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## Mammary Duct Ectasia

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### Continuing Education Activity

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Mammary duct ectasia is a benign, non-proliferative breast disease. It affects the large duct system. The exact cause is still unknown, but it may be considered a developmental aging process characterized by elongated, convoluted, weakened duct wall that presents with nipple discharge or palpable mass. This activity reviews the evaluation and treatment of mammary duct ectasia and highlights the main role of the caring physician to exclude breast malignancy and the role of interprofessional teamwork to provide an individualized best treatment option for this condition.

#### Objectives:

- This activity describes the histopathologic changes seen in the mammary duct ectasia (MDE).
- It outlines the various clinical presentations of the cases of mammary duct ectasia.
- It describes the typical imaging findings associated with mammary duct ectasia.
- It explains the importance of collaboration among the interprofessional team of surgeons, radiologists, and histopathologists to provide the best treatment for patients with mammary duct ectasia.

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### Introduction

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Mammary duct ectasia (MDE) is a non-proliferative inflammatory disorder of the large duct (milk duct) of the breast; as such, it affects the nipple and areola complex. In MDE, focal dilatation of the lactiferous duct system is due to endoluminal changes, as well as the loss of duct wall elastin, leading to abnormally dilated and tortuous lactiferous ducts with associated periductal inflammation and fibrosis. The patient commonly presents with intermittent nipple discharge of varying colors (ranging from white to green/black to grey), as well as pain and tenderness of the nipple and areola. Other symptoms can include an inverted nipple or a palpable breast "lump," though, in many instances, MDE is asymptomatic.

MDE can mimic more serious conditions, such as breast malignancy, or other benign processes, such as mastitis.

The clinical manifestations of mammary duct ectasia overlap with another benign inflammatory condition known as periductal mastitis, a condition that occurs at the nipple-areola complex (more commonly in smokers), and sometimes the two conditions cannot be distinguished from

each other on clinical assessment, with the final diagnosis possible only after histopathologic examination of the excised duct tissue with the affected surrounding tissue.[1]

## Etiology

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The exact cause of the disease process is still unclear, and some authors consider it a part of the aging process due to involuntional changes of the fatty peri-ductal tissue, but this hypothesis cannot fully explain cases reported in children and young adults. Pregnancy, lactation, and abortion history are all inconsistently related to the development of MDE. Histopathologic findings demonstrate plugging of the lactiferous duct system with thick secretions and cellular debris, with subsequent duct dilatation. It is not yet known what underlying factors initiate the disease.[1]

## Epidemiology

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The exact incidence of this abnormality is unknown. It is mainly seen in perimenopausal women 45 to 55, but it has rarely been reported in infants, teenagers, and the male breast. It is more common in smokers and those with congenital nipple inversions or malformations as well.[2][3]

## Pathophysiology

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It is uncertain if mammary duct ectasia and periductal mastitis (PDM) are to be considered as a single disease on a spectrum or as separate, distinct disease processes. More studies on etiology and ultrastructural changes are required to give more information on changes leading to duct ectasia. The presumed pathogenesis is that the affected duct becomes dilated and tortuous due to breast involution or other factors accumulating granular debris with numerous lipid-laden macrophages. A significant histological difference hinting these may be separate processes is that in MDE, there will be no epithelial proliferation near the opening of the duct, as opposed to PDM, where this is a cardinal feature. Periductal collagenization and fibrosis may eventually produce skin and nipple retraction, which may predispose to one or both conditions.

In periductal mastitis (PDM), the epithelial lining is intact, but there is a proliferative epithelium in the form of squamous metaplasia, beginning at the distal opening of the duct in the nipple and progressively extending deeper into the duct system. The resultant keratin production accumulates and then leaks out to interstitial space, inducing severe periductal reactive inflammation, culminating in collagen formation and interstitial fibrosis. Accordingly, many clinicians consider mammary duct ectasia and periductal mastitis as distinct disease entities with some shared clinical consequences and manifestations and resultant overlapping differential diagnoses.

