

Axillary Metastasis as the First Manifestation of Occult Breast Cancer in a Male Patient

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Key Words

Male breast cancer · Metastasis · Pathology · Hereditary nonpolyposis colorectal cancer · HNPCC

Summary

Background: The aim of this study was to investigate the clinicopathologic features of male breast cancer. **Case Report:** We present the clinicopathologic data of a 72-year-old male patient with occult breast cancer, who was diagnosed and underwent surgery in our hospital. The diagnosis was confirmed by histological examination, and the patient underwent modified radical mastectomy and axillary dissection. The histological examination showed no tumor foci in the resected breast tissue, but 2 of 15 dissected axillary lymph nodes were invaded by infiltrating ductal carcinoma. Immunohistochemistry staining was negative for both estrogen and progesterone receptors, but showed expression of p53 protein (+++), proliferating cell nuclear antigen (PCNA) (+++), Bcl-2 oncoprotein (+++), nm23 protein (++), multidrug resistance protein (MRP) (++), and human epidermal receptor (HER-2) oncoprotein (+++). 24 months after being diagnosed, the patient is alive without any residual or metastatic disease. **Conclusions:** Breast cancer is very rare in men, and the occurrence of occult breast cancer is even less common. Axillary metastases can present as the first manifestation of breast cancer in a male.

Schlüsselwörter

Mammakarzinom beim Mann · Metastasen · Pathologie · Hereditäres nicht polypöses Kolonkarzinom · HNPCC

Zusammenfassung

Hintergrund: Ziel dieser Studie war es, die klinisch-pathologischen Charakteristika des Mammakarzinoms beim Mann zu untersuchen. **Fallbericht:** Wir stellen die klinisch-pathologischen Daten eines 72-jährigen männlichen Patienten mit okkultem Mammakarzinom vor, der in unserer Klinik untersucht und chirurgisch behandelt wurde. Nach der histologischen Diagnosesicherung wurde eine modifizierte radikale Mastektomie mit axillärer Lymphknotenentfernung durchgeführt. Die histologische Untersuchung ergab keine Tumorfoci im entfernten Brustgewebe, aber 2 der 15 entfernten Achselhöhlenlymphknoten waren von einem invasiven Duktalkarzinom befallen. Die immunhistochemische Färbung war negativ für sowohl Östrogen- als auch Progesteronrezeptoren, aber zeigte positive Expression von p53-Protein (+++), PCNA (proliferating cell nuclear antigen) (+++), Bcl-2-Onkoprotein (+++), nm23-Protein (++), MRP (multidrug-resistance protein) (++) sowie HER-2 (human epidermal receptor)-Onkoprotein (+++). 24 Monate nach der Diagnosestellung ist der Patient am Leben und zeigt weder eine Resterkrankung noch Metastasen. **Schlussfolgerungen:** Das Mammakarzinom des Mannes ist äußerst selten, und das Auftreten eines okkulten Mammakarzinoms ist besonders ungewöhnlich. Axilläre Metastasen können die erste Manifestation eines Mammakarzinoms beim Mann sein.

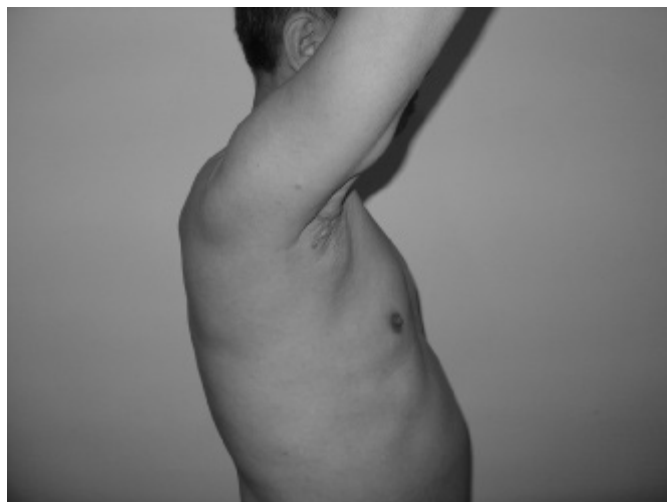


Fig. 1. External photo of the patient's chest showing an enlarged lymph node in the right axilla after biopsy, without a palpable breast mass (lateral aspect).

Introduction

Breast cancer is very rare in men, accounting for less than 1% of all breast cancers and less than 1% of all cancers in men [1, 2]. The occurrence of occult breast cancer in men is even less common [3, 4]. We report on a 72-year-old male patient with occult breast cancer diagnosed by histological examination and immunohistochemical (IHC) staining. This is the first case of occult breast cancer with axillary metastasis as the first manifestation seen at our hospital.

