

Nipple Adenoma of Breast: A Masquerader of Malignancy

Kanwal Aftab, Romana Idrees, Fozia Rauf and Naila Kayani

ABSTRACT

Nipple adenoma is a benign condition simulating malignancy such as breast carcinoma and/or Paget's disease clinically. In this study 19 cases diagnosed as nipple adenoma over a period of 14 years are described. The diagnosis was confirmed by histology alone. All patients were females with age ranging from 23 to 63 years. Most of the cases presented clinically with induration and ulceration accompanied by pain and itching. The diagnosis was clinically suspected in only 3 cases. This highlights the importance of histological diagnosis in all suspicious breast lesions. In one case, the clinical and histological diagnosis was incorrect leading to mastectomy. Complete local excision with clear margins is curative.

Key words: Nipple adenoma. Benign breast lesion. Florid papillomatosis of the nipple duct. Histopathology. Induration. Ulcer. Malignancy.

INTRODUCTION

Adenoma of the nipple is an extremely rare disease. About 200 cases have been reported in Europe and America, and 40 cases have been reported in Japan. No case series has been reported from Pakistan. The importance of recognizing these lesions stems from their resemblance to Paget's disease of the nipple clinically coupled with a histological picture that may be difficult to distinguish from ductal carcinoma.¹ Various histological patterns of nipple adenoma are described by Rosen as adenosis, papillomatosis, mixed proliferative and sclerosing papillomatosis.² The management and prognosis is entirely different from that of malignancy.

The evidence-based report describes a series of cases of nipple adenoma of the female breast.

METHODOLOGY

All cases diagnosed in the Section of Histopathology, Aga Khan University Hospital, between the period, January 1995- January 2008 as nipple adenoma were retrieved by using systemized nomenclature of medicine (SNOMED) coding system. Those that proved as nipple adenoma on histopathology were included and the rest were excluded. The selected cases were reviewed and clinical data including age, gender, clinical presentation and clinical diagnosis were recorded from files. Slides were reviewed for the size of the lesion and involvement

of margins. Results were described as measures of central tendency and dispersion for the studied variables.

RESULTS

Nineteen cases, diagnosed as nipple adenoma over a period of 14 years (1995- 2008) were included. All cases occurred in females with age range of 23-63 years and mean age is 40±11.8 years.

Most of the cases (n=11, 57%) presented clinically with induration of the nipple with ulceration accompanied by pain and itching and clinically suspected Paget's disease. Additionally ulceration and discharge was seen in 7 (36.86%) and 5 (26.3%) cases respectively. Two cases (10.5%) presented with nipple retraction and one case each presented as nipple mass and breast mass (Table I). The clinical diagnosis was nipple adenoma in 07 cases, Paget's disease in another 7 cases, carcinoma breast in 03 cases and chronic mastitis in 02 cases.

Table I: Clinical presentation of nipple adenoma.

Clinical presentation*	Number of cases
Induration of nipple with ulceration	11
Nipple discharge	5
Nipple Swelling	5
Nipple Retraction	2
Mass at nipple	1
Breast mass	1

*Some patients had more than one clinical presentation.

In all but one case, single small skin-covered fragments were received with average size of the lesion being approximately 0.5-1.8 cm (mean size=0.8±0.7 cm). The exceptional case mastectomy was received because of clinical suspicion of malignancy.

All cases showed histological spectrum of nipple adenoma like papillomatosis, adenosis and dense stroma (Figure 1, a and b). The predominant pattern was adenosis (7 cases, 36.8%) followed by mixed proliferation in 6 cases (31.5%), papillomatosis in 4

Department of Pathology, The Aga Khan University Hospital, Karachi.

Correspondence: Dr. Kanwal Aftab, Senior Instructor, Histopathology, Department of Pathology and Microbiology, The Aga Khan University Hospital, Stadium Road, P.O. Box. 3500, Karachi.

E-mail: kanwal.aftab@aku.edu

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cases (21.0%) and sclerosing papillomatosis in 2 cases (10.5%). Immunohistochemically double cell layer was confirmed by using antibodies against epithelial (cytokeratin CAM 5.2) and myoepithelial cells (ASMA and S-100) (Figure 2, a and b) in most of the cases. However, in one case clinically presenting as breast mass, an inaccurate histological diagnosis of ductal carcinoma was made followed by mastectomy. However, the mastectomy specimen, on extensive sampling did not reveal any invasive malignancy and review of the original biopsy revealed the error in diagnosis.

Status of margin of excision was also analyzed and in most cases the lesion was reaching the margin of excision in the initial excision biopsy specimen.

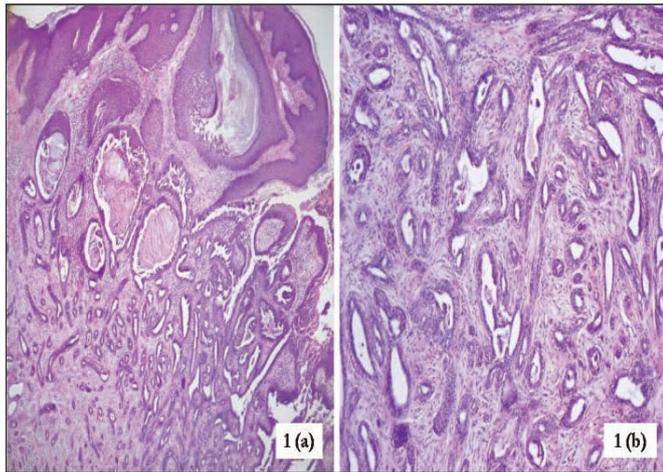


Figure 1: (a) Low power architecture of the nipple duct adenoma shows complex proliferation of tubular structures. (H&E stain, 10X). (b) Higher magnification reveals the presence of a double – cell layer. (H&E stain, 40X).

