Review Article

Breast concerns and disorders in adolescent females: a narrative review

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Background and Objective: Breast disorders are an important aspect of health care for adolescent females and this discussion presents principles for education and management of breast concerns as well as problems for this population of patients. Normal and abnormal breast development are considered. Breast pathology that is reviewed include congenital lesions as well as breast asymmetry, atrophy, tuberous breasts, fibroadenoma, cystosarcoma phyllodes, benign breast disease, mastalgia and other breast disorders.

Methods: An electronic search was performed on MEDLINE to identify relevant articles from 2010 to 2017.

Key Content and Findings: A review of relevant literature confirms that adolescent females have a variety of breast concerns and would benefit from the clinician asking these patients about this aspect of their body and dealing with issues that arise. Understanding of embryology and anatomy of the breast area is also important for clinicians in this regard. A careful and sensitive examination by the clinicians is important to help this young patients learn key information related to their sexuality and health.

Conclusions: A review of relevant literature confirms that adolescent females have a variety of breast concerns and would benefit from the clinician asking these patients about this aspect of their body and dealing with issues that arise. Understanding of embryology and anatomy of the breast area is also important for clinicians in this regard. A careful and sensitive examination by the clinicians is important to help this young patients learn key information related to their sexuality and health.

Keywords: Athelia; polymastia; fibroadenoma; mastitis; mammary hyperplasia; fibrocystic change

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Introduction

Breast disorders are an important aspect of health care for female adolescents (1-7). There are often unexpressed concerns the adolescent female has about her breast development. The breast examination may occur as part of an annual, comprehensive examination of the adolescent female or when specific concerns are expressed by her about breasts. The breasts are assessed in regard to their size, symmetry (or asymmetry) and for the presence of breast lesions, skin changes, tenderness or nipple pathology (such as areolar excoriations or discharge). Breast lesions are described in terms of their appearance, skin color, consistency, mobility, size, location, tenderness and associated warmth. The examination should document the presence or absence of lymphadenopathy (as axillary adenopathy) and hepatosplenomagaly. It is helpful to emphasize what is normal during the examination and teach about the importance of a regular breast examination when she is an adult. The family history of breast disease

Table 1 Breast concerns in adolescent females

Category	Conditions
Congenital and developmental conditions	Polythelia, inverted nipple, athelia, amastia, amazia, polymastia, bilateral breast hypoplasia, tuberous breasts, mammary hyperplasia
Benign breast mass or tumor	Fibroadenoma, fibrocystic change, benign cysts, pseudolumps, post-partum galactocele, traumatic fat necrosis, intraductal papilloma
Malignancy	Cystosarcoma phyllodes, adenocarcinoma, intraductal papilloma
Other	Mastitis, abscess, dermatitis, jogger's nipple, breast atrophy, galactorrhea, breast pain

(including cancer) influences the anxiety of the adolescent female and her parents if she presents with a breast concern. It may also encourage her to regularly check her breasts if a mother or other close relative has a breast cancer history. In the primary care medical practice, the adolescent female may present with a number of concerns related to the size, development, or appearance of breasts; the adolescent may also present with concerns about lump or swelling, nipple discharge or pain in the breast (*Table 1*) (1-19).

Methods

An electronic search was performed on MEDLINE to identify relevant articles from 2010 to 2017.

Embryology and development of breasts

During the fourth to sixth fetal week, epidermal cells migrate into mesenchyme forming the primitive mammary ridges or milk lines. Eventually thickening of ectoderm occurs extending from the axilla to the groin. During the tenth fetal week, there normally is atrophy of the upper and lower ridges, allowing the middle pectoral ridge to develop into normal breast tissue; the ridges become lactiferous ducts and mammary glands while surrounding mesenchyme becomes fibrous tissue and adipose tissue of breasts. Approximately 15–20 solid cords develop from secondary buds in each gland—these cords are the future milk ducts and lobes of the breast. The areola develops in the fifth fetal month and the nipple forms shortly after birth. During childhood, the breasts consist of epithelium-lined ducts with surrounding connective tissue.

