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Complex sclerosing lesion of the breast displaying progression to invasive cancer: A case report

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Abstract
A 70 year old lady presented with two lumps in the right breast since around fifteen years which were increasing in size since the past one year. Mammography showed a solid-cystic and a lobulated lesion in the right breast which were categorized as BIRADS (Breast Imaging- Reporting and Data System) category 4/5. On FNAC, a diagnosis of Atypical Ductal Hyperplasia, NHSBSP (National Health Service Breast Screening Programme) Category C4 was made and histopathologic examination advised. Subsequently right sided simple mastectomy was received the larger mass in which showed extensive areas of sclerosing adenosis with superimposed ductal carcinoma in situ. The subareolar mass showed a papillary lesion displaying epithelial overgrowth with features compatible with ductal carcinoma in situ. A thorough search revealed invasive nests in the vicinity of the papillary lesion. A diagnosis of Infiltrating Ductal Carcinoma arising in a multifocal complex sclerosing lesion with extensive intraductal carcinoma and intracystic papillary carcinoma was made. This case offers to display a pathologic continuum of sclerosing breast lesions evolving into atypical hyperplasias, intraductal carcinoma and invasive carcinoma. This falls in line with the current thoughts on premalignant nature of sclerosing lesions of the breast.

Keywords: Complex sclerosing lesion, sclerosing adenosis, ductal carcinoma in situ

Introduction

Case Presentation

A 70 year old lady presented with two breast lumps since around fifteen years for which she had not sought medical advice. She reported that the lumps were increasing in size since the past one year. She was advised radiological evaluation.

Mammography showed a well-defined hypoechoic cystic lesion measuring 4.9 x 4.2 cm with solid component noted within it in the retroareolar region at 11-12 o clock position of the right breast. Another lobulated lesion measuring 4.9 x 3.9 cm with internal vascularity and micro calcifications was noted in the lower outer quadrant at 7 o clock position of the right breast. It was categorized as BIRADS category 4/5.

At the time of FNAC, three lesions were palpable in the right breast. The first one was retroareolar, the second in the lower outer quadrant, both measuring around 4 cm each in diameter and a third smaller lesion along the lower inner quadrant measuring 2 cm in diameter.

Giemsa stained smears from the two larger lumps from which bloody fluid was aspirated showed similar morphology. They were markedly cellular. Loosely cohesive clusters of breast epithelial cells with admixed myoepithelial cells were seen. Cellular overcrowding and nuclear overlapping were observed. Microacinar formations were prominent. The cells showed mild anisokaryosis and nucleomegaly. Mitotic figures were increased in a few clusters. Background showed macrophages. On these bases, a diagnosis of Atypical Ductal Hyperplasia, NHSBSP Category C4 was made and histopathologic examination was advised.

Subsequently right sided simple mastectomy was received in which two masses were observed. The larger mass, which was being felt as two growths during local examination was found to be a continuous single mass. The subareolar mass, measuring around 4.5 cm in diameter was cystic and contained blood clots. Solid granular area was seen on one aspect of the cyst measuring 2.5 cm in diameter. This involved duct as seen while serial slicing of the specimen presented another solid cystic lesion measuring 4.5 cm, along the lower outer quadrant.

The third mass, along the lower inner quadrant was hard and irregular and measured around 2 cm. No lymph nodes were found. Microscopically, the larger mass showed extensive areas of sclerosing adenosis with superimposed ductal carcinoma in situ. Regularly spaced geometric 'cookie cutter' spaces were present throughout. The cells showed a mild degree of anisonucleosis and vesicular-hyperchromatic nuclei with coarse chromatin. The subareolar mass showed a papillary lesion confined in fibrotic cyst walls. Epithelial overgrowth with features compatible with ductal carcinoma in situ were seen to have replaced most of the fibrovascular cores. Calcification, apocrine metaplasia and collections of macrophages were present. A thorough search revealed invasive nests trapped in desmoplasia in the vicinity of the papillary lesion. A diagnosis of Infiltrating Ductal Carcinoma arising in a multifocal complex sclerosing lesion with extensive intraductal carcinoma and intracystic papillary carcinoma was made.

