Epidermal inclusion cyst of the breast: A literature review

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Abstract. An epidermal inclusion cyst (EIC) of the breast is a rare, benign condition that may potentially be malignant. The present study conducted a systematic review of the literature in order to identify pathological hypotheses, clinical characteristics, and diagnostic and treatment options. A search for relevant studies was conducted through the Scopus, Embase and Medline databases during September 2014. The search term employed was 'epidermal inclusion cyst breast'. Studies were selected if they contained adequate information regarding symptoms at presentation, diagnostic tools, pathology, characteristics, type of procedure performed and follow-up routines. A total of 35 papers describing 91 patients affected by EIC of the breast were identified. Following this, a total of 82 patients, including an additional case supplied from the present study, were selected for further analysis. EIC of the breast typically occurs during the fifth decade of life. A palpable mass of the breast was present in 65 (79%) patients. Ultrasonographic imaging was consistently utilized as a diagnostic tool in all the cases analyzed, whereas fine-needle aspiration cytology was used in 70% of the cases and mammography in 65%. No tumor recurrence was reported at a mean follow-up time of 53 months. The present study demonstrated that elliptical excision is the preferred treatment for EIC of the breast, with pathological analysis required to exclude malignancy.

Introduction

An epidermal inclusion cyst (EIC) of the breast is a rare condition that develops due to the proliferation and implantation of epidermal elements within a circumscribed space in the dermis (1). Growth of the EIC occurs through the accumulation of epithelial and keratinous debris, and it is formed by the inclusion of keratinizing squamous epithelium within the dermis, resulting in a lamellated keratin-filled cyst (2). Historically, EICs have been referred to using a number of different terms, including follicular infundibular cysts, epidermal cysts and epidermoid cysts. EICs may occur anywhere in the body, although they are most prevalent on the face, trunk, neck, extremities and scalp (1). EICs rarely develop in the breast-develops in the breast, it presents as a lump that is primarily localized in the periareolar region (3). The importance of this benign lesion lies in the differentiation between other non-neoplastic and neoplastic breast lesions (2). Furthermore, an association between EIC and squamous cell carcinoma has been reported (4). The incidence of malignant potential is highly variable (0.045-19.0%) and the true incidence remains uncertain (5).

The aim of the current literature review, with the addition of an individual case reported in the present study, is to identify and discuss the incidence, demographic occurrence, racial differences, clinical characteristics, pathology, and diagnostic and treatment options of this disease.

Materials and methods

Literature review. The literature search involved the use of the Scopus (www.scopus.com), Embase (www.embase.com) and Medline (www.ncbi.nlm.nih.gov/pubmed) databases during September 2014. Manual searching of reference lists of the relevant studies and previous reviews was also performed. No language restrictions were applied. The primary search term was conducted for any combination of the words 'epidermal inclusion cyst breast'. Studies were included if they contained adequate information regarding symptoms, EIC characteristics (size and location) and the type of procedures performed. In the case of duplicate publications, the latest and most complete study was included. Studies that dealt with locations other than the breast were excluded.

Data extraction. Two independent reviewers extracted data from each study using a predefined database form, which resulted in high interobserver agreement. The information included the names of the authors, the title of the study, the journal in which the study was published, the country and year of the study, the demographics of the patients, anamnestic information, the diagnostic tools used, the disease pathology and the treatment performed.

Following completion of data extraction from the included studies, the two independent reviewers discussed the results of the collected data and, if discrepancies were present, a consensus was reached by mutual agreement on the accuracy of the data.

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Key words: epidermal inclusion cyst of the breast, cancer, surgery

Statistical analysis. The data were entered into a computer spreadsheet and statistically analyzed through the use of SPSS software, version 21.0 (IBM SPSS, Armonk, NY, USA). Data were expressed as the mean ± standard deviation. Comparisons between groups were tested with Pearson's χ^2 test, either using Yates' correction or Fisher's exact test when appropriate for categorical variables, and Student's t-test for continuous variables. The association between tumor size (cut-off at 4 cm) and malignant transformation was analyzed and calculated using the Spearman's rank correlation coefficient method. The r value is reported for all linear regressions. P<0.05 was considered to indicate a statistically significant difference.

Results

Study data. The search identified 35 studies (1-35), describing the clinical course of 91 patients affected by EIC of the breast. Following a review of the literature, 8 studies that described 10 patients were excluded, as the complete studies could not be found or only partial data was available (28-35). The remaining studies fulfilled the inclusion criteria. A total of 81 patient cases were retrieved, to which an individual case reported by the present study was added, creating the final total of 82 cases available for the present analysis.

