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Occult Primary Breast Carcinoma Presenting as Isolated Cervical Lymphadenopathy: A Comprehensive Multimodal Management Approach

ABSTRACT

Background

Occult primary breast carcinoma (OPBC) is a rare clinical entity characterized by nodal metastasis without an identifiable primary breast lesion on imaging. Isolated cervical nodal presentation is exceptionally uncommon and poses significant diagnostic challenges.

Case Presentation

A 70-year-old postmenopausal woman presented with a painless, progressively enlarging swelling in the left posterior cervical region. Clinical breast examination, bilateral mammography, and contrast-enhanced breast MRI did not reveal any primary lesion. Fine-needle aspiration cytology demonstrated metastatic adenocarcinoma. Core biopsy with immunohistochemistry showed strong estrogen receptor and progesterone receptor positivity, GCDFP-15 positivity, CK7 positivity, and negativity for TTF-1 and CK20, confirming breast origin. The disease was staged as cT0 N3c M0 (AJCC 8th edition), Luminal A-like subtype.

The patient underwent selective cervical lymph node excision followed by adjuvant anthracycline-taxane chemotherapy, bilateral whole-breast and comprehensive nodal radiotherapy, endocrine therapy with letrozole, CDK4/6 inhibition with abemaciclib for two years, and adjuvant zoledronic acid.

Outcome

At 18 months of follow-up, the patient remains clinically and radiologically disease-free and has tolerated treatment well.

Conclusion

Isolated cervical lymphadenopathy may represent OPBC in postmenopausal women. Diagnosis relies heavily on immunohistochemistry. A multidisciplinary multimodal approach aligned with current evidence-based recommendations can achieve favorable short-term

outcomes in high-risk cases.

Keywords

Occult breast carcinoma; Cervical lymphadenopathy; ER-positive breast cancer;

Abemaciclib; Zoledronic acid; Multimodal therapy

1. INTRODUCTION

Breast cancer is the most frequently diagnosed malignancy in women worldwide, with approximately 2.3 million new cases reported in 2020 according to GLOBOCAN estimates [1]. Occult primary breast carcinoma (OPBC) is defined as metastatic breast carcinoma presenting without a detectable primary tumor on clinical examination or imaging. It was first described by Halsted in 1907 [2].

OPBC accounts for approximately 0.3–1% of all breast cancers [3]. Most patients present with axillary lymphadenopathy. Presentation as isolated cervical lymphadenopathy is extremely rare and often mimics head and neck malignancies, lymphoma, thyroid carcinoma, or metastatic adenocarcinoma of unknown primary origin [4].

The management of OPBC has evolved from radical surgical approaches to breast-conserving strategies combined with radiotherapy and systemic therapy tailored to tumor biology. We report a rare case of OPBC presenting as isolated left cervical lymphadenopathy in a 70-year-old woman managed with a comprehensive evidence-based multimodal approach.

2. CASE REPORT

2.1 Clinical Presentation

A 70-year-old postmenopausal woman (natural menopause at 52 years) presented with a painless swelling on the left side of the neck of six weeks' duration. She denied dysphagia, odynophagia, hoarseness, weight loss, fever, or night sweats. There was no history of

previous malignancy, radiation exposure, or family history of breast or ovarian cancer.

2.2 Clinical Examination

General examination was unremarkable with ECOG performance status 0. Local examination revealed a firm, non-tender, mobile lymph node measuring 2.5 × 2.0 cm in the left posterior cervical triangle (Level V). No other cervical, supraclavicular, or axillary lymphadenopathy was detected. Bilateral breast examination was normal. ENT evaluation including nasopharyngoscopy did not reveal any primary lesion.

2.3 Investigations

Laboratory investigations including complete blood count, renal and liver function tests were within normal limits. CA 15-3 was mildly elevated at 38 U/mL.

Contrast-enhanced CT of the neck and thorax demonstrated a single enlarged left Level V lymph node without necrosis. No primary lesion was identified in the head and neck region, thorax, or breasts. No axillary lymphadenopathy was noted.

Bilateral mammography was BI-RADS 1. Dynamic contrast-enhanced breast MRI did not identify any primary lesion.

Fine-needle aspiration cytology revealed metastatic adenocarcinoma. Ultrasound-guided core biopsy demonstrated metastatic adenocarcinoma replacing nodal architecture.