## Histopathology

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Excised duct specimens from patients with MDE reveal dilated lactiferous ducts with accumulated secretions, and potentially blood, in the intraductal space. The duct wall shows reduced elastin and inflammatory infiltrates with macrophages and plasma cells around the duct. Granulation tissue may fill the duct lumen. There is a lack of epithelial hyperplasia or apocrine metaplasia, and this is an important feature that distinguishes MDE from periductal mastitis (Zuska disease). In severe cases of mammary duct ectasia, duct obstruction is caused by fibrosis and not by epithelial hyperplasia. The presence of intraepithelial foamy histiocytes has to be carefully distinguished from Paget's spread of ductal carcinoma; cytokeratin and CD68 immunohistochemistry may be required to confirm this. Microabscesses are often seen in

severely complicated cases around dilated ducts. Calcifications are also seen in severe cases, and the presence of these calcifications on mammograms can mimic underlying malignancy, prompting biopsy for histopathological confirmation.

Transmission electron microscopic (TEM) studies of samples from patients with MDE have revealed some specific ultra-structural changes, such as denudation of the epithelial cells with focal loss of microvilli, which impairs duct clearance of the secretions. Widening of the interepithelial junctions with focal disruption of the T bars and periductal collagenization without inflammation may also be present; this helps differentiate MDE from PDM, where inflammation is always present.[4]

## History and Physical

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Mammary duct ectasia is frequently asymptomatic or only has subtle changes in breast texture that may go unnoticed until a nipple discharge is noticed. In breast clinics, nipple discharge is the third most common complaint and reason for medical consultation after mastalgia and a palpable lump in the breast.

Approximately 80% of women experience mammary discharge during their fertile lifetime, most of which are due to benign conditions. MDE is a benign condition that may be responsible for anywhere between 6% to 59% of patients presenting with nipple discharge.

The nipple discharge in MDE is variable, ranging from thick to thin, serous, dirty white, yellow, or green, and may fluctuate. It is usually unilateral, emanating from a single duct, though bilateral cases have been reported. If the discharge is bilateral, it is more likely to be due to fibroadenocystic disease, especially if it demonstrates a cyclical frequency. This variable presentation is part of the diagnostic challenge, as the traditional definition of pathological nipple discharge is defined as unilateral and spontaneous and frequently occurring from a single duct.

Essential elements of clinical assessment of nipple discharge include inquiry regarding discharge frequency, amount, color, whether it is spontaneous or provoked laterality, and single duct sourced or more (if able to be determined). Ideally, they can demonstrate the discharge during the examination, and the nipple can be observed under magnification.

Occasionally, patients with MDE present with small ovoid, well-defined subareolar, or periareolar tender masses associated with discomfort and erythema caused by dilated ducts filled with thick secretions and cellular debris. Upon pressing over the mass, nipple discharge appears from one duct opening. The nipple may be inverted in severe cases. Skin necrosis and ulceration are much more common in granulomatous lobular mastitis (GLM), a condition that may be associated with mammary duct ectasia. Still, the palpable mass in GLM tends to extend away from the nipple-areola complex. If secondary bacterial infection occurs, this can lead to the formation of a subareolar infection or abscess. In this setting, it can become difficult to distinguish MDE from periductal mastitis PDM or inflammatory carcinoma (which accounts for 1% to 6% of breast cancers). A trial of antibiotics with very close clinical follow-up is reasonable.

With repeated episodes of infection or with scarring from previous treatments or drainage attempts, more fibrosis is formed in the nipple-areola complex, which can potentially lead to nipple distortion or retraction. New-onset nipple retraction is a sign that must be investigated intensively, especially in a previously unknown patient. Assessment must exclude underlying malignancy, particularly when chronic pathologic changes lead to the formation of

microcalcifications behind the areola on the mammogram. A biopsy examination must be done to exclude carcinoma in these cases.

A clinical assessment of both breasts and axillae is required to determine the presence of lumps or lymphadenopathy, and a meticulous examination of the nipple-areola complex must be done. In the presence of active infection, a palpable tender axillary lymph node may be present.

MDE is rarely reported in neonates and childhood and should be low on the differential in these patients, but it can be a cause of nipple discharge, which tends to be bloody. The diagnosis is confirmed by an ultrasound study. This should not be confused with the physiologic nipple discharge that is due to maternal hormonal exposure.

In children, MDE tends to resolve spontaneously within two weeks, though it can take longer and is best managed conservatively. If the discharge continues for several months, surgical intervention is required in the form of a biopsy. Older children and adolescents should undergo a careful assessment to exclude the very rare juvenile secretory carcinoma and phyllodes tumors of the breast. It must be emphasized that any mass seen besides MDE must be biopsied.[5][6]

## Evaluation

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Breast pathologies, in general, are evaluated by a triple assessment approach, which includes clinical imaging and needle biopsy (tissue) assessment.

