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Original contribution

Atypical apocrine adenosis diagnosed on breast core biopsy: implications for management☆

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Summary Apocrine adenosis (AA) and atypical apocrine adenosis (AAA) are uncommon findings in breast biopsies that may be misinterpreted as carcinoma. The data from long-term follow up studies of open biopsies suggest that AAA is not a high-risk or precursor lesion. The clinical significance and risk implications of AAA diagnosed on core biopsy are not well established. The goal of this study was to determine the frequency of carcinoma in excision specimens after a core biopsy diagnosis of AA or AAA. We identified 34 core biopsies of AA (22) and AAA (12) performed between 1996 and 2014. The mean age at diagnosis was 60 years. The most common indications for core biopsy were calcifications (11), a mass or density (18), and a mass or density with calcifications (3). Two cases were detected on magnetic resonance imaging (MRI) studies. Available pathology reports and slides were reviewed, and surgical excision findings were correlated with core biopsy diagnoses. Of the core biopsies with AA or AAA, 7 also contained atypical ductal or lobular hyperplasia (AH) and 4 contained ductal carcinoma in situ or invasive carcinoma. In the absence of coexisting AH or carcinoma in the initial core biopsy specimen, none of the surgical excision specimens after a diagnosis of AA (2) or AAA (7) contained ductal carcinoma in situ or invasive carcinoma. AAA by itself is an uncommon core biopsy diagnosis that may not require surgical excision.

1. Introduction

In early descriptions of apocrine change and sclerosing adenosis (SA) of the breast, these histologic findings were regarded as benign and unlikely to be related to the development of carcinoma [1]. Subsequent long-term follow-up studies of patients with open biopsies established the cancer risk implications of many histologic types of benign breast disease (BBD) [2,3]. Among BBD categories, proliferative disease with atypia, or atypical hyperplasia (AH), was associated with the highest breast cancer risk [4–6]. By itself, apocrine change was associated with a relative risk (RR) of 1.2 for invasive carcinoma [7], and SA was associated with an RR of 1.7 [8]. Comparatively little is known about the risk associated with the presence of benign or atypical apocrine change in SA, often referred to as apocrine adenosis (AA) or atypical apocrine adenosis (AAA). In the Nashville cohort, AA showed an association with AH [9], but the cancer risk independent of coexisting AH is not well established. In a recent report from the Mayo BBD cohort, 2.7% (1/37) of patients with AAA alone developed invasive carcinoma, suggesting that AAA may not be a high-risk or precursor lesion [10].

AAA is part of the spectrum of apocrine lesions in the breast, ranging from benign apocrine change to apocrine ductal

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carcinoma in situ (DCIS) and invasive carcinoma. AA and AAA are of particular interest to pathologists because they can mimic patterns of DCIS and invasive carcinoma, potentially leading to the overdiagnosis of malignancy [9,11,12]. The diagnostic criteria applied to atypical apocrine proliferations are variable and not well validated in studies with clinical outcomes [13]. Features suggested to distinguish atypical or borderline apocrine lesions from apocrine DCIS include a threefold variation in nuclear size, prominent nucleoli, the absence of necrosis or architectural atypia, and limited extent [14–16]. Many of the same criteria have been applied to the diagnosis of AAA. In addition, studies reporting the highest RR of cancer for AAA may have included cases with cancerization of SA by apocrine DCIS [13,16].

With the widespread use of percutaneous core biopsy of the breast, attention has been focused on the risk of finding a carcinoma in an excision specimen after a core biopsy diagnosis of atypia. Several studies correlating core biopsy diagnoses of atypical ductal hyperplasia (ADH), atypical lobular hyperplasia, and flat epithelial atypia (FEA) with the frequency of carcinoma on excision have been published. However, no core biopsy series of AA or AAA have been reported. The objective of this study was to determine the frequency of carcinoma in excision specimens after a core biopsy diagnosis of AA or AAA. After almost any core biopsy diagnosis containing the term "atypical," most patients will be offered surgery to exclude the possibility of a more worrisome process. The data from this series may help distinguish patients who require surgery from those who may be offered clinical and radiologic follow-up as an alternative.

