Scientific Research Publishing

Case Reports in Clinical Medicine, 2025, 14(10), 573-578
https://www.scirp.org/journal/crcm
ISSN Online: 2325-7083
ISSN Print: 2325-7075

Secretory Carcinoma in the Axilla with Extensive Lymph Node Metastases: A Case Report

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How to cite this paper: Oza, T., Jefferson, J., Murray, G., Fleming, M.D. and Grey, C. (2025) Secretory Carcinoma in the Axilla with Extensive Lymph Node Metastases: A Case Report. *Case Reports in Clinical Medicine*, **14**, 573-578.
https://doi.org/10.4236/crcm.2025.1410073

Received: August 20, 2025
Accepted: October 12, 2025
Published: October 15, 2025

Abstract

Secretory carcinoma is a unique kind of carcinoma, most commonly occurring in the skin, breast, and salivary glands. It has distinct histological features and a characteristic genetic alteration t (12; 15) (p13; q25) translocation, which leads to the expression of the ETV6-NTRK3 fusion gene. This report details the case of a 52-year-old woman who presented with a history of recurrent swelling and tenderness of the right axilla. On examination, an 11.2 × 8.0 cm mass was found deep in the axilla. The tumor was removed through extensive surgery, including lymph node resection. Given the axillary location of the secretory carcinoma, we considered its origin to be either from the skin or axillary breast tissue. In this case, however, the tumor was found deep beneath the dermis, extending into the subcutaneous fat, without any breast tissue identified on histomorphology. Seven out of eight resected lymph nodes showed evidence of metastasis. The axillary location of this large tumor, combined with the extent of lymph node involvement, makes this case particularly unique. We aim to present our experience regarding the diagnosis, pathological analysis, and management of this patient.

Keywords

SCA (Secretory Carcinoma), SCB (Secretory Carcinoma of Breast), IHC (Immunohistochemistry), ETV6-NTRK3, Lymph Node Metastases, Axilla, FISH Testing

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1. Introduction

Secretory carcinomas of the skin share pathological characteristics with mammary-analog secretory carcinomas (MASCs) of the salivary gland and secretory breast carcinomas (SBCs). This novel tumor has only recently been identified in case reports and case series, first appearing in the literature in 2009 [1]. It was initially described in the breast and termed secretory breast carcinoma (SBC). Although the axilla is the most common site for secretory carcinoma of the skin (SCA), cases have been documented throughout the body [2]. Histologically, the tumor demonstrates round to ovoid glands, microcysts, and papillary structures filled with eosinophilic secretions, closely resembling the morphology of secretory carcinomas of the breast and salivary gland [3]. Most patients present between the fourth and seventh decades of life. The ETV6-NTRK3 fusion gene, resulting from the t (12; 15) (p13; q25) translocation, is a well-established molecular hallmark of this tumor type [4]. The prognosis for secretory breast carcinoma is generally favorable [5]. Surgical excision is the primary treatment, with recurrence rates reported as low [6]. We present a case of secretory carcinoma measuring 11.2 × 8.0 cm, originating in the axilla, with seven lymph nodes positive for metastasis.

2. Case Presentation

A 52-year-old woman with a history of swelling and tenderness in the right axilla was referred to surgical oncology, where a biopsy was performed. Histological analysis was consistent with secretory carcinoma. The patient reported that following the biopsy, the mass receded, and no nodule was palpable on physical examination. Despite recommendations for additional diagnostic and clinical evaluation, the patient did not return for follow-up.

Three years later, she returned with renewed swelling in the right axilla, and the mass was noted to be rapidly increasing in size. On physical examination in the surgical oncology clinic, a right axillary subcutaneous mass measuring approximately 12 cm was observed, protruding through the skin and accompanied by multiple enlarged lymph nodes. No signs of infection were present.

A PET scan revealed two hypermetabolic lesions in the right axilla, along with two to three subjacent hypermetabolic lymph nodes suggestive of metastasis. No evidence of distant metastasis was found. Complete surgical excision of the mass was performed via wide resection, along with regional lymph node dissection. The mass and eight lymph nodes were submitted for pathological evaluation.

Gross examination revealed a tumor measuring 11.2 × 8.0 cm, covered with skin and exhibiting surface ulceration. Histopathological analysis showed that the tumor was primarily located deep within the subcutaneous tissue. Epithelial tumor cells were arranged in variably sized glandular, papillary, and microcystic formations, many of which contained acidophilic secretions (**Figure 1**). The tumor cells exhibited eosinophilic cytoplasm, mild to moderate nuclear pleomorphism, prominent nucleoli, and both intracellular and extracellular secretions (**Figure 2**). The overall histology was classified as Grade 1, with a low mitotic rate

and moderate nuclear pleomorphism. All resection margins were confirmed to be free of tumor.

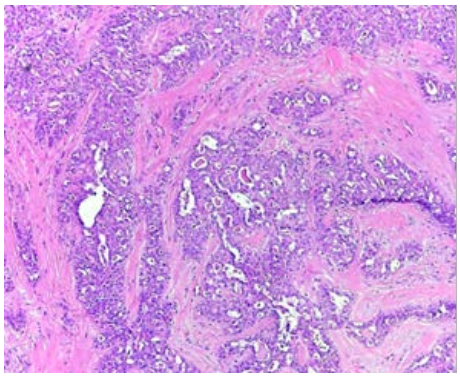

Figure 1. H&E stain (10×) showing secretory carcinoma with glandular features, secretions, and desmoplastic stroma.