Imaging assessments can include bilateral mammography, ultrasound examination, CT, MRI, and occasionally others such as galactograms or the recently introduced duct endoscopy.

Ultrasound examination is the imaging of choice for those younger than 35. Mammography, with or without ultrasound, is the methodology of choice for the 35+ age group, while MRI (more rarely CT) can be used in any age to assess cases of equivocal findings of concern further. Fine-needle aspiration (FNA) cytology and tissue confirmation will also be required in suspicious lesions and may be helpful in equivocal cases.

### Mammographic Findings in MDE

For symptomatic patients with typical clinical findings suggestive of MDE, such as nipple discharge near areolar lobulated soft to firm swelling with mild erythema, mammography may not be needed to make the diagnosis of MDE. Much more commonly, a lesion is seen during screening mammography, and for those without previous symptoms of MDE, the mammographic features may include microcalcifications, lobulated, partially smooth masses, nipple retraction, retro-areolar duct dilatation, and rarely speculated looking mass. These are more worrisome, prompting further evaluation to exclude malignancy.

The microcalcifications may be branching, small clusters, or scattered unilateral or bilateral with or without associated nipple retraction.

In a study of 40,003 women who underwent screening mammography, 14% had some of the above features suggestive of MDE that were confirmed with cytology or tissue biopsy when required. In 40% of those with mammographic findings that underwent biopsy had no other pre-biopsy features to suggest MDE, and merely the biopsy was required to rule out sinister pathology. Thus, incidental detection remains uncommon, though common enough to warrant consideration.

### Ultrasound (US) Findings in MDE

Breast ultrasound is indicated in all cases of nipple discharge. The US can show mammary duct dilatation, mixed solid and cystic mass close to the areola, solid mass, and abscess collection. Not all diagnoses can be made via US imaging, particularly in cases of MDE with solid mass formation.

In a study that assessed 72 cases of symptomatic MDE, areolar and periareolar masses were evident clinically with an average diameter of 40 mm and varied in size from 6 to 120 mm. These masses were most often located in retroareolar and periareolar areas and ovoid and undefined, inhomogeneous, and hypoechoic, with increased blood flow on Doppler and with mammary duct dilation. Abscess formation was seen in almost 49% of these symptomatic cases. These cases significantly overlapped in clinical presentation with other causes of granulomatous lobular mastitis.

Assessment with ultrasound is also required imaging for children presenting with nipple discharge. The typical US findings of MDE would show a hypoechoic heterogeneous oval mass, potentially lobulated, consisting of anechoic tubular structures representing the duct ectasia. These typical findings do not require further tissue or cytology confirmation unless the discharge continues for more than a few months.

### **Magnetic resonance imaging (MRI)**

There is no observable significant difference regarding the diagnostic utility of MRI versus US in patients with MDE.

MRI is used to assess cases of MED with a mass lesion that is very suspicious for undetected carcinoma.

The morphologic features on non-contrast MRI are nonspecific, but on dynamic contrast-enhanced (DCE)-MRI, the cases of MDE will show thick-walled lesions with circular enhancement with no enhancement in the center, resembling thickened pipe, representing a thickened duct. No enhancement is noted in the delayed phase, while malignant masses reveal heterogeneity with clear irregular borders.

Some MDE may be misdiagnosed as intraductal papilloma (IDP) on MRI, and here, MRI, in addition to the US images, decreases the rate of misdiagnosis.

### **Galactography or Ductography**

Galactography is still used as a second-line investigation for young patients with pathologic nipple discharge after US examination. It is used in cases without mass lesions and after excluding malignancy. It requires cannulation of the discharging duct with a very fine cannula (30 Ga), injecting a small amount of iodine-based radiopaque contrast material, and then taking CC view images. The main disadvantages of this investigation are that it is time-consuming, it may take up to 30 to 60 minutes to finish the examination, and it is more invasive than other modalities. Some duct openings are too small to be cannulated. Occasionally, a wrong duct may be cannulated and imaged, so there is a false-negative rate of approximately 6%. Mastitis or duct rupture are other rare potential complications.

