CASE REPORT
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A Rare Case of Syringomatous Tumor of the Nipple and Breast Reconstruction

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ABSTRACT

Syringomatous tumor, first described in 1983, is a rare benign clinical condition that can affect the breast. Its infiltrative form is often misidentified as malignant pathologies, as it can present as a subareolar lesion with suspicious clinical, mammographic, and ultrasound findings for malignancy. The exact origin of these lesions remains uncertain; however, they may manifest as a unilateral or bilateral subareolar nodule with symptoms such as pain, edema, nipple enlargement, and nipple discharge. Despite local infiltration, there is no evidence of regional or distant metastases. Local complete excision appears to be an adequate therapy, with only cases that were incompletely excised showing recurrence. Below is a case report of a syringomatous adenoma infiltrating the nipple, with complete resection and nipple reconstruction using oncoplastic techniques.

KEYWORDS: breast reconstruction; breast tumor; breast neoplasms.

INTRODUCTION

The areola-nipple complex (ANC) is the origin of various morphologically distinct tumors and related changes, stemming from the unique structures of the nipple, especially the intramammillary ducts, adjacent structures, and intramammillary stroma[1]. The syringomatous tumor of the nipple, a rare benign condition[2], was first described by Rosen in 1983[3].

Although benign, its tendency to infiltrate locally and recur if not completely excised can lead to it being mistaken for a malignancy.

The disease typically presents as a unilateral or bilateral subareolar nodule, accompanied by clinical manifestations such as erythema, pain, edema, nipple distension, and papillary discharge[4]. This case report aimed to address both the rarity of the condition and the significance of differentiating it from breast neoplasms, as well as to describe an alternative technique for nipple reconstruction.

CASE REPORT

A 55-year-old female patient, who experienced menarche at 11 years old and has had three children, her first at age 20, with breastfeeding lasting for 8 months. She had been using hormonal contraceptives for 12 years. She had been regularly consulting a mastologist to monitor nodules since March 2021. A mammogram (MMG) in November 2022 revealed nodular images and focal asymmetries (BI-RADS 3). An ultrasonography (USG) performed the same month showed a heterogeneous area of 2 cm at 9 o'clock and 4 cm from the nipple, which could correspond to either breast tissue or a solid nodule in the right breast (NRB), and another NRB of 0.8 cm at 6 o'clock and 3 cm from the nipple (BI-RADS 3); these nodules had been stable since August 2022. A fine needle aspiration (FNA) of the NRB at 9 o'clock revealed rare groups of typical ductal cells. During a routine consultation in November 2022, increased hardness was observed in the right nipple, covering more than two-thirds of its surface (Figure 1).

A magnetic resonance imaging (MRI) scan was requested, revealing intra-nipple enhancement in the right nipple extending 0.9 cm, categorized as BI-RADS 4. Additionally, a solid nodule in the left breast (NLB) was detected at 5 o'clock, 4.7 cm from the nipple, with a type II curve (Figure 1).

In February 2023, she underwent excision of two mammary nodules in her right breast and an incisional biopsy of the right nipple. The anatomopathological examination revealed that the nodules were fibroadenomas, measuring 1.2 cm and 0.6 cm. The nipple biopsy showed a syringomatous tumor of the nipple with compromised margins (specimen: 0.8 cm). Immunohistochemistry

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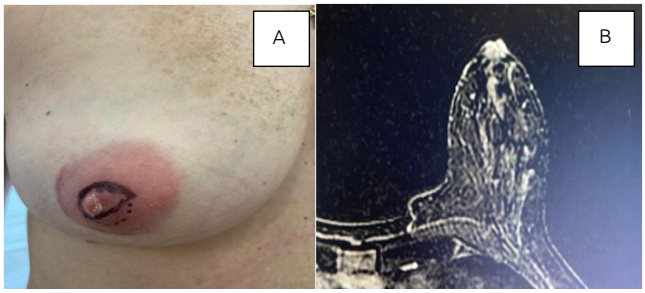

Figure 1. (A) Lesion in the right nipple affecting more than half of its volume and (B) MRI showing enhancement within the right nipple.

