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Adenoid Cystic Carcinoma of Breast: Clinicopathologic Study of Seven Cases

Raabia Nizamuddin², Nasir Ud Din¹, Romana Idrees¹ and Naila Kayani¹

ABSTRACT

Adenoid cystic carcinoma (ACC) of the breast is a rare type of tumor. Our objective was to determine the clinicopathologic features of breast ACC. We reviewed slides of breast ACC reported during 12 years. Seven cases were identified. Age ranged from 38 to 59 years (mean = 47 years). Mean tumor size was 2.3 cm (range 1.2 to 4 cm). Histologically, dominant cribriform pattern was seen in 4 cases, solid in 2 and tubular in one case. Mitotic figures ranged from 2 to 22/10 HPFs. Grades I and II were seen in 3 cases each while 1 was grade III. Post-surgical tamoxifen given in 3 cases, chemotherapy and radiotherapy in 2 and 1 case, respectively. Follow-up ranged from 12.5 - 138.5 months (mean = 61.25 months). One patient developed vertebral metastasis. Consistent with published data, this series indicated that ACC-breast has a good prognosis.

Key Words: Breast. Carcinoma. Adenoid cystic carcinoma. Prognosis.

Adenoid cystic carcinoma (ACC) of the breast is a rare type of tumor, seen in less than 0.1% of all breast carcinomas.¹ The first description of ACC by Geschickter dates back to 1945.² In most cases, it is shown to be less aggressive than ACC in other sites of the body, such as the lung, and salivary glands.³ The tumor consists of an epithelial and a myoepithelial component and is arranged in a variety of patterns, of which the cribriform and solid patterns predominate.⁴ Treatment options vary from simple lumpectomy to radical mastectomy. The exact incidence of ACC of breast in Pakistan is not known. In a large local study, it was seen that out of the 6718 cases of breast carcinomas, only 2 were found to be diagnosed with ACC.⁵ No case series on ACC-breast in Pakistan has been done to date. The aim of this study was to evaluate the findings from 7 patients with adenoid cystic carcinoma of the breast that were reported in our section.

The authors retrieved hematoxylin and eosin (H and E) stained slides of 7 cases of ACC of breast reported between 2002 and 2013 in the Section of Histopathology, the Aga Khan University Hospital (AKUH), Karachi, Pakistan. Four out of the 7 patients were treated at the AKUH. Clinical data of these 4 cases was obtained by reviewing past medical records, while those of the remaining 3 referral cases for histo-

pathology, was done via direct communication with the patient. Histological findings were reviewed by 2 pathologists. In 4 cases, immunohistochemical staining was performed: Cytokeratin Cam 5.2, CD10, S-100, p63 staining in 1 case, CD117 in 1 case, synaptophysin in 1 case, ASMA in 2 cases, 34-beta-E12 in 2 cases, cytokeratin AE1/AE3 staining in 2 cases. HER-2/neu and Estrogen/Progesterone receptor (ER/PR) testing was done in 2 cases.

The 7 cases occurred in women whose ages ranged from 38 to 59 years (mean = 47 years). A palpable lump was the main presenting complaint in 6 out of 7 cases, with 4 cases involving the left breast and 2 involving the right breast. Laterality was not known in 1 case. Two of the lumps were located in the periareolar region, 2 in the left upper quadrant, and 1 each in the right upper quadrant and the left lower inner quadrant. Three cases also involved associated skin with nipple retraction and tethering of the skin. Procedures performed included modified radical mastectomy, wide excision of the lesion, sentinel lymph node biopsy, needle localization excisional biopsy and lumpectomy.

Most of the tumors were firm in consistency and the colour of the tumors grossly was yellowish-pink, grey-brown and tan. One was noted to be well circumscribed while another had infiltrative borders (Figure 1). Hemorrhage was noted in 1 case. The tumor size ranged from 1.2 cm to 4 cm, with a mean tumor size of 2.3 cm.

Histologically, the tumor consisted of a ductal epithelial component and a basaloid myoepithelial component. The classic cribriform pattern was seen as a dominant component in 4 cases, in which large cystic spaces lined by basement membrane-like material is seen and as a small component in 1 case (Figures 2A and B). A tubular

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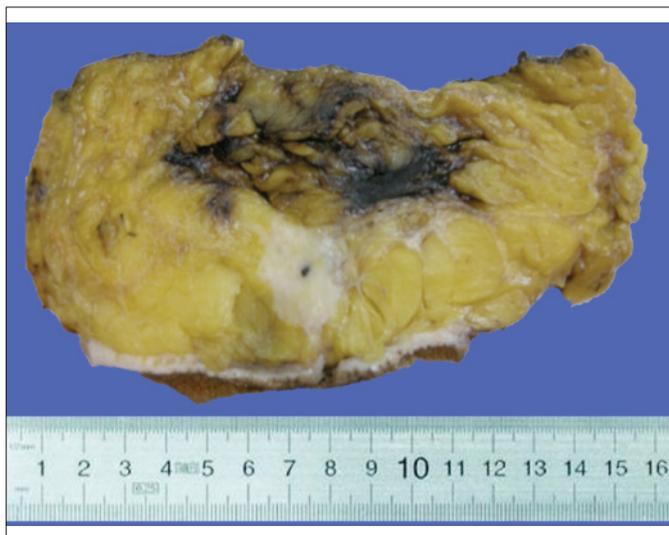


Figure 1: Gross appearance of ACC of breast. The tumor has grey-white solid cut surface.