MDE is diagnosed when the duct is more than 3 mm in diameter and smooth-walled without ductal filling defects. If MDE is confirmed, this may spare the patient from duct excision for diagnosis.

### **Nipple Discharge Cytology (NDC)**

NDC smears are commonly obtained in cases of pathologic nipple discharge, and they may provide useful diagnostic information. It is an easy, noninvasive test to perform but challenging to the cytopathologist. Since the majority of nipple discharges are due to benign lesions, the ability to detect malignancy by examination of NDC ranges from 45 to 82% with 0.9% to 2.6% false-positive rate. In cases of MDE, there will be foamy macrophages in a proteinaceous background with few normal duct cells.

The highest diagnostic ability of this test is seen when the discharge is due to benign papilloma, as the smears tend to have high cellularity and sometimes contain fragments of the papillary branching clusters.

Smears, in general, may show duct cells, foam cells, inflammatory cells, blood cells, and suspicious malignant cells. No evidence in the literature that mammary duct ectasia can be specifically diagnosed by NDC, although the cytologist can suggest the presence of a benign inflammatory condition.

### **Fiberoductoscopy (FDS)**

For patients who present with pathologic nipple discharge, FDS is a more recent option to investigate the underlying cause of the discharge. It allows direct visualization of small ductal growths and other morphological changes in the major lactiferous ducts and segmental ducts. It is the only modality to visualize the intraluminal space directly.

The main disadvantage is its non-availability. It is not indicated for multiple duct discharges.

Technically, the procedure is performed under local anesthesia. As with any new procedure, it has a learning curve, which will lead to a decrease in the failure rate. The cannulation rate is usually around 90% and can reach 100% with time. The scope is very delicate, with a diameter of 0.45 to 1.1 mm, and is introduced after serial dilatation of the duct opening with serial dilatory probes (lacrima probes can be used if specialized equipment is unavailable). Mammary ductal ectasia, single or multiple papillomata, and complete duct occlusion can all be visualized and accurately diagnosed via this intraluminal examination. This investigation is gaining popularity and is expected to replace galactograms gradually.

FDS will help to improve the diagnosis and treatment of pathologic nipple discharge by isolating those who need to have microdochectomy or other procedures and also may limit additional procedures such as open biopsies.

Minor complications can occur, such as local inflammation, which is self-limiting.<sup>[7][8][9][10][11][12][13]</sup>

### **Treatment / Management**

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Since the exact cause of MDE is still unknown, there is no specific treatment, and all treatments are aimed at symptom relief and excluding more malicious pathologies.

In mild cases that present only with intermittent nipple discharge, after excluding other diseases and confirming MDE, reassurance is adequate and all that is required.

Patients with discharge and discomfort are advised to treat symptomatically via applying warm compresses over the central part of the breast, wearing a supportive bra with breast pads to absorb any nipple discharge, and maintaining nipple and areola hygiene. These measures both ameliorate symptoms of MDE, as well as reduce the risk of infection.

MDE is a non-infective disease process, but as mentioned earlier, there is clinical overlap with periductal mastitis in terms of clinical manifestations, and the two diseases can exist together. Symptoms can mimic other infections, including mastitis or malignancy, particularly the former, including rubor, tumor, calor, and dolor. Bacteria such as *Staphylococcus aureus*, anaerobic *Streptococcus*, *Enterococcus*, and *Bacteroides* are the most commonly reported isolates from nipple discharge cultures in 60% to 80% of cases.

Oral antibiotics, effective against *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococci*, and *anaerobes* for ten days, should be prescribed. The majority of patients will improve dramatically with antibiotic treatment and pain medication. The periareolar discomfort and swelling will subside in the majority of cases.

If the localized infection progresses to abscess formation, the response will be partial or nil. The management protocol for breast abscesses is as follows: Aspiration with antibiotic cover is effective as a treatment when the abscess cavity is equal to or smaller than 4 cm in diameter; otherwise, incision and drainage are required for larger collections or if recurrent after aspiration. Bacterial culture and sensitivity should be done on any aspirated or drained material for more specific antibiotic therapy. Retrograde drainage through duct opening under ultrasound guidance is a procedure that can be successful when purulent discharge is seen from a single duct opening, though it is often more technically difficult and painful than direct aspiration.

