J Tokyo Wom Med Univ
76 (10・11) 430～434 (2006)

Mammary Ductoscopic Classification of Intraductal Breast Tumors

Takako KAMIO, Masako YAMAGUCHI, Tetsuya OHCHI, Kei AOYAMA and **Shingo KAMEOKA**

Department of Surgery II, Tokyo Women's Medical University, School of Medicine

(Accepted Sep. 12, 2006)

In examinations of intraductal abnormalities of patients presenting with abnormal nipple discharge, it is important to discover and diagnose minute lesions within the duct, to determine whether the lesion is benign or malignant, and to determine the extent of ductal spreading in the case of intraductal carcinoma. To date, ductoscopy has been conducted on 411 cases, and we have been classifying intraductal tumors based on our own mammary ductoscopic classification. In the present study, we verified the validity of the benign or malignant diagnosis of the 191 intraductal tumors observed by mammary ductoscopy that we examined histopathologically using this classification. With the mammary ductoscopic classification of intraductal breast tumors, the configuration of the tumors was classified into two major categories of pedicled type and broad-based type and the latter was further subdivided into hemispherical, uneven, and irregular-mass types. Then, the negative and positive predictive values were calculated with the pedicled type classified as benign and broad-based type as malignant with favorable results of 90.1% (n=121) and 84.3% (n=70), respectively.

The mammary ductoscopic classification of intraductal breast tumors proved to accurately reflect the histopathological characteristics of proliferation and progressive configurations of intraductal tumors, making the classification useful in diagnoses of intraductal tumors.

Key words: mammary ductoscopy, mammary ductoscopic classification, nipple discharge, intraductal papilloma, intraductal carcinoma

Introduction

Generally, abnormal nipple discharge in extrapuerperium is seen in 5-10% of outpatients and ranks third among chief complaints after tumor mass and breast pain[1]. Among the causes of abnormal nipple discharge is early-stage breast cancer[2], of which nipple discharge can be the only sign and should, therefore, never be overlooked. Examinations of intraductal abnormalities of patients presenting with abnormal nipple discharge are extremely important in the following aspects: diagnosis of the presence or absence of minute intraductal lesions, diagnosis of whether those lesions are benign or malignant, and to determine the extent of ductal spreading in the cases of intraductal carcinoma. In our department, in diagnosing abnormal nipple discharge, mammary ductoscopy has been used the most with the best results[3]. Mammary ductoscopy is capable of direct observation inside the ducts. Evaluation of whether the lesion is benign or malignant is done using the mammary ductoscopic classification of intraductal breast tumors. In the present study, we examined the validity of this classification.

Patients and Methods

Mammary ductoscopy is indicated when a discharge is observed from only one orifice, or even when there are nipple discharges from both nipples, or multiple orifice discharges, in cases of a bloody discharge from a single duct. During the 16 years from June 1990 through May 2006, there were 411 cases of abnormal nipple discharge in which mammary ductoscopy was conducted. There were 191 cases in which intraductal biopsy of the breast (IDBB) was performed during mammary duc-

toscopy for histopathological diagnosis or a surgical biopsy was performed after tumors had been observed by mammary ductoscopy.

In the present study, 220 cases were excluded. In those cases, 152 cases were found to be benign tumors by intraductal cytological biopsies or had no significant ductoscopic findings and were followed up. The remaining 68 cases had no significant findings with mammary ductoscopy, however, diagnoses were made of intraductal tumors by other diagnostic tools, such as ultrasonography and ductography. Incisional biopsies were then performed for these 68 cases to confirm the diagnoses. Twenty-two cases of these were cancer cases in which there was cancerous tissue in the peripheral regions that could not be reached by mammary ductoscopy, i.e., diagnoses were made considering the fact that no cancerous growth had spread to the nipple or proximal areas through the duct. This proves mammary ductoscopy is significant because it can be used for making decisions as to whether or not breast conserving surgery is indicated.