The patient was then referred to a tertiary care centre for further investigation and management.

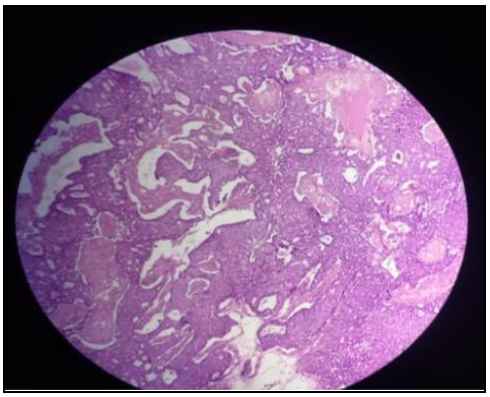

Fig 1: Sclerosing Adenosis with superimposed epithelial hyperplasia (H&E, 40X)

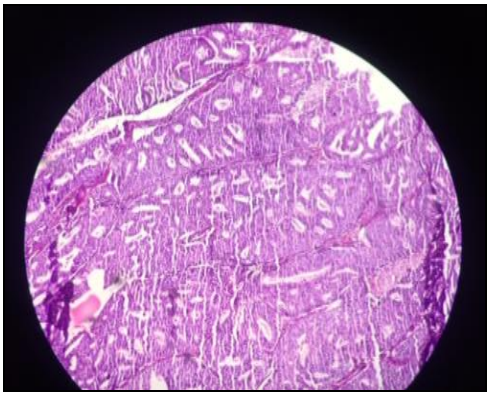

Fig 2: Sclerosing papillary lesion with features of intracystic papillary carcinoma (H&E, 40X)

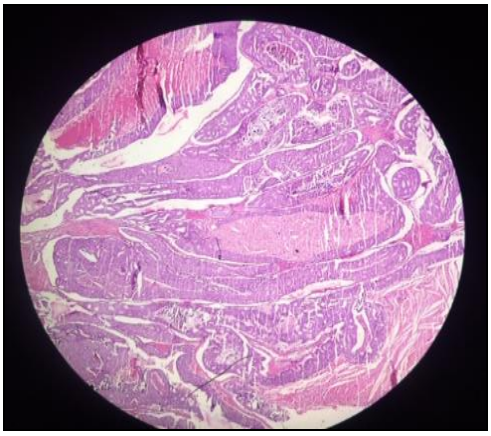

Fig 3: Papillary component of Complex Sclerosing Lesion showing collection of macrophages (H&E. 100X)

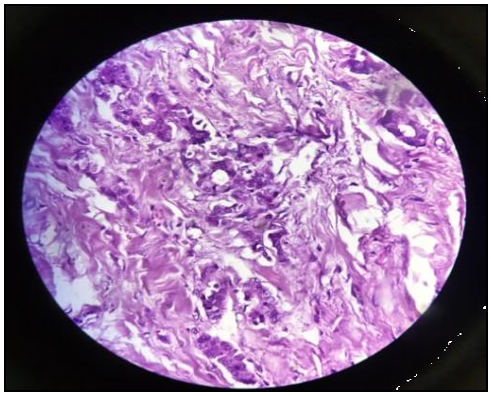

Fig 4: Invasive nests in a desmoplastic stroma (H&E, 100X)

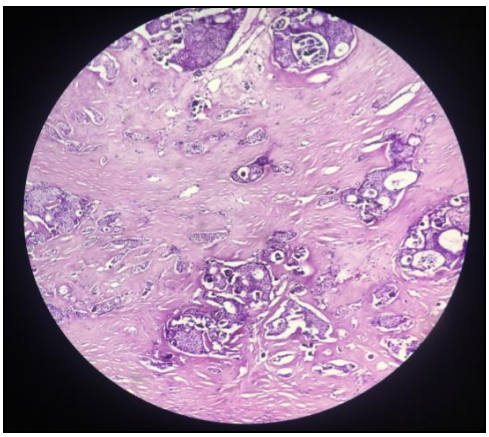

Fig 5: histological section demonstrating calcification.(H&E; 100X)

