Pathology - Research and Practice xxx (xxxx) xxx–xxx

Contents lists available at ScienceDirect

Pathology - Research and Practice

journal homepage: www.elsevier.com/locate/prp

Intracystic papillary carcinoma of the breast: Experience of a major Chinese cancer center

Jun Zhang[a,b], Tiemei Zhang[c], Nan Wu[a,b], Xinhua Zhao[d], Qingsong Wang[e], Yanyang Jiang[f], Ming Gao[g,*], Lin Gu[a,b,**]

[a] Department of Breast Surgery, Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center for Cancer, Tianjin's Clinical Research Center for Cancer, Key Laboratory of Cancer Prevention and Therapy, Tianjin, China
[b] Key Laboratory of Breast Cancer Prevention and Therapy, Tianjin Medical University, Ministry of Education, Tianjin, 300060, China
[c] Department of Endoscopy, Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center for Cancer, Tianjin's Clinical Research Center for Cancer, Key Laboratory of Cancer Prevention and Therapy, Tianjin, China
[d] Department of Breast Surgery, Hebei Province Qian an People's Hospital, Qian an, 064400, China
[e] Tianjin Research Center of Basic Medical Sciences, School of Basic Medical Sciences, Tianjin Medical University, Tianjin, 300070, China
[f] Department of Social Science, Florida State University, Tallahassee, FL, 32306, USA
[g] Department of Thyroid and Neck Tumor, Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center for Cancer, Tianjin's Clinical Research Center for Cancer, Key Laboratory of Cancer Prevention and Therapy, Tianjin, 300060, China

ARTICLE INFO

Keywords:
Breast cancer
Intracystic papillary carcinoma
Characteristics
Prognosis

ABSTRACT

Background: Intracystic papillary carcinoma (IPC) is a rare breast neoplasm. There are few studies focusing on its clinical features and limited data about its preoperative diagnosis,treatment and outcomes. The purpose of this study is to explore specific characteristics of patients with IPC, investigate its clinicopathological features, prognosis in China and confirm its surgery management.

Methods: We identified 111 patients with IPC from the registry of Tianjin Medical University Cancer Institute and Hospital between 2004 and 2017. Follow-up of cases dating back to January 1, 2004 was obtained from retrospective chart review and patient questionnaires. Differences in clinical features and survival of patients were assessed using the Kaplan-Meier method.

Results: The median tumor size was 2.25 cm. Median age was 62 years. In the cases of axillary lymph node dissection(ALND), only 1.1% (1/85) of patients with axillary lymph node metastasis were found. The diagnostic accuracy of preoperative Color Doppler ultrasound and Mammograms for IPC was 62.0% (62/100) and 63.5% (54/85) respectively. The median follow-up period was 52 (range2–149) months. The overall survival rate was 98.9%, 92.2%,and 85.6% at 2,5,and 10 years and the relapse-free rate was 99.1%,97.2%,and 92.0% at 2,5, and 10 years, respectively. The disease-specific survival rate was 100%.

Conclusion: Overall, we report some unique features of IPC in the Chinese population. The patients of IPC of the breast in China have more excellent prognosis than in Caucasian and other races. The diagnostic accuracy of imaging was low, and was easily misinterpreted as a cyst or benign disease. Preoperative core needle biopsies are very difficult for accurate pathological diagnosis of IPC. IPC is a localized disease with a low frequency of axillary lymph node involvement, rare distant metastases and excellent survival. The low incidence of axillary lymph node metastasis suggests that quadrectomy + sentinel lymph node biopsy (SLNB) and breast-conserving surgery is recommended for IPC.

1. Introduction

Intracystic papillary carcinoma (IPC) is an uncommon breast malignancy that accounts for between 0.5% and 2% of breast tumors, IPC also appears in men[1–3]. IPC often appears in postmenopausal women, the typical characteristics of IPC are the mass along with

* Corresponding author at: Department of Thyroid and Neck Tumor, Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center for Cancer, Tianjin's Clinical Research Center for Cancer, Key Laboratory of Cancer Prevention and Therapy, Tianjin, 300060, China
** Corresponding author at: Department of Breast Surgery, Tianjin Medical University Cancer Institute and Hospital, National Clinical Research Center for Cancer, Tianjin's Clinical Research Center for Cancer, Key Laboratory of Cancer Prevention and Therapy, Tianjin, Key Laboratory of Breast Cancer Prevention and Therapy, Tianjin Medical University, Ministry of Education, Huan Hu Xi Rd, Hexi District, Tianjin, 300060, China.
E-mail addresses: headandneck2008@126.com (M. Gao), doctorgulin@163.com (L. Gu).

https://doi.org/10.1016/j.prp.2018.01.006
Received 29 November 2017; Received in revised form 11 January 2018; Accepted 24 January 2018

bloody nipple discharge, imaging findings of round, oval, or lobulated circumscribed mass due to the appearance of the dilated duct rather than the tumor within it [4,5]. IPC was described for the first time in 1969, by McKittrick [6], as a variant of papillary ductal carcinoma developed in a cyst and surrounded by a fibrous capsule. In 2012, the WHO Working Group for the 4th edition regarded encapsulated (intracystic) papillary carcinoma is a distinctive variant of papillary ductal carcinoma, confined to a dilated cystic space and surrounded by a fibrous capsule, and characterized by thin fibrovascular stalks devoid of a myoepithelial cell layer, and a neoplastic cell population with histological features characteristic of low grade ductal carcinoma in situ. It can be present as an isolated lesion or associated with conventional non-papillary ductal carcinoma in situ and/or invasive ductal carcinoma [7]. The WHO Working Group reached a consensus that intracystic papillary carcinoma should be staged and managed like ductal carcinoma in situ (DCIS) [7,8].

