of sarcoidosis being regularly treated with HA injections without reporting adverse effects or sarcoidal cutaneous manifestations. Disease dormancy, filler composition or sheer luck can all be posited as potential factors. The absence of BDDE or other cross-linking chemicals in Prophilo's formulation makes the product more biocompatible than other traditional dermal fillers, possibly reducing the risk of foreign body reactions and granuloma formation.

Despite the positive clinical course of the patient in question, this publication is no way intended to encourage the use of injection HA treatment in patients with sarcoidosis. It should however serve as a reminder to specialists in the field to thoroughly interview patients with regard to prior medical conditions which may constitute a contraindication to treatment, and hence be erroneously omitted by patients.

Pre-treatment (2015) and progress photographs from 2016 to 2020 are reported in Figure 1.

During a conversation regarding tattoos in 2019, the patient reported having been diagnosed with histologically-confirmed pulmonary sarcoidosis in 2010 (Figure 2), and having been treated with 25 mg prednisone daily for 2 months with complete resolution of symptoms. The patient denied any subsequent symptoms, flares or relapses. Despite having been informed of the increased risk of cutaneous granuloma formation associated with dermal injections due to her personal history of sarcoidosis, the patient opted for continuing treatment and is currently still receiving HA injections twice a year. Hitherto no skin nodules nor other adverse cutaneous manifestations have been reported.



**Figure 2:** Left side: CT scan shows minimal septal thickening, in particular in the anterior segment of the left upper lobe and lower lingular lobe, associated with traction bronchiectasis. Symmetric hilar and mediastinal lymphadenopathy, particularly at the prevascular, aortopulmonary, pre- and subcarinal level. Such findings are compatible with a diagnosis of granulomatous disease (sarcoidosis). Absence of pleuro-pericardial effusion.

**Right side:** Histopathology of lung biopsy shows a non-caseating granuloma consisting of a well-formed and circumscribed conglomerate of epithelioid- and multinucleated-giant cells surrounded by occasional lymphocytes, typical of sarcoidosis.

## Declarations

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