There are three kinds of ductoscopes, different in their diameters and the materials of which they are made. The first ductoscopes we used were the rigid type with an external diameter of 1.2 mm. We then used the flexible ductoscope with a diameter of 0.75 mm. Since 1996, observations had been mainly performed with the semi-rigid ductoscope with a 0.8 mm diameter. The view of the ductscope consists of 10,000 pixels

Observations were made by inserting the ductoscope into the nipple through the duct. Evaluation of the configuration of the tumor was made by comparing it with the mammary ductoscopic classification of the intraductal breast tumors (Fig. 1).

Figure 2 shows the normal intraductal lumen. In the ductoscopic classification of intraductal breast tumors, the tumors were classified into two major types: the pedicled type which rises on a pedicle into a papilliferous mass from a normal smooth lumen (Fig. 3), and the broad-based type which proliferates along the intraductal lumen. On the broad-based type, moreover, further classifications were made for the following three subtypes (Fig. 4A-C): the hemispherical type with a smooth tumor surface that bulges out from the lumen (Fig. 4A), the uneven type with small bumps and hollows (Fig. 4 B), and the irregular-mass type with continuous luminal irregularities (Fig. 4C).

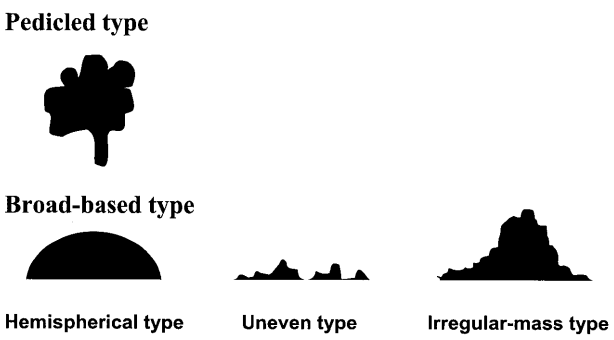

Fig. 1 Mammary ductoscopic classification of intraductal breast tumors

These classification results were then compared with histopathological diagnoses, and negative and positive predictive values for each type were calculated with the pedicled type as benign and the broad-based type as malignant.

Results

The breakdown of the histopathologic diagnoses of 191 cases gave: 17 cases (8.9%) of mastopathy, 103 cases (53.9%) of intraductal papilloma, and 71 cases (37.2%) of breast cancer (Table 1). At the same time, of the 71 breast cancer cases, 36 cases were noninvasive ductal carcinoma.

From results of contrasting ductoscopic classification of intraductal breast tumors and the histopathological diagnoses of the 121 cases diagnosed as the pedicled type which we thought were benign, 109 cases (90.1%) were histopathologically benign (Table 2). There were 14 cases (11.6%) of mastopathy, and 95 cases (78.5%) of intraductal papilloma. The negative predictive value is 90.1%, a favorable result. When we examined the 70 cases of the broad-based type, which we thought were malignant, we found 59 cases (84.3%) that were histopathologically proven to be malignant. The positive predictive value was 84.3% of the cases, also a favorable result. The positive predictive values for the three subtypes were: the hemispherical type, 13 of 19 cases (68.4%); the uneven type, 11 of 12 cases (91.7%); and the irregular-mass type, 35 of 39 cases (89.7%). The diagnostic results were quite favor-