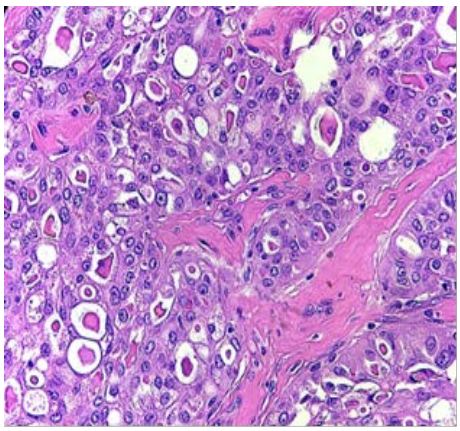

Figure 2. H&E stain (40×) showing glandular and microcystic architecture with luminal acidophilic secretions. Tumor cells exhibit eosinophilic cytoplasm and prominent nucleoli.

Immunohistochemical staining revealed pertinent negative markers, including ER (<1%), PR (<1%), and HER2 (score 0). Positive markers included GATA3, CK7, AE1/AE3, CK5/6, and S100. Based on the histological features, immunoprofile, and axillary location of the tumor, further molecular testing was pursued.

Interphase FISH analysis conducted on the tumor sample identified an NTRK3 (15q25.3) rearrangement in 48.0% of scored nuclei, exceeding the diagnostic threshold of 11.6%.

The combination of NTRK3 rearrangement, histological characteristics, and immunohistochemical profile supported the diagnosis of secretory carcinoma, favoring a cutaneous origin in this patient.

Of the eight submitted lymph nodes, seven were positive for metastatic involvement (**Figure 3**). Four demonstrated macro metastases, with the largest nodal deposit measuring 21 mm. The remaining three positive nodes contained isolated tumor cells.

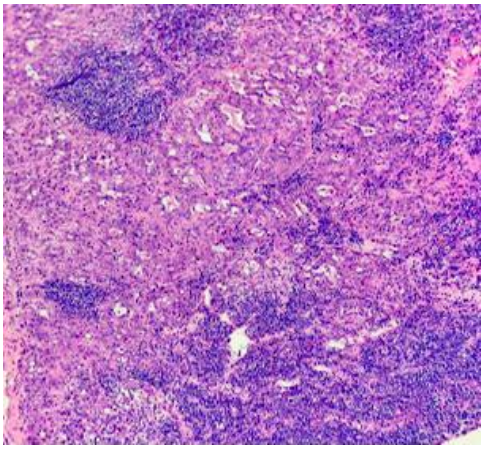

Figure 3. H&E stain (10×) demonstrating lymph node metastasis of secretory carcinoma.

3. Discussion

Secretory carcinomas arising from the skin, breast, and salivary glands share notable similarities in morphology and molecular alterations, suggesting they may represent a unified entity in certain respects [7].

In the present case, a 52-year-old female patient presented with a recurrent axillary tumor. Based on available data, the mean age of patients with secretory carcinoma is 50.3 years, with a median age of 44 years (range: 13 - 98 years), and 29.2% of patients are male. The axilla is reported as the most common site of presentation [7].

From the patient's history, it was evident that she had not undergone appropriate follow-up investigations or treatment during earlier encounters. She was diagnosed with secretory carcinoma involving the axillary region. In cases of axillary secretory carcinoma, the most important differential diagnosis is whether the tumor originates from the skin or the breast. Secretory breast carcinomas (SBCs) have been reported in the tail of the breast and in supernumerary breast tissue located in the axilla.

In our case, gross examination revealed that the tumor was covered by skin, and histologically, tumor cells were located deep beneath the dermis. No breast tissue morphology was identified. As per various studies the median size of SCA is 1.9 +/− 1.7 cm to 2.4 cm, although rare cases have documented tumors as large as 16 cm [8]. In this case, the tumor measured 11.2 × 8.0 cm at the time of resection, significantly exceeding the reported median size. The diagnosis of secretory carcinoma in this patient was supported by the presence of NTRK3 rearrangement, interphase FISH studies, histological features, and immunohistochemical staining patterns.

Treatment plans for secretory carcinoma are developed on a case-by-case basis, depending on patient demographics and tumor characteristics. The generally accepted approach for SCA includes complete tumor excision and lymph node dissection. Radiation therapy is often recommended for adult patients. Evidence sup-

porting the use of chemotherapy and endocrine therapy remains limited, whereas targeted therapy directed at the ETV6-NTRK3 fusion gene has shown promising responses.

Most patients have a favorable prognosis, although a minority may experience distant metastases [9]. Prolonged follow-up is advised in more aggressive cases, particularly those with distant spread or late recurrence. However, most patients maintain an indolent course with excellent outcomes.

In our case, given the primary axillary location of the carcinoma, wide resection of the axilla was an appropriate surgical approach. Due to delays in treatment resulting from lapses in follow-up, a follow-up PET/CT scan and a treatment plan were offered by the medical oncology team.

4. Conclusion

Secretory carcinoma involving the axillary area, particularly with a tumor size of 11.2 × 8.0 cm and associated lymph node metastases, represents a rare clinical entity. Although the patient's treatment course was complicated by gaps in follow-up, she underwent surgical management. With consistent surveillance and appropriate post-resection care, the prognosis remains favorable.

Declaration

Shared with consent for the purpose of advancing education and teaching; though not applicable to de-identified single case reports.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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