Analysis of Clinicopathological Features and Diagnosis and Treatment of 173 Cases of Pathological Nipple Discharge: Postprint

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Abstract

Objective: To analyze the clinical and pathological characteristics and follow-up of 173 cases of pathological nipple discharge, providing evidence for diagnosis and treatment.

Methods: Clinical data, postoperative pathology, and follow-up information of patients with pathological nipple discharge admitted to our hospital in 2015 were collected. Statistical analysis was performed using SPSS 22.0 software. Nonparametric variables were analyzed using chi-square test or Fisher' s exact test, while measurement data were compared using t-test or Mann-Whitney U test.

Results: No statistically significant differences were observed between the bloody and non-bloody discharge groups regarding age, unilateral/bilateral lesions, single/multiple duct discharge, disease duration, palpable mass on physical examination, positive mammography findings, or postoperative pathological types. A significant difference existed between the two groups in positive ultrasound findings (P=0.012). There was a significant difference between the groups in postoperative pathology indicating breast cancer (P=0.045). In the bloody discharge group, patient age showed a significant difference between benign and malignant lesion subgroups (P=0.014). Other clinical features demonstrated no significant differences. The median postoperative follow-up period was 17 months; no cases experienced recurrence, and breast cancer patients showed no recurrence, metastasis, or mortality.

Conclusion: Bloody discharge indicates a high risk of malignant breast lesions, with higher risk in older patients. However, non-bloody pathological discharge should not be neglected either. Most patients had positive preoperative ultrasound findings, particularly those with bloody discharge, yet preoperative

physical examination, ultrasound, and mammography could not provide effective basis for differentiating benign from malignant lesions. Timely surgical treatment represents an effective approach for definitive diagnosis and therapy, with favorable prognosis following timely surgery and postoperative follow-up.

Full Text

Preamble

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Retrospective Analysis of 173 Patients with Pathological Nipple Discharge

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Abstract

Objective: To analyze the clinical and pathological characteristics and follow-up data of 173 patients with pathological nipple discharge, and to provide evidence for diagnosis and treatment.

Methods: Clinical data, postoperative pathology, and follow-up information were collected from patients with pathological nipple discharge who underwent surgery in our hospital in 2015. Statistical analysis was performed using SPSS 22.0 software. Nonparametric variables were analyzed using chi-square test or Fisher' s exact test, while measurement data were compared using t-test or Mann-Whitney U test.

Results: No statistically significant differences were observed between the bloody and non-bloody discharge groups in terms of age, unilateral/bilateral lesions, single/multiple duct discharge, disease duration, palpable masses on physical examination, or positive mammography findings. However, a significant difference was found in positive ultrasound findings between the two groups (P=0.012). There was also a significant difference in postoperative breast cancer diagnosis between the groups (P=0.045). Among patients with bloody discharge, age showed a significant difference between benign and malignant lesion groups (P=0.014), while other clinical features showed no significant differences. At a median follow-up of 17 months postoperatively, no recurrence was observed in any cases, and no recurrence, metastasis, or death occurred in breast cancer patients.

Conclusion: Bloody nipple discharge indicates a high risk of malignant breast lesions, with even higher risk in older patients. However, non-bloody pathological discharge should not be ignored. Most patients had positive preoperative ultrasound findings, particularly those with bloody discharge, but preoperative physical examination, ultrasound, and mammography could not provide effective basis for distinguishing benign from malignant lesions. Timely surgical treatment is an effective means for definitive diagnosis and management, with favorable postoperative follow-up outcomes.

Keywords: pathological nipple discharge; bloody nipple discharge; breast cancer

Introduction

Nipple discharge is a common symptom of breast disease, with an incidence second only to breast mass and breast pain, accounting for 4.8%-7.4% of outpatient chief complaints [**?**]. Nipple discharge is divided into physiological and pathological types. The etiology of pathological nipple discharge includes intraductal papilloma, mammary adenosis, ductal ectasia, and breast cancer [**?**]. Among these, intraductal lesions are the main cause of nipple discharge, which can be classified as bloody or non-bloody. The latter includes serous and turbid mucoid types. This study retrospectively analyzed the clinical and pathological characteristics, diagnosis, and treatment of 173 patients with pathological nipple discharge to identify specific clinical-pathological features, particularly for bloody discharge, and to evaluate whether clinical diagnostic methods provide sufficient basis for management and whether treatment and postoperative follow-up are appropriate.