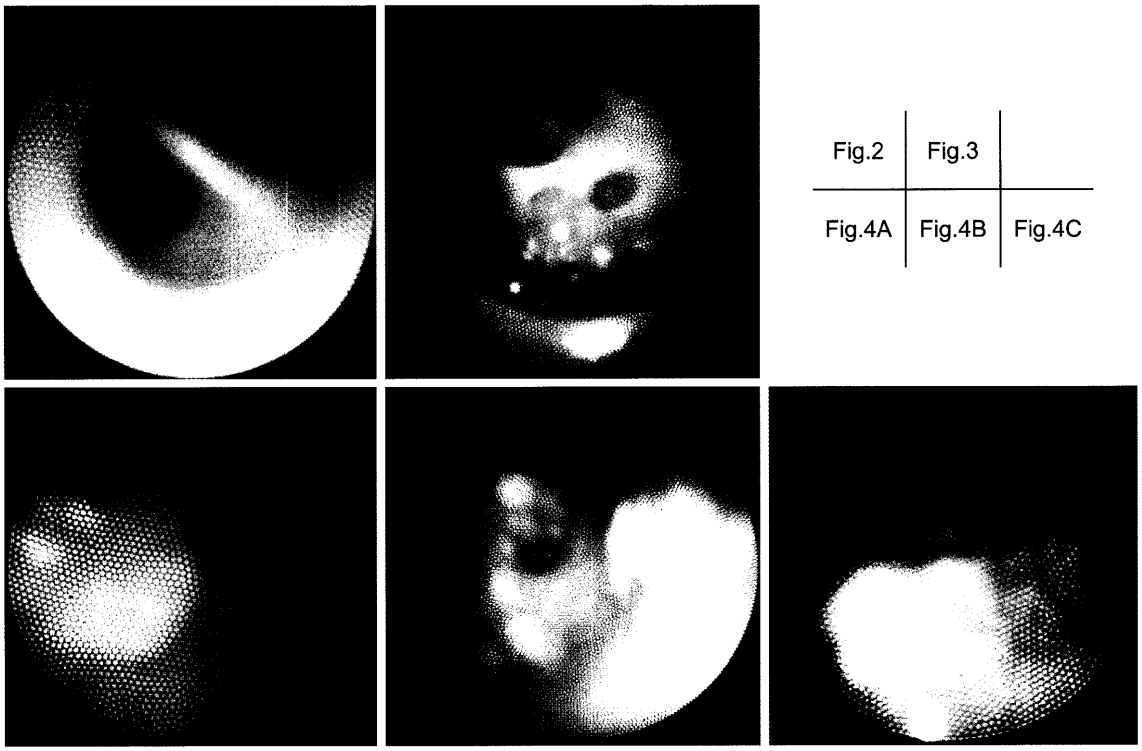

Fig. 2 Mammary ductoscopic findings of a normal duct
The duct extends to peripheral areas by repeated bifurcations. The ductal lumina is smooth.

Fig. 3 Mammary ductoscopic findings of the pedicled type
The pedicled tumor with a papillary proliferation that exhibits mobility, swaying back and forth with the introduction of a pulsed current of air. The ductal lumina around the tumor is smooth.

Fig. 4 Mammary ductoscopic findings of the hemispherical (A), the uneven (B) and the irregular-mass (C), broad-based type
A: The surface of the tumor is smooth and bulges out from the lumen.
B: Along the duct, the tumor is seen as having small bumps and hollows.
C: Along the duct, the tumor is seen as having an irregular and bulging proliferation.

Table 1 Histopathological diagnosis of intraductal breast tumors

Histology	n	%
Mastopathy	17	8.9
Intraductal papilloma	103	53.9
Carcinoma	71	37.2
Noninvasive ductal carcinoma	36	18.9
Invasive ductal carcinoma	35	18.3
Total	191	100

able for the uneven and irregular-mass types. And among 19 hemispherical type, 6 cases (31.6%) were benign tumors: 3 cases of mastopathy, and 3 cases of intraductal papilloma.

Discussion

Mammary ductoscopy enables direct viewing of minute proliferative changes in the intraductal lumina, the primary loci of breast cancer[4)~6)]. Along with the progress in the apparatuses and diagnostic technologies[3)7)], mammary ductoscopy is now an indispensable examination method for intraductal diseases with abnormal nipple discharge. Mammary ductoscopy is extremely useful in detection of breast cancer at an early stage and to determine whether or not breast conserving surgery is indicated according to the proximity of the cancer cells to the nipple.

We have been making our diagnoses based on the mammary ductoscopic classification of intraductal breast tumors that we developed which classifies the configuration of intraductal tumors into two major types: the pedicled type and the broad-based

Table 2 Correlation between mammary ductoscopic classification and histopathological diagnosis