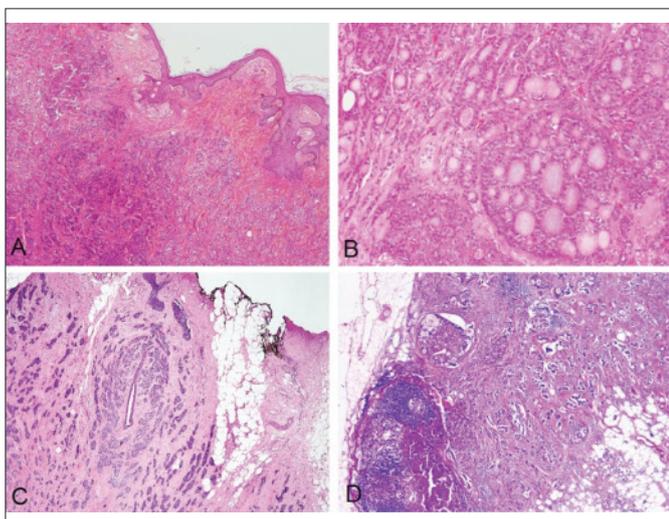


Figure 2: (A) Tumor is present beneath the skin as tubules and cribriform pattern (H&E, 4 x magnifications). (B) Predominant cribriform pattern with numerous cylinders containing homogenous acidophilic material (H&E, 10x magnification). (C) Arrangement of tumor tubules around a duct reminiscent of targetoid pattern (H&E, 4x magnification). Lymph node metastasis (H&E, 10x magnification).

pattern was seen as a dominant component in 2 cases and small component in 4 cases. In 1 case (case #5), the tumor tubules were seen to be arranged around ducts in a targetoid fashion, similar to that seen in lobular carcinoma (Figure 2C). In another case (case #6), secretions were seen in the tubules. A solid pattern was seen as a dominant component in 2 cases and small component in 2 cases, in which nests and clusters of cells were seen with pseudoglandular lumina. Sclerotic stroma was seen in 2 cases while hyalinized stroma was seen in 2 cases.

Typical characteristics of tumor cells in adenoid cystic carcinoma of the breast were seen as hyperchromatic nuclei, inconspicuous nucleoli and eosinophilic cytoplasm. Mitoses ranged from 2/10 to 22/10 high power fields. Infiltrative margins were seen in 2 cases (cases #1 and #5 in Table I). Three cases each were grade I and II, and one was grade III, according to the Modified Bloom and Richardson's grading system. Perineural invasion was noted in 3 cases. In the specimen of sentinel lymph node biopsy, 1 of the 8 lymph nodes was positive for metastasis (Figure 2D). In the modified radical mastectomy specimen, the lymph nodes were found to be tumor free (0/18) but did show reactive hyperplasia. In the excision biopsy specimen, the lymph nodes were also found to be tumor free (0/5). Evidence of extranodal metastasis was seen in the vertebral body in 1 case (case # 5). Immunohistochemical staining indicated cytokeratin AE1/AE3, CAM5.2, CD10, 34-Beta-E12 positive results in 1 case, 34-Beta-12 patchy positive in another case, CD117 in 1 case, HER-2/neu positive in 2 cases and ER/PR positive in 1 case. A special stain, PAS alcian blue, was positive in 1 case. The summary of all the findings are shown in Table I.

Three patients were started on tamoxifen after removal of the breast lump, 1 was started on radiotherapy and 2 underwent 5 cycles of chemotherapy. The follow-up period varied from 12.5 months to 138.5 months with a mean time period of 61.25 months. One patient lost to

Table I: Summary of cases of adenoid cystic carcinoma of breast (n=7).

Age	Procedure	Laterality	Tumor size	Growth patterns	Mitosis	Grade	IHC profile	Lymph nodes	Follow-up
51	Needle localization excision biopsy	Left	1.2x0.7	Cribriform	4/10	1	-	-	-
50	Lumpectomy	Left	3	Cribriform, tubular	5/10	1	ER/PR +ve	-	-
45	Frozen biopsy + Modified radical mastectomy	Right	3x2.7	Dominant component: Cribriform Small components: Tubular and solid pattern Perineural invasion	2/10	1	HER2/neu: +1	0/18	-
38	Lumpectomy	Not known	1.3x1.0	Dominant component: tubular Small component: cribriform	22/10	2	-	-	-
46	Excision biopsy	Left	4x2	Dominant component: Solid Small component: tubular pattern Perineural invasion +	12-13/10	2	-Cytokeratin AE1/AE3 +ve -Cytokeratin CAM 5.2: +ve -CD10: +ve -34-Beta-E12+ve	0/5	Vertebral body metastasis
59	Sentinel lymph node biopsy, wide excision of lesion	Right	2.5x2	Dominant component: Cribriform Small components: Tubular and solid pattern Perineural invasion +	12/10	2	-ER/PR +ve -Her2/neu: +ve	1/8 LNs positive for metastasis	-
40	Wide local excision	Left	1.5	Dominant component: Solid Small component: Tubular pattern No PNI	13/10	3	24BE12: patchy +ve CD117: +ve	-	-