Although IPC is considered a variant of ductal carcinoma in situ, some studies suggest that it may be metastatic, IPC is a low-risk invasive tumor [9–11]. Previous studies have focused on IPC in predominantly Caucasian populations [4,11], and studies of Chinese population have not been reported. Due to differencesin biology, behaviors and environment of different populations, the prognosis of the same disease may vary greatly in different countries. Therefore, it is important to analyze the data of people in China and the broader Asia-Pacific region. Because IPC cases are rare and there are no standardized treatment guidelines, only a few studies involving lymph node status and selection of surgical strategies [12,13]. Moreover, they have not focused on IPC in the preoperative diagnosis and postoperative biologic features. The aim of our observation was to elucidate the clinicopathological features and preoperative diagnosis, biologic features, variations in treatment pattern and survival of patients with IPC in the Chinese population.

2. Materials and methods

2.1. Ethics statement

All of the tissue samples were taken with informed consent of the patient. According to the latest revision of the Helsinki declaration, the program of sample analysis was approved by Institutional Review Board of the Tianjin Medical University Cancer Institute and Hospital. The research was approved by Institutional Review Board of the Tianjin Medical University Cancer Institute and Hospital.

2.2. Patient selection

111 patients of IPC were identified from 29,317 cases of breast cancer (0.38%) diagnosed between January 2004 and March 2017 at Tianjin Medical University Cancer Hospital, Tianjin, China. The pathologic material for each case of pure IPC was retrieved from the archive of the department and reviewed. All patients were confirmed to have IPC by a systematic independent review of the pathologic material by two breast pathologists who were blinded to patients' clinicopathological characteristics and outcomes. The patients' clinicopathlogical characteristics were obtained retrospectively from the medical records and evaluated as prognostic factors. 80 (72.1%) patients received modified mastectomy (MRM), 5(4.5%) patients accepted breast-conserving surgery, 20(18.0%) patients received quadrectomy, and the other 6(5.4%) patients received mastectomy. Surgical margins in excisional specimens were negative in all accepted breast-conserving surgery patients. All the patients received no radiation and/or chemotherapy before surgery. The majority of patients with ER+/PR+ tumor received hormonal therapy.

2.3. Immunohistochemical evaluation

The status of estrogen receptor(ER), progesterone receptor(PR), Her-2, Ki-67, and p53 was determined by immunohistochemistry(IHC). Formalin-fixed paraffin embedded tissue sections were employed in each case using a standard protocol. The immune reaction was evaluated independently by the 2 pathologists(L. F. and R. L.). ER and PR were classified as negative (less than 1%) and positive (1% or more) tumor cell nuclei staining [14]. Her-2 was scored for the intensity and the completeness of cell membrane staining based on guidelines. Her-2 (+++) was defined as positive. The immunohistochemistry is(++) for FISH assay [15]. Ki67 status was expressed in terms of percentage of positive cells, with a threshold of 20% of positive cells [16]. p53 classified as negative expression (fewer than 10%) and positive expression (10% or more) tumor cell nuclei staining [17]. Subtypes of breast cancer were defined by ER, PR, Ki67, and Her-2 status [16]: Luminal A, ER positive and/or PR positive, Her-2-, Ki67 < 20%;Luminal B, ER positive and/or PR positive, Ki67 ≥ 20%; HER2 over-expression, ER and PR negative and HER2 positive; Basal-like (triple negative), ER, PR and HER2 negative.

2.4. Statistical analysis

SPSS for windows 22.0 (Chicago, USA) was used for data statistical analyses. Relapse-free survival and overall survival was defined as the duration of time between the date of the first surgery and the date of first local relapses and died. Survival curves were determined by Kaplan-Meier survival curve (Log-rank).

2.5. Follow up

In the first year following surgery, patients were evaluated every three months in an outpatient setting. Patients were similarly evaluated every six months during years 2–5 and yearly thereafter. During the follow-up, local relapse and distant metastasis were observed through physical examination, Color Doppler ultrasound and chest X-ray. The last follow up for this study was conducted on 30. March 2017, the median follow-up period was 52 (range 2–149) months, overall survival and relapse-free survival data was obtained from medical records or by letter communication or telephone calls.

3. Results

3.1. Clinical findings

111 patients of IPC were identified from 29,317 cases of all breast cancer (0.38%) diagnosed between Jan 1, 2004 to Mar 31, 2017 at Tianjin Medical University Cancer Hospital, Tianjin, China. The age of the patients ranged from 18 to 87 years and the mean age and median age of 62 years and 62.1 years, respectively. The majority of IPC patients were women (98.2%, n = 109), and only 1.8%(n = 2) were male. 71.6%(78/109, Table 1) were postmenopausal and the remaining 28.4%(31/109, Table 1) were premenopausal. IPC was found that the probabilities are roughly the same on the left (50/111) and the right (61/111). Furthermore, 51.4% (57/111, Table 1) IPC patients were in the central quadrant of the breast; one patient (1/85, 1.1%, Table 1) presented with lymph node metastases in IPC. IPC was initially detected in 7 patients during breast cancer screening, and 32 patients detected a breast lump and bloody nipple discharge during self-examination.

3.2. Preoperative diagnosis

The diagnostic accuracy of preoperative Color Doppler ultrasound was 62.0% (62/100, Table 1). Color Doppler ultrasound demonstrates solid on complex cystic and solid masses that have mild to moderate posterior acoustic enhancement, with solid and cystic components in 63 patients and solid components in the other 37 patients. In addition to complex echogenicity, the most common Color Doppler ultrasound finding was regular shape 57.0% (57/100). Other findings included 46