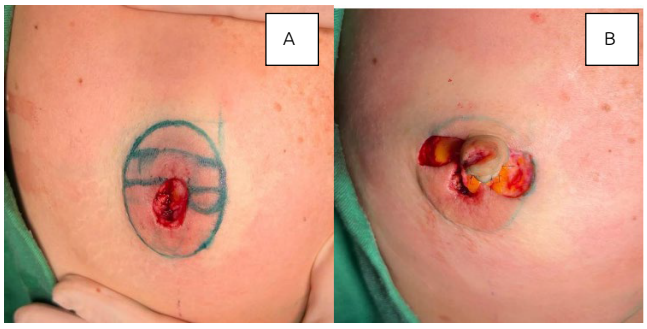

Figure 2. (A) Right breast after nipple resection with planned incision for the neomamilo and (B) assembly of the nipple after bringing the cylinder together.

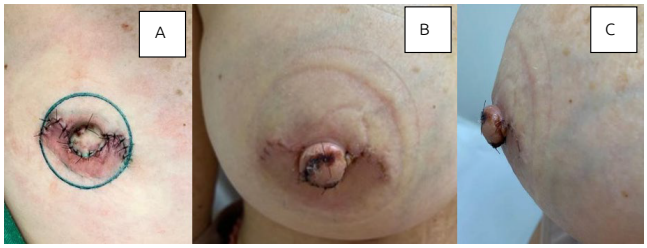

Figure 3. (A) Neomamilo after approximation of the areolar flaps to the nipple (immediate) and seventh postoperative day, (B) frontal view, and (C) lateral view.

confirmed the diagnosis, showing positivity for markers p63, cytokeratins 5/6, 14, and 8/18, estrogen receptor (ER) positive, and ki67 at 5%.

After analyzing the exams and reassessing the patient, it was decided to perform a complete resection of the tumor with margins and immediate nipple reconstruction. The surgery took place on July 20th, 2023. The entire right nipple and part of the base of the areola were resected (Figure 2).

After removing the nipple, it was sent for freezing and evaluated macroscopically, showing free margins. For nipple reconstruction using local flaps, and considering the patient did not have a contralateral donor nipple, the double-opposed periareolar/pouch flap technique was chosen. Modifications were made to the technique, positioning the upper closure portion of the nipple projection, which is normally central, laterally. The wings of the flap were marked with measurements of 1 cm in width and 1 cm at the base. Dissection began with the external wings, elevating them with a thin layer of subcutaneous fat. The papilla was then assembled and sutured together (Figure 2). The areolar flaps were sutured to the base of the papilla, and the incisions were approximated using single stitch sutures (Figure 3).

On the seventh postoperative day (POD), the areola stitches were removed (Figure 3), and on the 14th day, the stitches on the nipple were removed. The anatomopathological examination revealed a 1.5 cm syringomatous tumor of the nipple with free margins. The patient is currently scheduled for areola micropigmentation.

DISCUSSION

A syringomatous tumor typically presents as a solitary firm mass in the subareolar region or on the nipple and can occur within the breast parenchyma[2]. It may be clinically asymptomatic, sensitive, and painful on palpation, and/or present with itching and ulceration. The size varies from 1 cm to 3 cm in diameter[4]. The average age at presentation is 40 years, with an age range from 11 to 76 years[3]. Nipple inversion or discharge may be present[5]. It can be pathologically misdiagnosed as ductal breast carcinoma, which can lead to delays or errors in diagnosis. Timely management with histopathological correlation is essential, as it allows for less invasive surgical methods.

The imaging findings of a syringomatous tumor often resemble those of malignant tumors, making it difficult to distinguish from carcinoma on imaging studies such as MMG, USG, and MRI[2]. On MMG, it may appear as a high-density mass in the subareolar region with an irregular contour, spicules, or microcalcifications. On USG, it typically presents as a poorly defined mass with heterogeneous internal echoes[4]. Since fine needle aspiration or needle biopsy often fails to provide a definitive diagnosis, many cases are reported as suspected malignancies[4].