follow-up. None of the cases had recurrence of adenoid cystic carcinoma of the breast; however, vertebral body metastasis was seen in 1 case, 4 months after surgery. Benign histological findings, occasional foci of atypical lobular hyperplasia and microcalcifications were seen in 1 case, after which a lump excision was performed (case #1). In addition, a simple mastectomy and excision of axillary lymph nodes were performed to remove the residual tumor in another case (case #5). At the time of diagnosis, metastasis to a single lymph node was seen in 1 case (case #6).

Adenoid cystic carcinoma of the breast is a very rare tumor, seen in less than 0.1% of all breast carcinoma cases.¹ It is shown to be less malignant than ACC elsewhere in the body, such as the salivary gland, the tracheobronchial tree and the Bartholin's gland.³ In a case series on adenoid cystic carcinoma of the salivary glands by Nascimento *et al.*, local recurrence was seen in 37% of cases and metastasis in 50% of cases.⁶ In this case series, only 1 patient was found to have metastasis to a non-sentinel lymph node at the time of diagnosis and only 1 patient was found to have distant metastasis to the vertebral body after surgical removal of ACC-breast. One of the largest studies in the literature indicated that a mere 7 patients out of 225 presented with distant metastasis or unknown stage at the time of diagnosis,⁷ thus highlighting the difference in the degree of malignancy between the tumor and its counterparts elsewhere in the body.

The mean age at the time of diagnosis in this case series, 47 years, conforms to that seen in the vast majority of studies in the literature, where it is seen to fall in the 4th and 5th decade of life.^{3,8,9} The mean tumor size of 2.3 cm also falls in the size bracket most commonly seen in the literature of 1.8 to 3.7 cm.⁸

Histologically, as seen in previous studies in the literature, the cribriform and solid histological patterns are the dominant patterns seen while a tubular pattern is less commonly seen.^{4,8} The vast majority of studies in the literature show that ACC of the breast tumors are generally ER/PR and HER-2/neu negative and were shown to have a good prognostic value. However, there are some studies that indicate ER/PR positive ACC-breast tumors.⁹ In their study on the subject, Alpino and Clark noted that 46% of cases revealed a positive ER status and 36% showed a positive PR status.⁹ Three out of our 7 cases revealed a positive HER-2/neu and/or ER/PR status. None of these 3 cases resulted in local recurrence, while only 1 resulted in metastasis to 1 lymph node. Furthermore, an ER/PR positive status is very rarely seen in ACCs' more malignant counterpart tumors such as those seen in the salivary gland, suggesting that perhaps a positive ER and PR status does not significantly affect the prognosis of the tumor. Furthermore, it points to the cell origin of the tumor from

the breast's ductal element as opposed to its glandular element.¹⁰

Due to the rarity of the disease, the most optimal treatment option remains controversial. However, more often than not, simple mastectomy is considered to be the most preferred treatment modality.⁴ Local recurrence of ACC-breast is often seen to follow local excision,^{8,9} but it was not seen in any of these cases. Various treatment modalities were used in this case series, ranging from lumpectomy to radical mastectomy and most followed a good outcome.

Perineural invasion is reported to be a rare finding.^{3,6} However, in this case series, perineural invasion was seen in 3 of our cases, suggesting that it may be a poor prognostic factor for the disease.

No preferences to either breast or unilateralism were most common findings seen in the literature. In this case series, 4 cases occurred in the left breast, while the remaining 2 occurred in the right breast. Lymph node metastasis occurred in a case of ACC in the right breast, vertebral body metastasis occurred in a case of ACC in the left breast, and the remaining all cases had good prognosis, suggesting that laterality does not hold any significant value. There are multiple reports in the literature that indicate no significant predilection to either location of the lump in the central region or the upper quadrant. Similarly, our case series indicated that 3 of our cases occurred in the upper quadrant, 2 occurred in the central region and 1 occurred in the lower inner quadrant.

Consistent with data in the literature, this case series indicates that ACC-breast has a good prognostic value, with rare local recurrence after removal of the tumor and of distant metastasis. Other characteristics of the tumor were also seen in this case series, such as a small tumor size, preferential occurrence in the 4th and 5th decade of life, a dominant cribriform, and solid histological pattern. A positive ER/PR and HER-2/neu status does not seem to significantly alter the prognosis of the tumor. However, perineural invasion may play a role in worsening the prognosis of the tumor. It is difficult to definitely say which treatment modality is most effective. Perhaps, a larger study can validate our findings.

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