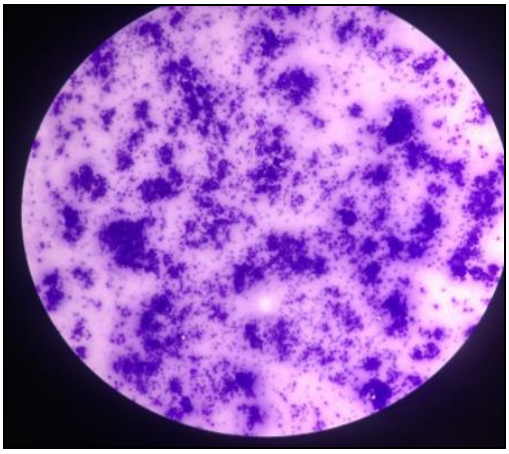

Fig 6: FNA smears showing loosely cohesive clusters of Brest epithelial cells with tendency for microacinar formations. (H&E: 40X)

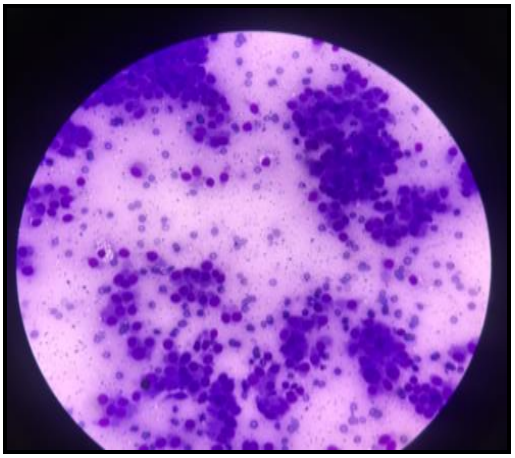

Fig 7: FNA smears showing some degree of anisonucleosis, nucleomegaly and nuclear overlapping. (H&E; 100X)

Discussion

Radial Scar (RS) or Complex Sclerosing Lesion (CSL) is a pathological entity characterized by a fibroelastotic core with entrapped ducts [1]. It may be associated with atypical and typical epithelial hyperplasia, adenosis, papillomatosis, ductal carcinoma in situ (DCIS) or invasive carcinoma within or adjacent to RS [2].

Here we present a complex sclerosing lesion which is unique in that it is multifocal and is associated with infiltrating carcinoma, extensive intraductal carcinoma in foci of sclerosing adenosis as well as papillary lesion with features of inracystic papillary carcinoma.

Some authors have suggested using the term "radial scar" for lesions measuring <1 cm, whereas the term "complex sclerosing lesion" was reserved for lesions measuring 1 cm or larger [3]. Our patient presented with masses measuring around 4.5 cm and 2 cm and were classified as complex sclerosing lesions.

Although sclerosing adenosis is often found as a microscopic lesion accompanying fibrocystic diseases, it rarely presents as a palpable mass when it is designated as adenosis tumour or nodular sclerosing adenosis [4] The present case showed on histology components of complex sclerosing lesions-sclerosing adenosis and intracystic papillary carcinoma, presenting as multifocal palpable masses.

Radial scar/CSL has been associated with both age and lesion size; lesions smaller than 6–7 mm or in women under the age of 40 are not correlated with cancer, but patients over 50 years of age with lesions greater than 2 cm are at a slightly higher risk [5]. Jacobs *et al.* found that radial scars were associated with an even greater risk of carcinoma breast in women with larger or multiple radial scars [6]. These findings corroborate with the findings in our patient in whom invasive and in situ cancer were found. She had larger, multiple lesions and her age was 70 years.

