

CASE REPORT

**MULTIPLE LOWER EYELID NODULES IN BREAST CANCER
PATIENT WITH HISTORY OF DERMAL FILLERS:
A CASE REPORT**

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ABSTRACT

Introduction: Dermal filler injections have been associated with several complications, including migration to other areas and forming nodules due to the presence of foreign bodies or granulomatous reactions may develop, which encapsulates the filler. Fillers might also be associated with malignancy. The presence of such complications must be removed with reconstructive surgery.

Patient and Methods: We present a case of breast cancer patient with a history of dermal filler injection to the lower eyelid. The nodules in the lower eyelid was surgically removed, and the lower eyelid, particularly the muscle, was reconstructed to provide a good cosmetic result. The nodules were also pathologically examined to confirm the diagnosis. Reconstruction of the lower eyelid was conducted with care by noting the aesthetic aspects.

Results: A local muscle flap was easy to harvest and handle, and provided good results. It is also important to consider malignancy to treat the patient thoroughly. The pathology examination confirmed the diagnosis of metastasis. This case is unique because the nodules developed in the patient may be associated with metastasis of the cancer or the dermal filler injection.

Summary: Our reconstruction technique leads to a good cosmetic result. There are no sign of complications and recurrence at 3 months following the procedure.

Keyword: lower eyelid nodules, breast cancer, dermal filler, metastasis

Pendahuluan: Injeksi *filler* kulit telah dihubungkan dengan beberapa komplikasi, meliputi migrasi ke area lain, pembentukan nodul sebagai reaksi benda asing, atau reaksi granulomatosa yang mengakibatkan terjadinya enkapsulasi *filler*. *Filler* juga dapat dihubungkan dengan keganasan. Komplikasi yang terjadi hanya dapat ditangani dengan operasi rekonstruksi.

Pasien dan Metodologi: Kami melaporkan kasus pasien kanker payudara dengan riwayat injeksi *filler* kulit pada kelopak mata bawah. Nodul pada kelopak mata bawah diangkat melalui pembedahan, dan kelopak mata bawah terutama otot direkonstruksi untuk memberikan hasil kosmetik yang baik. Nodul juga diperiksa secara patologis untuk mengonfirmasi diagnosis. Rekonstruksi kelopak mata bawah dilakukan dengan hati-hati dan memperhatikan aspek estetika.

Hasil: Flap otot lokal mudah diambil dan dikendalikan, serta memberikan hasil yang baik. Pertimbangan adanya keganasan pada pasien penting untuk penatalaksanaan secara menyeluruh. Pemeriksaan patologi mengonfirmasi diagnosis metastasis. Kasus ini unik karena nodul yang terjadi pada pasien mungkin berhubungan dengan metastasis kanker atau injeksi *filler* kulit.

Ringkasan: Teknik rekonstruksi kami memberikan hasil kosmetik yang baik. Tidak ada tanda-tanda komplikasi dan kekambuhan pada 3 bulan setelah operasi.

Kata Kunci: nodul kelopak mata bawah, kanker payudara, *filler* kulit, metastasis

Conflicts of Interest Statement:

The author(s) listed in this manuscript declare the absence of any conflict of interest on the subject matter or materials discussed.

INTRODUCTION

Dermal filler injections have been used widely for aesthetic purposes especially in the face. These procedures have gained popularity for their rapid and predictable results. Even when administered by experienced and professional physicians, dermal filler injections might cause some complications such as nodule or granuloma formation (most common), cellulitis, dermatitis, skin necrosis and tyndall phenomenon.¹ Yet, there are many incompetence doctors even not a physician perform these procedures, especially in Indonesia.

The most common used dermal filler is hyaluronic acid (HA) due to the least likely resulting in complication. HA can also be used on the lower eyelid for rejuvenation. However, one possible complication is a chronic inflammation.² The chronic inflammatory reaction might be delayed and recurrent.³ Chronic inflammation is associated with malignancy and metastasis.⁴ We authors report a rare case of lower eyelid nodules associated with dermal fillers and breast cancer.

PATIENT AND METHOD

A 44-year-old woman with breast cancer was consulted to a plastic surgeon due to bilateral lower eyelids blepharitis. Ophthalmologist did not find any abnormalities in both eyes. She did not feel any pain, tenderness and itchiness, only slight soreness. because the swelling was getting bigger within time (Figure 1).



Figure 1. 44 year-old woman with breast cancer presented with swelling on right lower eyelids.

One year prior to consultation, she had dermal filler injections into her both lower eyelids. After that, she felt swelling on the lower eyes. She had her eyes checked by ophthalmologist but the result was normal. Then, the swelling was getting larger within time. From physical examination, diffuse swelling with multiple irregular subcutaneous nodules in the lower right eye was found. We diagnose the

patient with chronic inflammation caused by dermal fillers based on the history and clinical manifestation. The swelling subsided with antibiotics and anti-inflammatory agents. However, the skin nodules persisted (Figure 2).