Case report. A 70-year-old woman was referred to the Department of Surgery, Policlinico Umberto I (Rome, Italy) in June 2013 due to a painful and rapidly growing palpable mass in the left breast. The medical history of the patient was notable due to previous addictive breast plastic surgery and subsequent implant removal due to rupture. Physical examination identified a round, firm lesion that was non-adherent to the overlying skin in the lower outer quadrant of the left breast. Ultrasonography exhibited a solid, heterogeneously hypoechoic, well-circumscribed mass measuring 3.1x3.0 cm. An excisional biopsy was performed with an ellipse of skin. Pathological examination of the mass detected breast lobules and EIC (Fig. 1). The patient provided written informed consent.

Demographics. Of the 82 patients, there were 60 females (73%) and 8 males (10%), while in 14 cases (17%) the gender was unspecified. The mean age at presentation was 48±14 years (median, 47 years; range, 20-85 years). EIC was identified in the majority of cases within the Asian and Caucasian populations (28 and 22 cases, respectively). The right side was affected in 24 patients (29%) and the left in 32 (39%). Out of 68 patients from whom information was retrieved, 11 (13%) had undergone previous cosmetic breast surgery and 7 (19%) had experienced previous trauma. Neither a family history of breast disease or previous/current hormonal medication was noted. Furthermore, a predisposition to develop EIC of the breast was not observed with oral estroprogestinic therapy or genetic patterns. No specific information regarding weight, body mass index and biochemical tests were available, and no patients had associated EIC at other body locations. The postoperative course was uneventful. The patient remained alive without signs or symptoms of recurrence at a follow-up of 27 months.

Clinical presentation. A total of 65 patients (79%) presented with a palpable mass of the breast. Local discomfort was
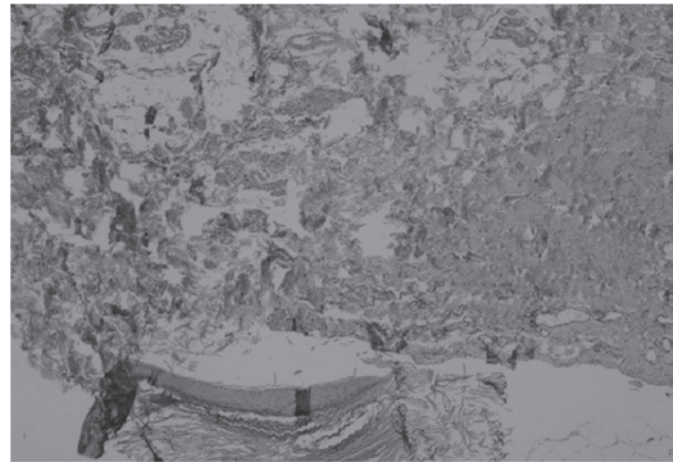

Figure 1. Pathological analysis of an EIC of the breast as presented in a 70-year-old patient. Breast lobules may be observed in the upper section of the image, and the EIC may be observed in the lower section. Stain, hematoxylin and eosin; magnification, x100; EIC, epidermal inclusion cyst.

associated with 55 cases (67%), inflammation with 27 (33%), spontaneous rupture with 10 (12%) and ulceration with 3 (4%).

Tumor characteristics. At presentation, the mean tumor size was 4±3 cm (median, 3 cm; range, 1-10 cm). The mean growth period of the breast mass was 25±42 months (median, 12 months; range, 1-264 months).

Diagnostic tools. Ultrasonographic imaging, mammography, fine-needle aspiration cytology (FNAC) and FNA biopsy (FNAB) were the diagnostic tools that were used, either alone or in association, to investigate the presence of an EIC of the breast. A total of 22 patients were studied using ultrasonographic imaging and exhibited a solid, well-circumscribed and complex, or heterogeneous, appearance. Notably, an ꞌonion-ringꞌ appearance, with alternating concentric hyperechoic and hypoechoic rings was observed in 3 patients, and in 1 patient, this also extended into the dermis. Ultrasonographic imaging was demonstrated to consistently provide an accurate diagnosis.

A total of 24 patients underwent a mammography, which demonstrated a well-circumscribed mass with homogeneous increased density in 19 patients. However, in 5 cases, the mammography was misleading. Magnetic resonance imaging was performed in 2 patients and demonstrated a fluid-like signal with variable low-signal components on T2-weighted images, and a peripheral rim enhancement on gadolinium-enhanced images. FNAC was performed in 21 patients and FNAB in 17. An accurate diagnosis was achieved in 15 (71%) and 11 (65%) cases, respectively. In 10 cases, the diagnostic flowchart from the relevant studies was not available.