Some researchers have reported the usefulness of immunohistochemical staining for p63 or S-100 protein[5,6]. However, in the present study, staining was performed for Ki-67, a prognostic and predictive marker for breast cancer[7]. Ki-67 is expressed during the G1, S, G2, and M phases of the cell cycle but not during the resting G0 phase. Therefore, high levels of Ki-67 indicate a tumor with high proliferative potential. In other words, Ki-67 staining helps differentiate between benign and malignant tumors and predict prognosis.

The presence of a myoepithelial layer in syringomatous tumors is not completely indisputable, but it is commonly mentioned in the literature due to positive reactions for "myoepithelial cell markers" such as p63 or Ck5/6. Recently, however, immunohistological findings have demonstrated that syringomatous tumors of the nipple are p63+ Ck5/14+ proliferations of progenitor cells in the nucleus,

which differentiate into glandular (Ck8/18) and squamous cells (Ck10/13). Differentiations into myoepithelial cells (actin, CD10, calponin, etc.) are much rarer and usually only focal in these tumors. Therefore, in the context of syringomatous tumors, the expression of p63 and high molecular weight cytokeratins Ck5 and/or Ck14 cannot be used as an indication of myoepithelial differentiation[1].

Pathologically, the tumor appears grossly ill-defined, with a firm to resistant consistency and a gray or white cut surface[8]. Histologically, the lesion is composed of tubules, ducts, and strands of small, uniform, generally basophilic cells that infiltrate the dermis of the surrounding skin and the stroma of the nipple[8]. Proliferating ducts, lined by one or multiple layers of metaplastic squamous cells, may be present. These cellular nests often have a teardrop or comma-shaped appearance, and tumor cells can infiltrate the stroma between smooth muscle bundles and even into the perineural region[4].

Histologically and clinically, syringomatous adenoma of the nipple is often mistaken for tubular carcinoma or low-grade adenosquamous carcinoma of the breast. Special attention from pathologists and clinicians is crucial to avoid incorrect diagnoses and unnecessary treatments[4].

The histopathological diagnostic criteria for syringomatous tumor include:

- Location in the dermis and subcutaneous tissue of the nipple or areola;
- Irregular tubules, compressed or comma-shaped, infiltrating into bundles and/or smooth muscle nerves;
- Presence of myoepithelial cells around the tubules;
- Presence of cysts lined with stratified squamous epithelium and filled with keratinized material;
- Absence of mitotic activity and necrosis[4].

Due to its rarity, the syringomatous tumor presents an intriguing diagnostic challenge. Differential diagnoses include primary malignant breast carcinomas such as low-grade adenosquamous carcinoma and tubular carcinoma. Tubular carcinoma typically occurs deep in the breast, often located in the upper quadrant, lateral to or away from the nipple. If it extends to the nipple, it may cause nipple retraction or Paget's disease. Tubular carcinoma is also more commonly ER positive, whereas syringomatous tumors are usually ER negative. Syringomatous tumors are benign and have not been reported to metastasize. However, they can exhibit local recurrence if not completely resected[6]. Therefore, the ideal initial management involves complete resection with histologically negative margins. If the margins appear involved, reexcision is recommended.

In patients with negative margins after removal of the entire syringomatous tumor, there was no evidence of recurrence during a follow-up period of 1 to 6 years[9]. However, patients with positive margins after local surgical excision experienced tumor recurrence[10]. Therefore, careful monitoring to detect local recurrence is considered necessary[5]. Most recurrences were treated with local reexcision. However, since syringomatous tumors of the nipple generally occur in the dermal and subcutaneous regions of the nipple or areola[3]; appropriate management often requires total resection of the ANC.

If the tumor is so close to the nipple that preserving it is impossible, and the patient wishes to preserve it, an appropriate treatment regimen must be selected. In these cases, however, careful postoperative monitoring is mandatory[2]. Jones et al.[10] reported recurrence times ranging from 1.5 months to 4 years. Therefore, the duration of follow-up should exceed 5 years if complete resection is not performed.