Case Report

A 72-year-old male patient presented with a painless and enlarged lymph node in the right axilla, which had developed over the past 6 months, without any palpable breast mass (fig. 1). His medical history showed no evidence of liver disease; no medication had been taken; and in particular, there was no history of hormonal treatment. Axillary lymph node biopsy showed an infiltrating ductal carcinoma (IDC) which was suspected to have metastasized from the breast. The patient was admitted, and a series of physical, X-ray, and ultrasonic examinations was carried out. However, no other foci were found in the body. Liver function was normal. The biopsy slice was circulated, and opinions were sought from fellows of other hospitals. Pathologists eventually concluded that this was a case of occult breast cancer. The patient underwent modified radical mastectomy and axillary dissection on 11 April 2006. Histological examination of paraffin sections stained with hematoxylin and eosin (HE) revealed no tumor foci in the breast, but 2 of 15 removed axillary lymph nodes were invaded by IDC. Histological examination showed the lymph tissue to be massively and diffusively infiltrated with large and relatively round tumor cells that were tightly cohesive and displayed round to ovoid nuclei and a thin rim of cytoplasm with an occasional intracytoplasmic lumen (fig. 2). IHC staining showed negative expression of both estrogen receptors (ER) and progesterone receptors (PR), but positive expression of p53 protein (+++), proliferating cell nuclear antigen (PCNA) (+++), Bcl-2 oncoprotein (+++), nm23 protein (++), multidrug resistance protein (MRP) (++), and human epidermal receptor (HER-2) oncoprotein (+++). The patient

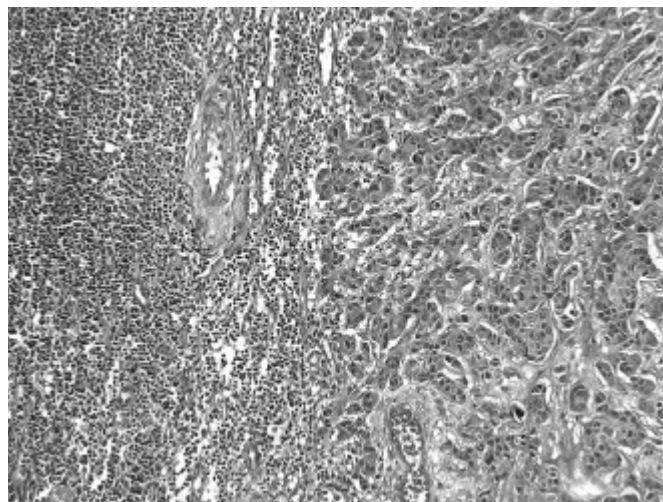


Fig. 2. Infiltrating ductal carcinoma metastasized into an axillary lymph node; lymph node tissue invaded by large and relatively round tumor cells (HE stain, original magnification $\times 200$).

did not receive any endocrinotherapy, chemotherapy, or radiotherapy after his operation. 24 months after being diagnosed he is alive without any residual or metastatic disease. Follow-up is still continuing.

Discussion

Breast cancer is very rare in men. Epidemiological studies showed that the rate of male breast cancer is 0.5–1% in most Western countries, and 6% or more in Tanzania and Central Africa [1, 2]. The reasons for this geographic variability remain unclear. Recent epidemiologic data suggest that the incidence of male breast cancer has been steadily increasing [5]. However, the pathogenesis of male breast cancer is still unclear. Epidemiologic risk factors may include prostate cancer and associated endocrinotherapy, gynecomastia, occupational hazards (e.g., exposure to electromagnetic fields, polycyclic aromatic hydrocarbons, high temperatures), dietary factors (e.g., meat intake, fruit and vegetable consumption), and alcohol intake. Recently, scientists have paid more attention to potential genetic factors [5, 6]. Mutation of the BRCA1, BRCA2, and MMR genes may play a very important role in the onset of male breast cancer; other genetic factors involved may include the AR gene, the CHEK2 gene, cytochrome P45017 (CYP17), the XXY karyotype (Klinefelter's syndrome), and the PTEN tumor suppressor gene associated with Cowden syndrome. The BRCA1 and BRCA2 germline mutation is known to be associated with hereditary breast cancer [7]; and the MMR germline mutation (especially hMLH1) is associated with hereditary nonpolyposis colorectal carcinoma (HNPCC). Some researchers regard breast cancer, and especially male breast cancer, as part of the HNPCC tumor spectrum, and believe breast cancer might be an extracolonic manifestation of HNPCC [8, 9]. Therefore, if a male patient

presents with breast cancer, we should not only examine the breast lesion, but also inquire about the patient's family history and past medical history which may be helpful for clinical diagnosis and therapy.

As a form of male breast cancer, occult breast cancer is particularly rare. It usually presents with lymph node metastases of the axilla, supraclavicular fossa, and infraclavicular fossa as the first manifestation [10]. In our case, the patient presented with axillary lymph node metastases as the first manifestation. The most common causes of malignant axillary lymph nodes include lymphoma and metastasis from breast cancer, lung cancer, melanoma, and squamous cell cancer. Hence, relevant examinations must be carried out to find foci and avoid misdiagnosis. Research shows that in approximately 50% of cases of occult breast cancer no tumor foci can be found in the breast specimen [11], as was the case with our patient. The final diagnosis was made after a number of pathologists had

been consulted and a series of examinations for differential diagnosis had been carried out, with the histological examination and IHC staining of metastatic lesions being particularly important in the diagnosis of occult breast cancer.

The currently recommended surgical therapy is modified radical mastectomy with axillary dissection. It was reported that male breast carcinomas have a higher positive rate for hormone receptors than female breast carcinomas, and so adjuvant hormonal therapy is theoretically very promising [12]. In our case, although the tumor cells were negative for ER and PR, the expression results of PCNA, P53, Bcl-2, nm23, MRP, and HER-2 protein were similar to other reports [1, 3, 6]. Since the patient was in his 70s, his family did not agree to him undergoing endocrine therapy, chemotherapy, or radiotherapy after the operation. However, the patient's prognosis is very promising; he has remained cancer-free for about 24 months after being diagnosed. Follow-up is still continuing.

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