Pathology. EIC of the breast was benign in 72 patients (88%), and had transformed into squamous cell carcinoma in 10 patients (12%). In 3 cases, the congenital development of a cyst secondary to an obstructed hair follicle or pore was theorized. Whilst in 11 cases, an injury to the epidermis subsequently resulting in fragments being implanted deeply in the breast tissue was hypothesized, and in 3 cases, EIC was

believed to have developed following squamous metaplasia of normal columnar cells within a dilated duct in cases of fibrocystic disease (1 case), fibroadenoma (1 case) or a phyllodes tumor (1 case). A significant correlation between tumor size and malignant transformation was observed (P<0.01, r=0.459).

Surgical excision. Surgical excision of the mass was performed in 70 patients (85%). The remaining patients did not undergo surgery.

Follow-up. At a mean follow-up time of 53±62 months, no problems associated with the surgery or recurrence of the EIC of the breast were reported. The long-term survival of the patients affected with malignant transformation of the EIC was not reported.

Discussion

Despite the literature containing abundant case reports and reviews, several concerns remain regarding the incidence, etiology, diagnosis and treatment of EIC. The present study analyzed the current international literature with the aim of understanding this rare occurrence somewhat further.

To date, the international literature has reported 90 cases of patients who have been affected by EIC of the breast. To the best of our knowledge, the first histologically defined case of EIC of the breast was reported in December 1900 at The Johns Hopkins Hospital (Baltimore, MD, USA) (5). From the literature, it can be determined that EIC of the breast typically affects individuals in the fifth decade of life, and males are observed to be affected in a small proportion of cases (1-28). This type of tumor is naturally slow growing. The spontaneous rupture of large cysts was noted in 10 cases, releasing non-absorbable keratin, which acts as an irritant and subsequently leads to secondary foreign body reactions, granulomatous reactions or abscess formation.

A previous history of trauma or surgery appears to be associated with the development of this benign tumor, but other theories have been postulated (1-28). A unique pathogenesis cannot be concluded, but it is believed that, in the majority of cases, EIC of the breast may be congenital, arising from cell nests that remain from specific cells, including the embryonic mammary ridge. EIC of the breast may also develop from obstructed hair follicles. Furthermore, pilosebaceous structures may become inflamed, leading to a cystic reaction in the dermis, or be created by squamous metaplasia of normal columnar cells within a dilated duct in the case of fibrocystic disease, or in fibroadenoma or phyllodes tumors.

Physical examination regarding the diagnosis of EIC is unreliable (1-28). EIC of the breast typically appears as a smooth, round nodule, the nature of which cannot be detected through this method. Ultrasonographic imaging consistently achieved an accurate diagnosis (1,2,7-17,22,23,25,26), whilst mammography achieved accuracy in 79% of the reported cases (6-12,15-17,21-27). Magnetic resonance imaging was used in only 2 cases (16,25), but it was also observed to consistently identify EIC of the breast accurately. FNAC (2,8,16-19,25-27) and FNAB (1,2,7,8,14,15,18,22,23,25) may also aid the diagnosis, but these methods are less reliable when compared to ultrasonographic imaging. The present literature review demonstrated that ultrasonographic imaging is the diagnostic tool of choice to achieve the accurate characterization of EIC.

During the review process, it was identified that the association between EIC of the breast and malignant tumors was 12% (5,27). Malignant transformation appears to occur more frequently in EIC of the breast as opposed to EIC affecting other body areas, and this may be associated with the pathogenesis of EIC of the breast from squamous metaplasia of the mammary duct epithelium. Furthermore, a significant correlation between tumor size and malignant transformation was identified. Therefore, the presence of a lesion of <1 cm localized in the breast parenchyma may be differentiated from a large fibroadenoma or phyllodes tumor, and even from a malignant breast neoplasm with benign features, including mucinous carcinoma.

If the diagnosis is accurate, asymptomatic small-sized lesions (<2 cm diameter) do not require treatment. An excisional biopsy is not required if typical ultrasonographic findings are exhibited. However, EICs of the breast that are large and palpable, and possibly causing the patient physical and psychological discomfort, will require surgical excision through an elliptical incision. The removal of the entire cyst wall is recommended for pathological analysis and to prevent recurrence or malignant transformation.

In conclusion, EIC of the breast is a rare occurrence and the pathogenesis remains unknown. Future studies should focus on the identification of the predisposing factors, including hormone therapy or genetic predisposition, that may influence the development of this disease.

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