We opted for complete resection of the lesion, which occupied more than 2/3 of the nipple. This resulted in the excision of the entire nipple and part of the areola, yielding a 1.6 cm specimen with free margins. We also chose to perform immediate nipple reconstruction.

CONCLUSION

Nipple adenoma, also known as syringomatous cystadenoma, is a rare type of benign tumor that can occur on the skin or cutaneous appendages, such as sweat glands and sebaceous glands. Clinically, it mimics Paget's disease of the nipple or malignant breast lesions. Due to its rarity, nipple adenoma can easily be overlooked as a differential diagnosis in clinical practice.

The possibility of a syringomatous tumor should be considered when a patient presents with nipple discharge and erosion, with or without a palpable nodule beneath the nipple. This condition also presents a challenge for histological diagnosis. Accurate histological and immunohistochemical analysis is important to distinguish nipple adenoma from invasive carcinoma.

Due to the risk of recurrence, resection with clear margins should generally be recommended. In cases where resection results in compromised margins, follow-up may be required.

Written informed consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal. This report was approved by the Ethics Committee under number 6.639.583.

AUTHORS' CONTRIBUTIONS

JLAA: Writing – original draft, Writing – review & editing, Supervision, Validation. UWS: Project administration, Resources, Software. MLMD: Formal analysis, Investigation, Funding acquisition. WP: Formal analysis, Conceptualization, Data curation, Investigation, Funding acquisition. DTSMN: Project administration, Formal analysis, Conceptualization, Data curation, Writing – original draft, Writing – review & editing, Investigation, Methodology, Funding acquisition, Resources, Software, Supervision, Validation, Visualization.

REFERENCES

1. Gutjahr E, Streng A, Aulmann S, Flechtenmacher C, Toberer F, Heil J, et al. Pathologie der Mamillenregio. Der Pathologe. 2020;41:515-22. https://doi.org/10.1007/s00292-020-00790-z
2. Ishikawa S, Sako H, Masuda K, Tanaka T, Akioka K, Yamamoto Y, et al. Syringomatous adenoma of the nipple: a case report. J Med Case Rep. 2005;9:256. https://doi.org/10.1186/s13256-015-0739-9
3. Rosen PP. Syringomatous adenoma of the nipple. Am J Surg Pathol. 1983;7(8):739-45. PMID: 6660349.
4. Oo KZ, Xiao PQ. Infiltrating syringomatous adenoma of the nipple: clinical presentation and literature review. Arch Pathol Lab Med. 2009;133(9):1487-9. https://doi.org/10.5858/133.9.1487
5. Carter E, Dyess DL. Infiltrating syringomatous adenoma of the nipple: a case report and 20-year retrospective review. Breast J. 2004;10(5):443-7. https://doi.org/10.1111/j.1075-122X.2004.21518.x
6. Mrklić I, Bezić J, Pogorelić Z, Ilić N, Tadić T, Buljević V, et al. Synchronous bilateral infiltrating syringomatous adenoma of the breast. Scott Med J. 2012;57(2):121. https://doi.org/10.1258/smj.2011.012012
7. Yerushalmi R, Woods R, Ravdin PM, Hayes MM, Gelmon KA. Ki67 in breast cancer: prognostic and predictive potential. Lancet Oncol. 2010;11(2):174-83. https://doi.org/10.1016/S1470-2045(09)70262-1
8. Rosen PP. Patologia mamária. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 2001.
9. Suster S, Moran CA, Hurt MA. Syringomatous squamous tumors of the breast. Cancer. 1991;67(9):2350-5. https://doi.org/10.1002/1097-0142(19910501)67:9≤2350::aid-cncr2820670923≥3.0.co;2-d
10. Jones MW, Norris HJ, Snyder RC. Infiltrating syringomatous adenoma of the nipple. A clinical and pathological study of 11 cases. Am J Surg Pathol. 1989;13(3):197-201. https://doi.org/10.1097/00000478-198903000-00003