In cases with consistent or recurrent symptoms and swelling, excision of the involved duct and surrounding inflammatory tissue is performed, termed a “microdochectomy.” An intraoperative swab for culture and sensitivity from the wound site is advisable when inflamed tissues are dissected. However, in MDE alone, the cultures are mostly sterile, but when MDE is associated with periductal mastitis, 50% or more of the swabs will be positive. There is no evidence in the literature to suggest that MDE predisposes to cancer development; hence, routine biopsy is not indicated, and the decision must be individualized and based on patient risk factors independent of MDE.

More aggressive procedures and major mammary duct excision may be required for smokers or those patients with recurrent periductal mastitis associated with duct ectasia and duct fistulation. [14][15][1]

## Differential Diagnosis

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**Periductal mastitis (PDM)** is the most difficult condition to differentiate from MDE. There is an overlap in clinical manifestations and imaging findings. Medical literature still has some controversies and overlaps between MDE and PDM. Absence of smoking history, presence of more severe inflammation, higher frequency of acute exacerbations, and fistulae are more common in PDM. The final diagnosis is often impossible without histopathology.

**Granulomatous lobular mastitis (GLM)** is a rare inflammatory condition of the breast that affects lobular and ductal components associated with the formation of noncaseating inflammatory granulomatous mass. The mass is usually a presenting symptom, located slightly away from the nipple and tender on palpation. A lumpectomy or segmental mastectomy is often required for histopathology to confirm the diagnosis.

**Fibrocystic disease**, usually more diffuse manifestations, cyclical discomfort, nipple discharge from multiple openings, bilaterality, and palpation of cysts away from the nipple-areola region all point toward fibrocystic disease. Ultrasound is usually diagnostic.

**Ductal carcinoma in situ (DCIS)** or intraductal carcinoma, when located close to the areola, can be difficult to distinguish since calcifications are also seen with MDE. Imaging is helpful; a needle biopsy is required for final diagnosis.

**Intraductal papilloma** must be excluded in cases of pathologic blood nipple discharge. In MDE, the discharge is multi-colored, but younger patients may have a bloody nipple over the course of MDE. The absence of palpable thickened tubal structure in the subareolar area with always bloody in favor of intraductal papilloma. Diagnosis is confirmed by high-resolution ultrasound, discharge smear cytology, fiberoctoscopy, and histopathology of the microdochestomy specimen.

## Prognosis

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The prognosis is generally good since it is a benign disease that does not pose any increased risk of malignancy. Although the severity of the disease is variable, the cure can occur spontaneously with no specific treatment; at the other extreme, patients with a severe course of the disease may require medical or surgical therapies. Survival is not affected and remains similar to a healthy same-age population.

## Complications

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Recurrent attacks of inflammation, infection, and fistulation are the main complications; these complications require redo procedures and wider duct excisions with resultant scarring of the areola region.

## Consultations

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A general or breast surgeon's opinion is required, and they will provide management and follow-up. Support from radiology and histopathology departments is essential.

## Deterrence and Patient Education

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There are no measures to suggest to prevent MDE in view of the fact that etiology is still unknown, but generally, patients who start with mild disease with nipple discharge need to be educated on wearing a supportive bra with breast pads to absorb any nipple discharge to maintain nipple and areola hygiene to prevent secondary infection.

Patients will be reassured about the benign nature of MDE. Abstaining from smoking reduces the development of periductal mastitis, which can make the course of the disease more severe and with a higher rate of recurrences.

Patients should seek a general or breast surgeon's opinion to exclude malignancy.

## Enhancing Healthcare Team Outcomes

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Mammary duct ectasia is like many other benign diseases that have low morbidity and without mortality. It is not adequately researched. The medical literature solely relies on sporadic case reports and case series studies regarding investigations and management.

There are no randomized controlled trials on treatment options; hence, there is no consensus on therapeutic modalities. Treatment decisions are made similarly to a known range of associated problems with the same or other diseases.

The main role when dealing with patients with MDE for the general or breast surgeon is not to miss breast malignancy.

Good communication and teamwork involving a general or breast surgeon, radiology department, and histopathology are essential for individual case discussions aiming to provide the best choice of therapeutic management.

The treatment outcome is mainly related to the chronicity and severity of the disease. Generally, the prognosis remains good by the fact that MDE is a benign disease with no increased risk of malignancy.

More research is required to disclose the exact etiology and disease prevention or control in the future.

## Review Questions

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