Figure 2. After administration of antibiotics and anti-inflammatory agents, the swelling subsided but the skin nodules persisted

Then, excision and reconstruction surgery was performed for therapeutic and diagnostic. Transcutaneous lower blepharoplasty technique was used. Incision along the lower lid transcutaneous (subciliary) was made. There were multiple white spots along the subcutaneous and muscle area. Multiple masses were felt and seen along the muscle. Excision of the white spots and masses was conducted and sent to the pathology (Figure 3). Local muscle flap (orbicularis oculi) was elevated and preserved to support the lower eyelid (Figure 4).

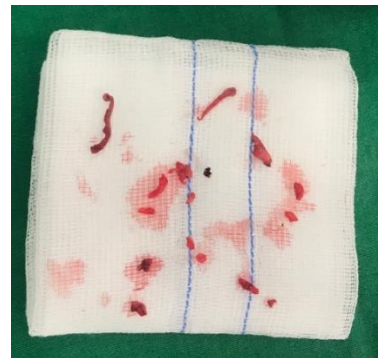


Figure 3. Multiple masses were excised and sent to pathology department.



Figure 4. Local muscle flap was elevated and preserved to support the lower eyelid.

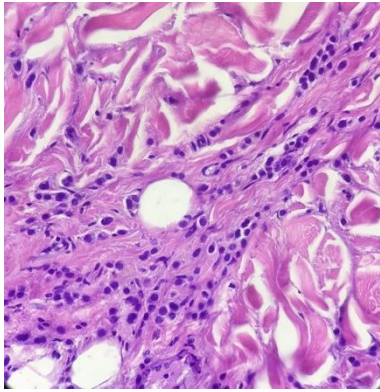


Figure 5. Pathology examination

RESULTS

Three months after the surgery, there was no complication. The patient was satisfied with the surgery result. Histologic examination revealed that the nodules were invasive lobular carcinoma metastasis (Figure 5). In the end, the patient was referred to the former oncologist for further treatment.

DISCUSSION

The lower eyelid nodules in the patient was first diagnosed as chronic inflammation due to history of HA filler injection.³ A 5-year retrospective review showed a case of HA, the most common filler used, caused unseen, painless yet palpable nodules.¹ These nodules might be developed because of body reaction to the foreign bodies. HA among other dermal fillers was the least likely resulting in complication. HA filler injections had been used in the lower eyelid for nonsurgical rejuvenation.² Chronic inflammation and nodules development as delayed complications of HA fillers had been reported in several studies.⁵⁻⁷ The first treatment given to the patient, antibiotic and anti-inflammatory agents, were accordance to the initial diagnosis. Those treatments had been reported to successfully treat inflammatory nodules due to HA filler.¹ Yet, the lower eyelid nodules still not subsided after those treatments.

Metastases to the eyelid were very rare, representing only 0.1-0.3% of all eyelid lesions.⁸ In breast cancer patients, cutaneous metastases only occurred in small number. Breast cancers had the highest rate of cutaneous metastases among internal malignancies which accounted for 35% to 40%.⁹⁻¹⁰ Infiltrating ductal carcinoma was the most type of breast cancers that causing

cutaneous metastases. While, lobular carcinoma type, which is the same with the case, was only accounted for 15% of cutaneous metastases from breast cancers. Cutaneous metastases might be the first sign of breast cancer metastases.¹¹ The most common location was on the chest ipsilateral to the primary breast malignancy.¹²

The relationship between HA and malignancy had been observed. HA was an essential element of the extracellular matrix of all animal tissues. It regulated several normal physiological processes such as diffusion of nutrients, metabolites, and hormones between cells. HA was also involved in wound healing process such as stimulates fibroblast proliferation, migration and collagen production.¹³ HA also regulated cell proliferation and motility through the cell membrane receptor CD44.¹⁴ HA has been used as a dermal filler through tissue engineering application.¹⁵ HA was likely contributing to tumor cell growth, proliferation, and metastases via its interaction with the CD44 receptor.¹⁶

Chronic inflammation had been thought to be associated with malignancy. Many cancers arose from infections, chronic irritation and inflammation. Inflammatory cells were the main components in the neoplastic processes such as cell proliferation, survival and migration.¹⁷ Various inflammatory mediators substantially contributed to metastasis, facilitated tumour cell invasion, extravasation and metastatic outgrowth.^{18,19} In this case, we were wondering whether chronic inflammation because of dermal filler might be related to the metastasis.