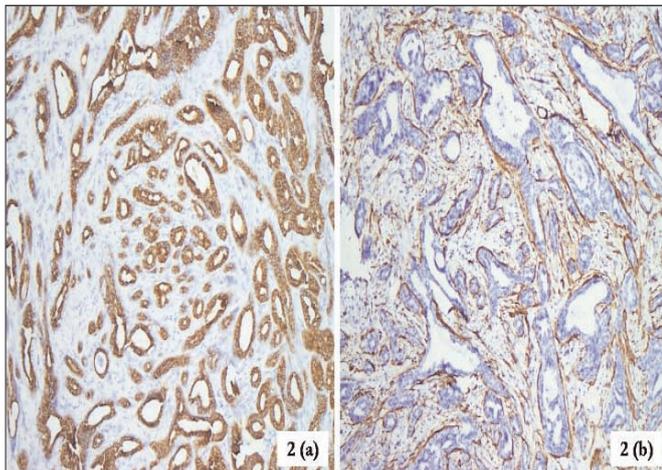


Figure 2: (a) Immunohistochemical stain CK CAM 5.2 highlights epithelial cells (40X). (b) Immunohistochemical stain ASMA highlights the myoepithelial cells. (40X).

DISCUSSION

Nipple adenoma is a compact proliferation of small tubules lined by epithelial and myoepithelial cells, with or without proliferation of epithelial component, around the collecting ducts of the nipple.³ It was first described in 1955 and is variably referred to as adenoma of nipple,

erosive adenosis or florid papillomatosis.² In previous reports of surgical case, the frequency of adenoma was 0.02%.¹

Nipple duct adenoma, usually a unilateral lesion occurs predominantly in the female breast, but it also occurs occasionally in the male breast.⁴ The patients range in age from newborn to 89 years, with the average age reported between 43 and 45 years in larger series.⁵ Clinical features like soreness, ulceration and swelling of the nipple, sometimes with discharge, may simulate Paget's disease.^{3,6-8} In literature, nipple discharge is the most common complaint present in 65-70% of the patients, followed by enlargement and induration of the nipple associated with ulceration.⁵ In this series a history of nipple discharge was present in only 5 cases (26.3%), and majority (11 cases, 57.8%) presented with induration of the nipple with ulceration (Table I).

In 7 cases (36.8%), clinical diagnosis was Paget's disease. The microscopic picture, of a nipple adenoma however, is distinctive enough to be distinguished easily from Paget's disease.

Microscopically, Rosen and Caicco described 4 distinct growth patterns of nipple adenoma, but these do not appear to have any prognostic significance, nor is there any evidence that they differ in pathogenesis.⁶ Sclerosing papillomatosis pattern is the one most to mimic carcinoma. In this series, one case was diagnosed on small biopsy as invasive carcinoma due to this mimicry. The features used to identify this lesion as benign include the presence of 2 cell types, a dual population of epithelial and myoepithelial cells (confirmed by immunohistochemical evaluation),⁹ an oval nuclear shape, a lack of atypia, presence of streaming, the formation of peripheral clefts and the absence of a cribriform pattern.⁷ The epithelial proliferation may show atypia and necrosis, a finding which leads to frequent misinterpretation of the changes as carcinoma.⁵ Western literature also cites a number of earlier studies in which these lesions were diagnosed as carcinomas followed by mastectomies. Thus, this diagnostic pitfall is well recognized in literature. In this study 2 patients underwent unnecessary major surgery.

The coexistence of carcinoma and nipple adenoma has been noticed before by many investigators, and the reported incidence of this phenomenon varies in different studies. Fisher *et al.* found that, in a group of 967 patients with carcinoma, 1.2% had associated nipple adenoma.¹⁰ In this series, only one patient had a history of infiltrating ductal carcinoma. The patient subsequently presented with induration of the nipple with ulceration and clinician suspected Paget's disease of the nipple, but on excision showed histological picture of nipple adenoma. In a quarter of cases in one series nipple adenoma was an incidental finding in mastectomy specimens removed for breast cancer.⁵ Another author

described the nipple adenoma as an incidental finding in the resected breast for invasive breast cancer and high Ki-67 labeling index in the tumour cells in the superficial region as compared to the deeper region. He postulated that in nipple adenoma sign and symptoms are associated with the destruction of the epidermis of the nipple by the invasion of benign tumour cells with high proliferation.¹¹

Complete excision with a narrow rim of uninvolved breast tissue is adequate treatment. In this series except one case of mastectomy, all the tumours were reaching the margin of excision. In two cases, there was recurrence due to incomplete excision of the lesion. This shows the importance of complete local excision with a rim of uninvolved breast tissue for adequate treatment. Appropriate histological evaluation of the lesion along with immunohistochemical assessment and clear margins remains the optimum method of managing these clinically and histologically challenging lesions.

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