



## A Multilayer Hyaluronic Acid Approach for Vulvovaginal Atrophy: A Case Report

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### Abstract

**Background:** Vulvovaginal atrophy is associated with structural and functional changes that may significantly affect quality of life, particularly in patients with limited eligibility for hormonal therapy.

**Case Presentation:** A 48-year-old woman with symptoms of vulvovaginal discomfort and sexual dysfunction was treated using a multilayer approach combining PEGDE-crosslinked and non-crosslinked hyaluronic acid formulations.

**Results:** Improvement in tissue condition was observed using the VeTH scale, with resolution of most parameters. The total FSFI-6 score increased from 6.0 at baseline to 24.0 at 6-week follow-up, indicating a clinically meaningful improvement in sexual function.

**Conclusion:** This case suggests that a multilayer hyaluronic acid hydrogel-based approach may represent a safe and effective non-hormonal option for the management of vulvovaginal dysfunction.

**Keywords:** Vulvovaginal atrophy, Hyaluronic acid; Multilayer approach; PEGDE-crosslinked hyaluronic acid; Calcium hydroxyapatite; Sexual function

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### Introduction

Women experience a gradual decline in hormonal activity starting in their forties, ultimately leading to menopause. Reduced levels of estrogen and androgens are associated with structural and functional changes within the vulvovaginal tissues, including decreased elasticity, reduced adipose tissue in the labia majora, and increased tissue sensitivity. These alterations may result in diminished lubrication, heightened sensitivity to mechanical stimuli, and activation of nociceptive pathways, contributing to pain and discomfort [1]. While hormonal therapies remain the standard approach, their long-term use may be limited, and some patients, particularly those with a history of oncological disease or chronic conditions may not be suitable candidates for such treatments. This highlights the need for effective non-hormonal therapeutic options [2]. Injectable Hyaluronic Acid (HA)-based treatments have gained increasing attention as a potential approach to improving tissue hydration, elasticity, and structural support. In the vulvovaginal region, cross-linked HA may provide not only volumetric enhancement but also functional benefits, contributing to improved tissue integrity and protection of sensitive anatomical structures [3,4].

Loss of volume or structural support of the labia majora, whether age-related or secondary to childbirth or weight loss, may disrupt the anatomical balance of the vulvar region. This may lead to increased exposure of the vestibule and labia minora, resulting in heightened sensitivity, discomfort, and dyspareunia. In such cases, restoration of the anatomical contour of the labia majora may improve both mechanical protection and overall patient comfort [4]. Beyond volumetric effects, HA-based treatments may also support tissue hydration and contribute to the maintenance of the extracellular matrix environment within the lamina propria. This layer, rich in fibroblasts, collagen, and elastic fibers, plays a key role in preserving tissue resilience and function [5].

Sexual dysfunction significantly affects quality of life and intimate relationships; given the multifactorial nature of vulvovaginal dysfunction, functional impairment and anatomical alterations



**Figure 1:** Clinical photographs before, during and after treatment demonstrating improvement in vulvovaginal tissue condition.

frequently coexist, requiring a comprehensive and individualized approach [6-9]. Various injection techniques have been proposed to address functional symptoms and restore tissue hydration in the vulvovaginal area; however, standardized treatment protocols are yet to be established.

The aim of this case report is to present the effectiveness and safety of a combined approach using a Poly) Ethylene Glycol) Diglycidyl Ether (PEGDE) crosslinked hyaluronic acid as a non-hormonal strategy for the management of vulvovaginal discomfort and sexual dysfunction.

### Case Description and Treatment Approach

A 48-year-old perimenopausal woman, with a normal Pap smear, normal gynecological ultrasound, and negative vulvovaginal swabs, presented seeking vulvovaginal rejuvenation due to symptoms consistent with vulvovaginal atrophy. These included dryness, vulvar itching, vestibular burning independent of sexual activity, pain, and post-coital microlesions. She also reported anhedonia and dyspareunia during intercourse, with post-coital vaginal burning and dysuria. Vulvar itching unrelated to sexual activity was exacerbated by wearing underwear and panty liners, causing persistent daily discomfort. A layered treatment approach using different Hyaluronic Acid (HA) formulations was proposed to address multiple aspects of the condition simultaneously and to improve overall tissue quality. In this case, the following products were used: a PEGDE-crosslinked HA (28 mg/mL; Neauvia Intense Rose), a PEGDE-crosslinked HA (26 mg/mL) enriched with Calcium Hydroxyapatite (CaHA) (Neauvia Stimulate), and a non-crosslinked HA (18 mg/mL) enriched with CaHA (Neauvia Hydro Deluxe Rose). All products contained glycine and proline, amino acids commonly associated with collagen structure and metabolism. The procedure was performed with the patient in the gynecological position following standard disinfection of the external genital area. Local anesthesia was achieved by injecting 1 mL of lidocaine into the subcutaneous tissue of the labia majora bilaterally, approximately 1 cm from the vestibular margin. Access was obtained using a 16 G needle, followed by the use of an 18 G cannula. From the entry point, 1 mL of PEGDE-crosslinked HA (28 mg/mL, with glycine and proline) was injected into the deep dermis using a retrograde fan technique. The procedure was performed symmetrically on both sides, ensuring even distribution of the product and restoration of the natural contour of the labia majora. This technique allows for volumization while preserving natural anatomy and minimizing the risk of uneven product distribution. A second layer was then applied using 0.5 mL of PEGDE-crosslinked HA (26 mg/mL) supplemented with 1% CaHA, glycine, and proline, injected into the superficial dermis using the same retrograde

fan technique. The total volume of crosslinked HA did not exceed 1.5 mL per side. In the vulvar vestibule, a non-crosslinked HA (18 mg/mL, with 0.01% CaHA, glycine, and proline) was administered using a three-point injection technique (V-spot), consisting of three injections of 0.1 mL each (one central and two lateral). Additionally, targeted microinjections of the same formulation were performed in selected anatomical areas, including the clitoral region (so-called O-shot) and the anterior vaginal wall (so-called G-spot), in the lower third of the vagina, approximately 1.5 cm from the urethral meatus, using small volumes (0.1 mL per point).

