

## Clinical and pathological characteristics of occult breast cancer and review of the literature

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### Summary

**Purpose:** Occult breast cancer is defined as axillary metastasis without clinically and/or radiologically evident primary tumor. In female patients presenting with isolated axillary nodes with adenocarcinoma, the most likely primary cancer is an invasive breast carcinoma. Herein we present our experience over this issue, together with a brief review of the literature about this clinically challenging condition.

**Methods:** We retrospectively analyzed 1215 consecutive breast cancer patients treated at our clinic between 2004-2010. Four of these patients presented with axillary nodal metastasis without clinical and radiological evidence of a primary breast tumor.

**Results:** The incidence of occult breast cancer in our clinic was 0.32%. Median follow-up was 8 months. All patients were alive and remained free of disease at the end of the follow-up period.

**Conclusion:** The prognostic factors for occult breast carcinoma are similar to that of its overt counterpart. The number of axillary lymph node involved and the hormone receptor status are considered significant prognostic predictors. Further studies with randomization and longer follow-up are needed for the establishment of a safe management plan.

**Key words:** axillary metastasis, breast cancer, occult, treatment

### Introduction

Occult breast cancer is defined as axillary nodal metastasis of adenocarcinoma without clinically and/or radiologically evident primary tumor. The differential diagnosis of an adenocarcinoma with metastasis to the axillary lymph nodes includes cancer from the breast, ovary, uterus, lung, thyroid, pancreas, stomach, colon, rectum and kidney. In female patients presenting with isolated axillary nodes harboring adenocarcinoma, the most likely primary cancer is an invasive breast carcinoma. This may arise from an ipsilateral or contralateral primary breast cancer (0.3-1%) [1-4].

The best radiological modality with which to investigate the primary site has been discussed extensively. Most studies suggest magnetic resonance imaging (MRI) when mammography and breast ultrasonography fail to indicate relevant breast pathology [5-9]. Since 1907 when Halsted first identified occult breast carcinoma presenting with axillary metastasis [10],

the treatment of choice has been local treatment (either mastectomy or radiotherapy) with axillary lymph node dissection [11]. Axillary dissection without mastectomy or radiotherapy [11] or even observation alone has been advocated [12]. Further studies found that observation alone showed a higher incidence of subsequent primary breast cancer (14-83%) when compared with patients receiving whole breast irradiation or at least axillary radiotherapy (12-33%) [1,13]. Axillary dissection with subsequent whole breast irradiation is increasingly viewed as the best treatment modality [1,14,15].

In this article we present our experience with occult breast carcinoma, together with a brief review of the literature about this clinically challenging condition.

### Methods

We have retrospectively analyzed 1215 consecutive breast cancer patients treated in our clinic between

2004-2010. Four (0.32%) of these patients presented with axillary metastasis without clinical and radiological evidence of a primary breast tumor. Physical examination was unremarkable. All patients with occult primary tumor underwent bilateral breast contrast-enhanced MRI and CT scan of the chest, abdomen and pelvis. The diagnosis of their axillary disease was confirmed with fine-needle aspiration cytology (FNA) and core biopsy.

## Results

The incidence of occult breast cancer in our clinic among all breast cancer patients was 0.32%. The clinical and pathological characteristics of these patients and the chemotherapy regimens given are summarized in Table 1. Median follow up was 8 months (range 4.8-30). All patients received whole breast irradiation except one with stage IIIC disease who received also regional nodal irradiation. All patients were alive and free of disease at the end of the follow-up period.

## Discussion

Axillary dissection with subsequent whole breast irradiation is increasingly viewed as the best treatment modality in occult breast cancer [1,14,15]. Occult breast disease means T0 cancer at the time of diagnosis and axillary metastasis, which, even at this early stage, might indicate the aggressive nature of the tumor. In a case report by Yamaguchi et al. a lymph node biopsy obtained from a radiologically occult breast cancer was stained positive with VEGF-C and D [16], two markers that are reported to be associated with aggressive behavior in breast cancer [17]. However, the results of several reports show occult breast cancer has a better prognosis than overt disease in comparable stages [18-20].

Previous studies have shown that in most cases benign and malignant lymph nodes could not be reliably distinguished from each other using mammography. In a study by Walsh et al. the only distinguishing feature of a malignant lymph node on mammography was its greater size ( $\geq 34$  mm) [21]. Ultrasonography increases the sensitivity and specificity of the assessment of lymph node nature [22], especially in patients with dense mammary tissue. In a study by Chan et al. the addition of ultrasonography to mammography significantly increased the sensitivity (detection from 78 to 94%) [23]. When ultrasonography fails to show a significant lesion further radiological tests are indicated. MRI of the breast has a high sensitivity of 85-100% and specificity of 35-95% [1,24]. In some studies FDG-PET scan, with or without CT scan, is reported to have sensitivity of 96% and specificity of 100% [1,25]. Despite this sophisticated technology at our disposal, a small number of patients still present with occult breast carcinoma.

In such patients lymph node biopsy should always be obtained to confirm the diagnosis. An adenocarcinoma staining for hormone receptors (ER, PR) in lymph node biopsy strengthens the diagnosis and also provides prognostic and therapeutic insight since the primary tumor may never be found [26,27]. Complete excision of a suspicious lymph node is rarely indicated as core needle biopsy is a safe and minimally invasive method. Rao et al. compared core needle biopsy vs. FNA and sensitivity was 82 and 75%, respectively [28]. We performed FNA followed by core needle biopsy in all our patients.

Once the diagnosis of occult breast carcinoma is made, axillary dissection is indicated in all cases but mastectomy is increasingly replaced by radiotherapy in these cases [29,30]. Studies favoring mastectomy have also been reported [29]. Sentinel node identification poses challenges as in every breast cancer patient. The blue dye does not cross to the contralateral axilla compared to the radioisotopic method. Since sentinel

**Table 1.** Characteristics of patients with occult breast cancer

Patient no.	Age (at diagnosis)	Histology	Lymph node status	Stage	ER/PR/Her-2	Chemotherapy	Hormonotherapy	Radiotherapy	Follow-up (months)
1	43	Infiltrative ductal carcinoma	N1	IIA	+/-	ACX4	+	+	30
2	50	Metastatic carcinoma	N3	IIIC	-/+	TACX6	+	+	8
3	51	Infiltrative ductal carcinoma	N2	IIIA	+/-	TACX6	+	+	4.8
4	50	Metastatic carcinoma	N1	IIA	+/-	ACX4	+	+	26

Tamoxifen and aromatase inhibitors were given for pre and postmenopausal patients.

AC: doxorubicin+cyclophosphamide, TAC: docetaxel+doxorubicin+cyclophosphamide, ER: estrogen receptor, PR: progesterone receptor

lymph node can be found in both axillae, preoperative lymphoscintigraphy in patients with occult axillary metastases of possible breast origin may add important information if applied properly. The prognosis of patients with axillary metastasis without identifiable breast mass is comparable to stage II disease with 5-year survival of 50-87%, depending, at least in part, on the number of lymph nodes involved [18-20]. The prognostic factors of occult breast carcinoma are similar to that of its overt counterpart. The number of axillary lymph node involvement and the hormone receptor status are considered significant prognostic factors [18,19]. Further studies with randomization and longer follow-up are needed for the establishment of a safe management plan.

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