2. Materials and methods

This study was approved by the Cleveland Clinic Institutional Review Board. Breast core biopsies with a diagnosis of AA or AAA from January 1, 1996, to February 11, 2014, were retrieved from the Anatomic Pathology information system CoPathPlus (Cerner Corporation, Kansas City, Missouri) using the search terms "apocrine," "adenosis," and "breast." The initial search results included 34 core biopsies with AA or AAA from 31 patients from 1996 to 2014. The indications for core biopsy and patient age at core biopsy were recorded for all cases. For all core biopsies, the presence and type of coexisting (in the same core) or concurrent (in a concurrent ipsilateral core biopsy) atypia or carcinoma were recorded. Cases with coexisting atypia or carcinoma and cases without a subsequent surgical excision pathology report in CoPath were excluded from further study. Cases with another pattern of atypia, carcinoma in situ, or invasive carcinoma in ipsilateral core biopsies performed concurrently or within 4 months of the core biopsy with AA or AAA were also excluded. For the remaining patients, core biopsy findings were correlated with the histologic findings in surgical excision specimens.

AA cases showed a whorled lobulocentric pattern of sclerosis and a cell population with granular eosinophilic cytoplasm typical of apocrine change. Biopsies with AAA showed similar overall architecture with cytologic atypia that tended to be variable (Fig. 1). Nuclear enlargement and prominent nucleoli were evident in foci with atypia. None of the cases contained necrosis or an architectural pattern that would meet criteria for ADH or DCIS.

All available surgical pathology reports and slides for excision specimens after a core biopsy diagnosis of AA or AAA alone were reviewed. The presence and location of calcifications were included in the pathology reports for the core biopsies and the excision specimens. The submitted sections for all of the excision specimens included biopsy sites. One patient had 2 sites with AA on core biopsy, and 1 patient had 3 sites with AAA on core biopsy. Each core biopsy site was individually correlated with a corresponding excision specimen when possible. Excision specimens containing AA or AAA and another pattern of atypia were classified based on the coexisting pattern of atypia.

3. Results

A total of 34 core biopsies from 31 patients were initially identified, 22 with AA and 12 with AAA (Table). The mean and median ages for all patients were 60 and 58 years, respectively. Two core biopsies were magnetic resonance imaging (MRI)–guided, 13 were stereotactic, and 19 were ultrasound guided. The indication for biopsy was calcifications in 11, a mass or mammographic density in 21 (3 of which were associated with calcifications), and an enhancing lesion on MRI in 2 cases. One patient with AA had a history of invasive carcinoma in the ipsilateral breast, and 1 patient with AA had a history of DCIS in the ipsilateral breast. Six patients, 3 with AA and 3 with AAA, had a history of invasive carcinoma in the contralateral breast. One patient with AAA had a history of AH in the ipsilateral breast.

Of the 22 core biopsies with AA (Fig. 2), 18 were excluded from further study. Eleven did not have an available pathology report for an excision, and 7 had a more advanced lesion in the same core or a concurrent ipsilateral core biopsy. In the 7 core biopsies with AA and coexisting or concurrent atypia or carcinoma, 5 had AH, 1 had DCIS, and 1 had invasive carcinoma (Table). Of the 4 core biopsies with AA alone and a subsequent surgical excision, 2 of the excision specimens contained AA and FEA. Two of the core biopsies with AA alone were from 1 patient who also had a core biopsy with AAA several years later, and that core biopsy was immediately followed by surgery as discussed below. Neither of the surgical specimens after a core biopsy diagnosis of AA alone contained DCIS or invasive carcinoma.

Of the 12 core biopsies with AAA (Fig. 3), 5 had a more advanced lesion in the same core or a concurrent ipsilateral