Written informed consent was obtained prior to the procedure; the treatment approach was selected based on clinical judgment and individual patient assessment.

### Results

Changes in vestibular tissue condition were assessed using a Vestibular Trophic Health (VeTH) scale, a multi-item clinical tool incorporating evaluation of petechiae, pallor, thinning, dryness, and redness (10), where lower scores indicate improved tissue condition. At baseline, the patient presented with impaired vestibular trophism, with VeTH scores indicating the presence of petechiae (1), pallor (2), thinning (3), dryness (3), and redness (1). Following treatment, a marked improvement was observed across all assessed parameters. Petechiae, pallor, dryness, and redness resolved completely (score 0), while thinning showed a substantial reduction (from 3 to 1) (Table 1). These findings were consistent with the clinical observation of improved mucosal hydration, color, and tissue integrity, as well as with the patient-reported reduction in burning and discomfort.

The FSFI-6-6 is a validated 6-item short-form screening tool widely used in female sexual medicine research [11]. It comprises one question per domain (desire, arousal, lubrication, orgasm, satisfaction, and pain), each scored from 0 or 1 to 5, reflecting sexual function over

**Table 1:** VeTH scale scores before and after treatment (0 = absent, higher scores indicate greater impairment).

	petechiae	pallor	thinning	dryness	redness
Before	1	2	3	3	1
After	0	0	1	0	0

**Table 2:** FSFI-6 domain scores and total score before and after treatment. Domain scores are weighted; total score ranges from 2.0 to 36.0.

	desire	arousal	lubrication	orgasm	satisfaction	pain
Before	2	1	1	0	1	1
After	4	4	4	3	5	4

the previous four weeks. The total score is the simple sum of the six item scores, ranging from 2 to 30, with higher scores indicating better sexual function. A total score of 19 or below indicates female sexual dysfunction. In this case, the total FSFI-6-6 score increased from 6 at baseline to 24 at 6-week follow-up (Table 2), representing a clinically meaningful improvement in tissue condition compared to baseline as illustrated in the clinical photographs (Figure 1).

## Discussion

Over the past decade, there has been a growing use of both Hyaluronic Acid (HA)-based treatments and energy-based devices in the management of sexual dysfunction, vaginal laxity, and Genitourinary Syndrome of Menopause (GSM), as well as in improving the appearance of the external genitalia. Several studies have confirmed the efficacy and safety of HA injections in the labia majora, with satisfactory results and a low rate of adverse events [3,12]. Despite growing demand for such procedures, the evidence base remains limited and standardized protocols have not yet been established. The use of HA allows for meaningful tissue revitalization using a relatively simple outpatient procedure with a low risk of complications [3,12]. In the presented case, a PEGDE-crosslinked HA hydrogel was selected for its potentially favorable safety profile compared to conventional crosslinking agents. PEGDE may reduce immune recognition of the complex, thereby lowering immunogenicity and antigenicity [3,13,14]. This material demonstrates biomimetic properties supporting physiological tissue integration, high biomechanical compatibility, favorable rheological characteristics, and a reduced inflammatory profile [13,14]. These properties may also support its compatibility with energy-based co-treatments [10].

In this case, the use of different HA formulations was associated with improvement across all evaluated domains, including both functional and aesthetic aspects. Treatment with HA-based fillers in the labia majora is a repeatable and reversible procedure with a low adverse event profile, making it a valuable therapeutic option in the management of hypotrophy in this area. It should be noted that certain components of the treatment protocol, including injections in the clitoral region and anterior vaginal wall, remain investigational techniques with limited published evidence regarding both efficacy and safety. These were applied based on clinical judgment and informed patient consent, but their contribution to the observed outcomes cannot be isolated in this case. The main limitations of this report include the small sample size (n=1), the absence of a control condition, the short follow-up period (6 weeks), and the use of assessment instruments that are partially subjective. Nonetheless, the post-treatment FSFI-6 total score of 24, exceeding the diagnostic cutoff of  $\leq 19$ , indicates that the patient no longer met the criteria for female sexual dysfunction at the 6-week timepoint. Further studies with larger patient populations and extended follow-up are needed to confirm these findings and establish optimal treatment protocols.

## Conclusion

This case report suggests that a multilayer approach combining PEGDE-crosslinked and non-crosslinked HA formulations supplemented with CaHA may represent a safe and effective non-hormonal option for vulvovaginal discomfort and sexual dysfunction,

addressing both structural and physiological aspects of the condition. The physicochemical properties of PEGDE-crosslinked HA may further support its compatibility with energy-based co-treatments, potentially enhancing combined therapy outcomes.

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