After excision surgery, reconstruction of the lower eyelid in this patient were using the transcutaneous blepharoplasty method. This technique might be associated with several complications such as lower eyelid malposition, lid retraction and ectropion.²⁰ Transconjunctival lower eyelid blepharoplasty might reduce the risk of lower eyelid retraction.²¹ It was also important to use local muscle flap (orbicularis ori) to support the eye and prevent the complication. Another strategy was lateral canthal support to obtain an excellent aesthetic result and maintain the natural appearance of the eyelid shape.²⁰ In this case, we did those strategies and the result was excellent.

SUMMARY

Nodules found in patient with history of dermal fillers is not always caused by the foreign body reaction. It is important to think of malignancy when doing surgeries as a plastic the possibility of malignancy although it is very rare such as in this case. We suggest there might be a correlation between dermal filler injection and metastasis. Further studies are needed to find an association between hyaluronic acid dermal filler with malignancy. Reconstruction of the lower eyelids should be conducted with careful and think about the aesthetic unit to avoid any complications. To the best of our knowledge this is the first report of breast cancer metastasis to lower eyelids related to dermal fillers.

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REFERENCES

- Daines SM, Williams EF. Complications Associated With Injectable Soft-Tissue Fillers A 5-Year Retrospective Review. *JAMA Facial Plast Surg*. 2013;15(3):226-231.
- Lee S, Yen MT. Nonsurgical Rejuvenation of the Eyelids with Hyaluronic Acid Gel Injections. *Semin Plast Surg*. 2017 Feb;31(1):17-21.
- Artzi O, Loizides C, Verner I, Landau M. Resistant and recurrent late reaction to hyaluronic acid-based gel. *Dermatol Surg*. 2016;42:31-37.
- Shalapour S, Karin M. Immunity, inflammation, and cancer: an eternal fight between good and evil. *J Clin Invest*. 2015 Sep;125(9):3347-55.
- Bhojani-Lynch T. Late-Onset Inflammatory Response to Hyaluronic Acid Dermal Fillers. *Plast Reconstr Surg Glob Open*. 2017 Dec;22;5(12):e1532.
- Haneke E. Managing complications of fillers: Rare and not-so-rare. *J Cutan Aesthet Surg*. 2015;8:198-210.
- Alsaad SM, Fabi SG, Goldman MP. Granulomatous Reaction to Hyaluronic Acid: A Case Series and Review of the Literature. *Dermatol Surg*. 2012;38:271-276
- Goodier MA, Jordan JR. Metastatic Breast Cancer to the Lower Eyelid. *Laryngoscope*. 2010;120 Suppl 4:S129.
- Riley FC. Metastatic tumors of the eyelids. *Am J Ophthalmol*. 1970;69(2):259-264.
- Mansour AM, Hidayat AA. Metastatic eye lid disease. *Ophthalmology*. 1987;94(6): 667-670.
- Mayer JE, Maurer MA, Nguyen HT. Diffuse cutaneous breast cancer metastases resembling subcutaneous nodules with no surface changes. *Cutis*. 2018 Mar;101(3):219-223.
- Lookingbill DP, Spangler N, Helm KF. Cutaneous metastases in patients with metastatic carcinoma: a retrospective study of 4020 patients. *J Am Acad Dermatol*. 1993;29(2, part 1):228-236.
- Edwards PC, Fantasia JE. Review of long-term adverse effects associated with the use of chemically-modified animal and nonanimal source hyaluronic acid dermal fillers. *Clin Interv Aging*. 2007;2(4):509-19.
- Stern R. 2003. Devising a pathway for hyaluronan catabolism: are we there yet? *Glycobiology*, 13:r105-15.
- Fakhari A, Berkland C. Applications and emerging trends of hyaluronic acid in tissue engineering, as a dermal filler and in osteoarthritis treatment. *Acta Biomater*. 2013 Jul;9(7):7081-92.
- Hill A, McFarlane S, Johnston PG, et al. The emerging role of CD44 in regulating skeletal micrometastasis. *Cancer Letts*. 2006;237:1-9.
- Coussens LM, Werb Z. Inflammation and Cancer. *Nature*. 2002 Dec 19; 420(6917): 860-867.
- Peinado H, Lavotshkin S, Lyden D. The secreted factors responsible for pre-metastatic niche formation: old sayings and new thoughts. *Semin Cancer Biol*. 2011;21, 139-146.
- Qian BZ, Pollard JW. Macrophage diversity enhances tumor progression and metastasis. *Cell*. 2010;141, 39-51.

20. Codner MA, Wolfli JN, Anzarut A. Primary Transcutaneous Lower Blepharoplasty with Routine Lateral Canthal Support: A Comprehensive 10-Year Review. *Plast Reconstr Surg.* 2008 Jan;121(1):241-50.
21. Jacono AA, Moskowitz B. Transconjunctival versus Transcutaneous Approach in Upper and Lower Blepharoplasty. *Facial Plast Surg.* 2001 Feb;17(1):21-8.