Methods

1.1 Clinical Data

We collected clinical data, postoperative pathology, and follow-up information from 173 patients with pathological nipple discharge (bloody, yellow serous, or turbid mucoid) who were hospitalized and underwent surgery in our hospital from January 2015 to December 2015. All 173 patients were female, aged 24-90 years with a median age of 43 years. The median disease duration was 3 months. Among them, 119 cases (68.7%) had bloody discharge and 54 cases (31.2%) had non-bloody serous discharge. Single-duct discharge was present in 171 cases, with only 2 cases showing multiple-duct discharge. Unilateral nipple discharge occurred in 168 cases, while 5 cases had bilateral discharge.

1.2 Preoperative Examination

All patients underwent preoperative physical examination, ultrasound, and mammography. Twenty-three patients had palpable breast masses on physical examination, while 150 had no palpable masses. Ultrasound examination revealed low-echo lesions within the breast or ductal system, or high-echo lesions, in 111 patients, while 62 patients had no positive ultrasound findings. Mammography detected breast masses or calcifications in only 35 patients, with 138 patients showing no abnormalities.

1.3 Surgical Treatment

All 160 patients initially underwent excision of the diseased duct and associated lobule using the methylene blue retrograde localization technique. Based on intraoperative frozen section or paraffin pathology results, 4 breast cancer patients underwent central quadrantectomy including the nipple-areola complex, 3 patients underwent central quadrantectomy plus sentinel lymph node biopsy, 14 patients underwent simple mastectomy plus sentinel lymph node biopsy, 1 patient underwent simple mastectomy only, and 5 patients underwent modified radical mastectomy. Additionally, 9 patients underwent breast mass excision plus diseased duct and lobule resection, while 4 patients underwent breast mass excision only.

1.4 Pathological Results

Postoperative paraffin pathology revealed 27 cases of breast cancer, including 6 invasive carcinomas, 19 ductal carcinomas in situ, and 2 other types (mucinous carcinoma and neuroendocrine carcinoma). Patients who underwent sentinel lymph node biopsy or axillary lymph node dissection showed no lymph node metastasis. Atypical hyperplasia was found in 15 cases. Benign lesions were predominantly intraductal papilloma (92 cases), with other benign lesions including mammary adenosis (21 cases), fibroadenoma (4 cases), and ductal ectasia (14 cases).

1.5 Postoperative Treatment and Follow-up

Postoperatively, 23 patients received endocrine therapy, including 12 treated with selective estrogen receptor modulators (SERMs) and 11 with aromatase inhibitors (AIs). Four patients underwent postoperative radiotherapy. One patient with bloody nipple discharge, multiple masses, and age younger than [text incomplete]···

1.6 Statistical Methods

Measurement data were expressed as mean ± standard deviation. Statistical analysis was performed using SPSS 22.0 software. Categorical variables were analyzed using chi-square test or Fisher' s exact test, while measurement data

were compared using t-test or Mann-Whitney U test. The significance level was set at =0.05.

Results

2.1 Clinicopathological Analysis of Bloody vs. Non-bloody Discharge (Table 1)

No statistically significant differences were observed between the bloody and non-bloody discharge groups in age, unilateral/bilateral lesions, single/multiple duct discharge, disease duration, palpable masses on physical examination, or positive mammography findings. However, a significant difference was found in positive ultrasound findings between the two groups (P=0.012). Postoperative breast cancer diagnosis also showed a significant difference between groups (P=0.045), while the distribution of pathological types showed no significant difference.

2.2 Analysis of Clinical Data for Benign vs. Malignant Lesions in Bloody Discharge (Table 2)

Among patients with bloody discharge, age showed a significant difference between benign and malignant lesion groups (P=0.014). Other clinical features, including single/multiple duct discharge, unilateral/bilateral presentation, and positive findings on physical examination, ultrasound, or mammography showed no significant differences.

2.3 Follow-up

At a median follow-up of 17 months postoperatively, no recurrence, metastasis, or death occurred in patients with breast cancer pathology. Among patients with benign pathology, 5 developed new breast masses during follow-up, manifested as hypoechoic nodules on ultrasound, all managed with observation. One patient developed inflammatory lesions in the operated breast requiring surgical excision. Another patient developed contralateral non-bloody nipple discharge 5 months postoperatively, which was managed surgically.

Discussion

Pathological nipple discharge often indicates breast disease, particularly increased risk of malignant breast disease. In this study, breast cancer and atypical hyperplasia accounted for 24.28% of pathological nipple discharge cases, while intraductal papilloma accounted for 53.18%, consistent with literature reports [**?**]. Therefore, clinically, when patients present with pathological dis-

charge symptoms, including bloody, yellow serous, or turbid mucoid discharge, heightened vigilance and timely surgical treatment are warranted.