Immunohistochemistry results are summarized below:

Table 1. Immunohistochemical Profile

Marker	Result	Interpretation
ER	Strongly positive (>80%)	Supports breast origin
PR	Positive (>60%)	Supports breast origin
GCDFP-15	Positive	Breast specificity
CK7	Positive	Upper tract epithelial origin
HER2	Negative (1+)	Luminal A-like subtype
TTF-1	Negative	Excludes lung/thyroid origin
CK20	Negative	Excludes gastrointestinal origin

The immunoprofile confirmed metastatic carcinoma of breast origin.

2.4 Diagnosis and Staging

A diagnosis of occult primary breast carcinoma with isolated left cervical nodal metastasis was established. According to the AJCC 8th edition, the disease was staged as cT0 N3c M0 [5]. The tumor was ER-positive, PR-positive, HER2-negative (Luminal A-like).

2.5 Management

The case was discussed in a multidisciplinary tumor board.

Surgery

Selective excision of the involved cervical lymph node was performed. Histopathology confirmed metastatic adenocarcinoma consistent with breast origin without extranodal extension.

Chemotherapy

Adjuvant anthracycline-taxane chemotherapy was administered (AC-T regimen): Doxorubicin 60 mg/m² and Cyclophosphamide 600 mg/m² every 3 weeks for 4 cycles, followed by Paclitaxel 175 mg/m² every 3 weeks for 4 cycles.

Radiotherapy

Following chemotherapy, bilateral whole-breast external beam radiotherapy was delivered (50 Gy in 25 fractions). Comprehensive nodal irradiation included left cervical levels II–V, supraclavicular region, axillary levels I–III, and internal mammary chain.

Endocrine Therapy

Letrozole 2.5 mg daily was initiated after radiotherapy with planned duration of at least 5 years.

CDK4/6 Inhibition

Abemaciclib 150 mg twice daily was commenced concurrently with endocrine therapy for a planned duration of 2 years based on eligibility criteria from the monarchE trial [13–16].

Bisphosphonate Therapy

Zoledronic acid 4 mg IV every 6 months was initiated for bone protection and potential reduction in bone recurrence risk [17–20].

2.6 Follow-Up

At 18 months, the patient remains clinically and radiologically disease-free. Treatment was well tolerated. Mild arthralgia from letrozole and low-grade diarrhea from abemaciclib were managed conservatively. Bone mineral density remained stable.

3. DISCUSSION

OPBC is an uncommon entity representing less than 1% of breast cancers [3]. Cervical nodal presentation is particularly rare and often leads to extensive evaluation for head and neck primaries before breast origin is considered.

The exact pathogenesis remains unclear. Hypotheses include spontaneous regression of a microscopic primary tumor or persistence of disease below imaging detection thresholds. Even high-sensitivity breast MRI cannot completely exclude microscopic multifocal disease.

Immunohistochemistry plays a pivotal role in diagnosis. Strong ER and PR expression with GCDFP-15 positivity and absence of TTF-1 and CK20 staining strongly supports breast origin in metastatic adenocarcinoma involving cervical lymph nodes. A structured panel approach prevents misclassification.

Management parallels that of high-risk node-positive early breast cancer. Anthracycline-taxane chemotherapy remains a well-established adjuvant regimen in node-positive disease [27,28]. Sequential administration prior to endocrine therapy is standard practice. The addition of abemaciclib reflects evolving evidence in high-risk HR-positive, HER2-negative disease, with demonstrated improvement in invasive disease-free survival and emerging overall survival benefit in eligible patients [14–16].

Adjuvant zoledronic acid provides both bone protection during aromatase inhibitor therapy and reduction in bone recurrence and breast cancer mortality in postmenopausal women [20].

Bilateral breast irradiation was considered appropriate in this case because tumor laterality could not be determined despite comprehensive imaging. While data remain limited, this strategy may reduce the risk of occult intramammary recurrence in selected patients after multidisciplinary evaluation.

Longer follow-up is required to determine durability of disease control. The rarity of cervical-only OPBC and the relatively short follow-up period limit definitive conclusions regarding long-term outcomes.

4. CONCLUSION

Occult primary breast carcinoma may rarely present as isolated cervical lymphadenopathy. A high index of suspicion and targeted immunohistochemistry are essential for accurate diagnosis. A multidisciplinary multimodal treatment strategy incorporating surgery, chemotherapy, radiotherapy, endocrine therapy, CDK4/6 inhibition, and bisphosphonate therapy can achieve favorable short-term outcomes in high-risk patients.

CONFLICT OF INTEREST

None declared.

FUNDING

No funding received.

ETHICAL STATEMENT

Written informed consent was obtained from the patient for publication.

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