This case offers to display a pathologic continuum of sclerosing breast lesions evolving into atypical hyperplasias, intraductal carcinoma and invasive carcinoma. This falls in line with the current thoughts on premalignant nature of sclerosing lesions of the breast. In some studies, radial scar/complex sclerosing lesion was not found to be independently associated with an increased breast cancer risk, but only secondary to the frequent association of RS/CSL with other proliferative disease.[7] However, view is largely held based on multiple studies that complex sclerosing lesions may serve as a milieu for the development of atypical epithelial proliferations, including atypical intraductal hyperplasia and DCIS [8]. Jacobs *et al*., for instance, found that radial scars were associated with a doubling of the risk for breast cancer, regardless of the type of primary breast disease [6].

Radiologically complex sclerosing lesions reveal a radiolucent central core and radiating spicules, which is indistinguishable from invasive carcinoma mammographically as well as histopathologically.[9] the present case showed solid-cystic and lobulated lesions with internal vascularity and micro calcifications which were categorized as BIRADS 4/5.

Calcifications are common in RS/CSL and are often associated with the proliferative changes and sclerosing adenosis that coexist with these lesions. These calcifications are usually not helpful with respect to differentiating benign from malignant disease at imaging [10]. Facilities for breast ultrasound, MRI, Digital Breast Tomosynthesis, core biopsy are not available at our centre.

On aspiration, papillary breast lesions usually yield highly cellular smears containing clusters of ductal cells, often with a papillary configuration [11]. The papillary nature of one of the two lesions could not, however, be appreciated on cytology smears from our patient.

The cytology of fibrocystic changes, papillary lesions, radial scars, fibroadenoma, low-grade ductal carcinoma, or apocrine carcinoma often appear similar. The role of FNA cytology in the diagnoses of sclerosing or papillary lesions breast lesions is said to be, therefore, limited [12]. Although we could not determine the papillary nature of one of the masses on cytology, detection of subtle features that suggested atypical hyperplasia even in the absence of frankly dysplastic features led to histopathological examination of the lesions and detection of malignancy.

In the present case, clusters of breast epithelial cells with probable myoepithelial cells were seen in a background of macrophages. Collections of macrophages within the fibro vascular cores of the papillary lesion were observed on histology. These observations stand in contrast with the knowledge that myoepithelial cells, apocrine cells and histiocytes are suggestive of a benign proliferation [12]; as extensive intraductal carcinoma and foci of infiltrating

carcinoma were subsequently seen on histology.

As a rule, micro calcifications are not a common feature of papillary lesions, whether benign or malignant. When micro calcification is encountered, it is most frequently in the setting of a sclerosing papilloma [12]. Micro calcifications were observed in histology slides from the cystic-granular papillary growth in our patient, albeit only in association with areas of sclerosis.

Calcification is one of the common features of ADH, studies have found calcification to be present in up to 70% of the ADH cases, and that calcification didn't have a significant independent association with higher risk. Research is impending to assess if intra-ductal calcification and stromal calcification correlate with different risks [13].

The distinction of benign and malignant proliferative lesions based on hematoxylin-eosin (H&E) morphology can be very challenging. This has led to a considerable increase in the number of different antibodies available for use in the diagnosis of breast lesions [13]. A combination of ME cell markers (p63, calponin, CD10) and antibodies to high molecular weight cytokeratins, such as CK5/6 and 34þE12; and estrogen receptor (ER) has been known to be useful in the differentiation of benign and neoplastic proliferations of the breast.[12] The present case showed the presence of myoepithelial cell marker p63 only at the epithelial-stromal surface in the papillary lesion; and strong and complete positivity for ER in the regions of proliferation and invasion. Subsequently, foci of invasive carcinoma entrapped in desmoplasia were detected by thorough re-sampling. The findings in our patient concur with research that has observed invasive cancers in radial scars to have favorable biological profiles - positivity for estrogen and progesterone receptors, apart from a low proliferative index [14].

In conclusion, sclerosing lesions can present as palpable masses and display varied histologic patterns–sclerosing adenosis and papillary lesions; with superimposed typical and atypical epithelial hyperplasias which serve as fertile soils for the development of invasive cancer. Sclerosing lesions with hyperplasias must be sampled thoroughly to rule out progression into invasive carcinoma.

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