Zervoudis et al. [**?**] reported that pathological nipple discharge caused by breast lesions is mostly unilateral and single-duct. Our study found 171 cases of single-duct discharge and only 2 cases of multiple-duct discharge, with 168 cases of unilateral discharge and 5 cases of bilateral discharge, consistent with literature reports. However, no significant differences were observed between bloody and non-bloody discharge groups or between benign and malignant lesion groups within the bloody discharge cohort regarding single-duct or unilateral presentation. This may be because multiple-duct or bilateral nipple discharge is often considered benign and not referred for surgery, resulting in small sample sizes for these categories.

Most scholars consider bloody nipple discharge a high-risk factor for breast cancer. Chen et al.' s [**?**] meta-analysis concluded that patients with bloody nipple discharge have higher breast cancer risk than those with other discharge types. Wang et al. [**?**] reported that the rate of precancerous lesions/malignancy in the bloody discharge group was significantly higher than in the non-bloody group. However, some scholars believe there is no absolute correlation. Morrogh et al. [**?**] reported that bloody discharge does not predict malignant lesions or high-risk pathology, and non-bloody discharge cannot exclude malignancy. Our study found a significant difference in breast cancer incidence between bloody and non-bloody discharge groups, indicating that bloody discharge suggests high risk of breast cancer. However, in the non-bloody discharge group, the incidence of breast cancer was 7.4% and atypical hyperplasia was 7.4%, suggesting that non-bloody pathological discharge should not be overlooked. Regarding pathological types, all breast cancers in the non-bloody group were ductal carcinoma in situ, while nearly one-third of cancers in the bloody group were invasive carcinoma. We conclude that bloody discharge warrants greater clinical attention.

Regarding clinical examination, Lippa et al. [**?**] reported that "suspicious" pathological discharge such as bloody discharge has more clinical and imaging findings than "benign" pathological discharge. Our study found that the bloody discharge group had significantly more positive ultrasound findings than the non-bloody group, consistent with literature reports. However, no differences were observed in palpable masses or mammography findings, possibly related to denser breast tissue in Asian women making mammographic lesion detection difficult. Among benign and malignant lesions within the bloody discharge group, none of the three examinations showed significant differences. Therefore, the presence of masses and findings on ultrasound or mammography cannot provide effective clinical evidence for distinguishing malignant from benign lesions in bloody discharge, consistent with literature reports [**?**, **?**].

Due to low sensitivity of color Doppler ultrasound and mammography in diagnosing nipple discharge, traditional ductography and discharge cytology have high misdiagnosis rates. Teboul first applied ductoscopy in the 1990s [**?**] to address the challenges of etiological diagnosis and lesion localization. However,

since multiple lesions are most common within ducts and ductoscopy typically examines only 1-2 ducts, it cannot assess the overall breast condition. Additionally, most breast cancers originate in terminal ducts that are difficult to reach with ductoscopy. Furthermore, ductoscopy provides only morphological diagnosis with low accuracy, and biopsy specimens obtained are often insufficient for effective pathological assessment [**?**]. Xu et al. [**?**] reported that ductoscopy detected malignant lesions in only 53.3% of patients with bloody nipple discharge. Washington University School of Medicine performed ductoscopy on 121 patients with nipple discharge from 2006-2010, and 44% of patients with negative ductoscopy results were still found to have ductal carcinoma in situ or invasive carcinoma [**?**]. Therefore, negative ductoscopy results should not lead to reduced vigilance. Moreover, ductoscopy often causes duct wall injury and cessation of nipple discharge, potentially masking the condition [**?**]. Ductoscopy also cannot provide effective evidence for nipple discharge diagnosis.

In the benign and malignant lesion groups with bloody discharge, age showed significant differences, with older patients (mean age 54.04) presenting with bloody discharge being more likely to have malignant lesions than younger patients. This is consistent with the peak incidence age of breast cancer [**?**].

In this study, most postoperative malignant pathology cases were ductal carcinoma in situ, with only 0.03% being invasive carcinoma, and no axillary lymph node metastasis was observed. No recurrence or metastasis of malignant lesions was observed during follow-up. Among benign lesions, only one case developed inflammatory lesions requiring surgical treatment, while other postoperative nodules were considered benign and managed with observation.

In summary, this study suggests that bloody nipple discharge indicates high risk of malignant breast lesions, with even higher risk in older patients. However, non-bloody pathological discharge should not be ignored. Most patients had positive preoperative ultrasound findings, particularly those with bloody discharge, but preoperative physical examination, ultrasound, and mammography cannot provide effective basis for distinguishing benign from malignant lesions. Timely surgical treatment is an important means for definitive diagnosis and therapeutic management, with favorable postoperative follow-up outcomes for patients undergoing prompt surgical intervention.

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Note: Figure translations are in progress. See original paper for figures.