Ductoscopic classification	Histology			Total (%)
	Mastopoathy (%)	Intraductal papilloma (%)	Carcinoma (%)	
Pedicled type	14 (11.6)	95 (78.5)	12 (9.9)	121 (100)
Broad-based type	3 (4.3)	8 (11.4)	59 (84.3)	70 (100)
Hemispherical type	3 (15.8)	3 (15.8)	13 (68.4)	19 (100)
Uneven type	0 (0)	1 (8.3)	11 (91.7)	12 (100)
Irregular-mass type	0 (0)	4 (10.3)	35 (89.7)	39 (100)
Total	17 (8.9)	103 (53.9)	71 (37.2)	191 (100)

type[3]. The classification is an accurate reflection of histopathological characteristics, i.e., a benign tumor proliferates locally and perpendicularly within the duct lumen, whereas cancerous tissue proliferates and spreads along the intraductal lumen[8]. The author of the present study, focused on this essential concept of the nature of intraductal tumor proliferation, the same concept used to develop the previous classification of ultrasonographic images of the mammary duct[9)~11)]. In the present study, the negative predictive value of the pedicled type and positive predictive value of the broad-based type have been extremely favorable, and it has been confirmed that each of these types accurately reflects the histopathological characteristics, which clarified the validity of the mammary ductoscopic classification of intraductal breast tumors.

Considering the three subtypes of the broad-based type of intraductal tumors, the positive predictive values of both the uneven and irregular-mass types are high, and these types are an accurate reflection of the histopathological characteristics. On the other hand, the hemispherical type was as low as 68.4% in terms of the positive predictive value. Therefore, further clarification of the points of distinction for the hemispherical type is warranted.

In addition to our mammary ductoscopic classification, the Association of Mammary Ductoscopy has recently proposed another type of mammary ductoscopic classification[12] that classifies ductoscopic findings into three types: the polypoid type (solitary, multiple), combined type, and superficial type. Their classification differs from ours such that in theirs the number of tumors is considered, the way of evaluating the shape, however, is similar in noting the developmental direction of the tumor (whether developing perpendicularly or horizontally to the duct wall). Our pedicled type corresponds to their polypoid type. In the broad-based type, the hemispherical type in our classification is included in the polypoid type, while the uneven type in ours is the superficial type in theirs, and our irregular-mass type corresponds to their combined type.

Makita et al[13] examined 129 cases using the classification by the Association of Mammary Ductoscopy. They found that 88.5% of the polypoid solitary type was benign (54 of 61 cases). Of the polypoid-multiple type, combined type, and the superficial type, the rates of malignancy were 65% (13 of 20 cases), 88.9% (16 of 18 cases), and 96% (29 of 30 cases), respectively. The positive predictive values for the combined and superficial types are high while the same is low (65%) for the polypoid-multiple type in which the number of tumors is considered. This latter point still requires further consideration. When comparing our classification with that of the Association of Mammary Ductoscopy in the rates of correct diagnoses, there were 84.3 vs 85.3% and 90.1 vs 88.5%, respectively, for the positive predictive value and negative predictive value.

Regarding the histopathological diagnoses of the tumors visualized by mammary ductoscopy, new methods for performing biopsies with ductoscopy have recently been devised to make it possible to identify tumors on a one-to-one basis[3)7)14)]. By making further detailed comparisons of the tumor images and histopathological diagnosis, expectations are high for achieving further improvements in diagnostic accuracy.

Conclusions

Mammary ductoscopy makes it possible to observe the intraductal lumina to make the diagnoses of intraductal tumors in patients presenting with abnormal nipple discharge and is, therefore, a quintessential examination method. The mammary ductoscopic classification of intraductal breast tumors accurately reflects the histopathological characteristics of proliferation and progressive patterns in intraductal tumors that primarily occur from the lumen of the duct and, therefore, is indispensable in the diagnoses of intraductal tumors. Major clinical results have been achieved by mammary ductoscopy using this classification. We are convinced that mammary ductoscopy will make further major contributions in diagnoses and treatments of breast diseases that target early and minute lesions.

References

1) **Leis Jr HP**: Management of nipple discharge. World J Surge **13**: 736–742, 1989
2) **Ohuchi N, Furuta A, Mori S**: Management of ductal carcinoma in situ with nipple discharge. Cancer **74**: 1294–1302, 1994
3) **Kamio T**: The system and technique of duct endoscopy. Jpn J Breast Cancer **10**: 61–70, 1995
4) **Teboul M**: Echo-histological "Acino-Ductal Analysis". Preliminary results. Ultrasound Med Biol **14** (Suppl I): 89–95, 1988
5) **Okazaki A, Okazaki M, Asaishi K et al**: Fiberoptic ductoscopy of the breast: A new diagnostic procedure for nipple discharge. Jpn J Clin Oncol **21**: 188–193, 1991
6) **Makita M, Sakamoto G, Akiyama F et al**: Duct endoscopy and endoscopic biopsy in the evaluation of nipple discharge. Breast Cancer Res Treat **18**: 179–187, 1991
7) **Nagase J**: Endoscopical diagnosis and treatment for the intraductal lesions of the breast. Jpn J Breast Cancer **10**: 263–273, 1995
8) **Haagensen CD**: Disease of the Breast. 2nd ed.W.B Saunders Co. (1971)
9) **Kamio T**: Ultrasonographic diagnosis of nonpalpable breast tumor. Jpn J Med Ultrasonics **17**: 293–307, 1990
10) **Kamio T, Kameoka S, Hamano K**: Ductal echography: Classification of ducts. *In* Breast Ultrasound Update (Madjar H, Hackeloer B-J eds), pp174–182, Karger, Freiburg (1993)
11) **Kamio T, Kameoka S, Hamano K et al**: Indication for breast conservative surgery by ultrasonography. Jpn J Breast Cancer **11**: 656–664, 1996
12) **The Association of Mammary Ductoscopy**: Endoscopic classification of intraductal lesions. Proceeding of 6th Annual Meeting of Japanese Association of Mammary Ductoscopy (2001)
13) **Makita M, Akiyama F, Gomi N et al**: Endoscopic classification of intraductal lesions and histological diagnosis. Breast Cancer **9**: 220–225, 2002
14) **Makita M, Akiyama F, Gomi N et al**: Endoscopic and histologocal findings of intraductal lesions presenting with nipple discharge. Jpn J Breast Cancer **19**: 575–582, 2004

乳管内腫瘍に対する乳管内視鏡分類

東京女子医科大学　医学部　第二外科学（主任：亀岡信悟教授）

神尾（カミオ）　孝子（タカコ）・山口（ヤマグチ）　昌子（マサコ）・大地（オオチ）　哲也（テツヤ）・青山（アオヤマ）　圭（ケイ）・亀岡（カメオカ）　信悟（シンゴ）

異常乳頭分泌症例に対する乳管内の検索は，乳管内微小病変の存在診断や良悪性の鑑別診断，さらに，病変が乳癌の場合には癌の乳管内進展状況を把握する上で重要である．我々は1990年6月に乳管内視鏡検査を開始し，これまで異常乳頭分泌症例411例に対して乳管内の観察を行い，独自に作成した乳管内腫瘍に対する乳管内視鏡分類に基づいて乳管内腫瘍の評価を行ってきた．今回，乳管内視鏡検査で病変が捉えられ良悪性の鑑別診断を行ったのち病理組織学的な検索により確定診断の得られた乳管内腫瘍191例について，乳管内視鏡分類を用いた良悪性診断の妥当性について検証した．191例の病理組織学的診断の内訳は，乳腺症17例(8.9%)，乳管内乳頭腫103例（53.9%），乳癌71例（37.2%）であった．また，乳癌71例中36例（50.7%）は非浸潤性乳管癌であった．乳管内視鏡分類では，腫瘍の形態を有茎型，広基型の2型に大きく分類し，さらに広基型については半球型，凹凸不整型，不整隆起型の3型に亜分類している．有茎型を良性，広基型を悪性として算定したnegative predictive valueおよびpositive predictive valueはおのおの90.1%（n:121），84.3%（n:70）と良好であった．さらに，広基型の亜型別にpositive predictive valueをみると，半球型68.4%（n:19），凹凸不整型91.7%（n:12），不整隆起型89.7%（n:39）であり，凹凸不整型と不整隆起型の診断成績は良好であったが，半球型は，31.6%が良性腫瘍であり，この型の診断精度向上が今後に残された課題であると考えられた．

乳管内視鏡分類は，乳管内腫瘍の病理組織学的な増殖，進展様式の特徴を的確に反映しており，乳管内腫瘍の診断に極めて有用である．乳管内視鏡による診断は，今後，早期・微小病変をターゲットにした乳腺疾患の診断と治療にさらに大きく貢献し得るものと確信する．