As puberty develops, the breasts of the female undergo major changes under the influence of estrogen (adipose and ductal development), progesterone (lobar, areolar growth) and normally, after pregnancy, prolactin (lactation). Other hormones also influence the development of breasts in utero, including growth hormone, insulin, thyroxine and adrenal corticoids. The progression of breast development in puberty is identified in five stages called the Tanner Stages or Sexually Maturity Ratings. This represents research initiated by Stratz in 1909, modified by Reynolds and Wines in 1948, and finalized by Tanner in 1962.

Thelarche or the breast budding stage (Tanner stage or sexually maturity stage 2) signals the onset of puberty. Thelarche may begin as early as age 6 in African-American adolescent females and 7 in Caucasian adolescent females in the United States. Approximately 15% of Caucasian females and 48% of African-American females develop thelarche between 8 and 9 years of age. Females who have no breast development by age 13–14 are classified as having delayed puberty.

During the menstrual cycle, the breasts increase in size up to 50%; during the early follicular phase, there may be an increase in edema fluid in the breasts. An optimal time for breast examination is during days 4 to 12 of the menstrual cycle, when edema fluid is minimal. Increased vascular permeability develops in the luteal phase and some develop a watery discharge from the breasts just before menstruation. During pregnancy the breast weight may double along with ductal secretion and increase in aerolar pigmentation.

Congenital and developmental concerns

Polythelia

Polythelia, presence of supernumerary nipples or nipple-areolar complexes, is a congenital lesion (polythelia, polymastia, or a combination) usually located along the embryonic milk line (1,2,5). Polythelia is noted in 1% to 2% of the general population and is typically asymptomatic as well as familial. It can be associated with urologic and cardiovascular defects. Such lesions can be found on the embryonic milk lines from the axilla to the groin; sometimes

they may be found on the back or buttocks. The differential diagnosis includes a mole, melanoma and hemangioma. The diagnosis rarely necessitates an excisional biopsy. Excision can be done if the diagnosis is unclear and/or the adolescent requests removal.

Inverted nipple

An inverted nipple, reported prevalence between 1.8% and 3.3%, does not project beyond the breast surface and is seen at birth, usually bilateral (1,2,4). In most cases, it reverts to a normal position in a few weeks after birth, but can persist adolescence. Its differential diagnosis includes a bifid nipple and a depressed nipple (with ducts opening in a depressed area within the areolar center). An inverted nipple can lead to cosmetic deformity and chronic areolar abscesses (with swelling, infection and pain). If the inversion first occurs during adolescence or adulthood, a diagnosis of duct ectasia or malignancy should be considered. Inverted nipple can be a source of distress and anxiety for the adolescent and if persistent, surgical treatment options should be considered.

Athelia

Athelia is a rare congenital anomaly in which the nipple is absent either unilaterally or bilaterally. It can be a familial condition with no other associated anomalies (1,2,4). Athelia can also be seen in the offspring, where the mother was exposed to exogenous androgens during pregnancy. If the nipple is absent, breast tissue may develop at puberty.

Polymastia

Polymastia or supernumerary breast is not as common as polythelia, occurs along the embryonic milk line, and can be unilateral or bilateral as well as familial (1,2,4). Its typical location is on or below the normal breast on the chest or upper abdomen and various combinations can be seen: areola, nipple and/or glandular tissue. The differential diagnosis includes moles and hidradenitis suppurativa. Problems may arise at puberty or during pregnancy and/or lactation. This accessory tissue is usually removed for cosmetic and/or diagnostic reasons, but other indications include an axillary location and the presence of lactation.

Amastia

Congenital amastia, complete absence of breast tissue, nipple and areola, is rare and typically unilateral. It may be seen with the Poland syndrome in which, there is amastia, pectoralis muscle aplasia, rib defects, radial nerve aplasia, webbed fingers, and brachysyndactyly (1,2,4). Amastia that is acquired (versus congential) may occur because of breast bud excision, damage from irradiation or other injury. Another similar condition is amazia, which refers to absence of one or both mammary glands; while, the nipple and areola are present. In both, amastia and amazia, a surgical consultation is needed for appropriate surgical options.

Breast asymmetry

One breast may begin development before the other and thus, asymmetry of breasts in adolescent females is quite common and may be persistent in 25% (1,2,4). Breast injury may cause acquired breast asymmetry such as seen with pre-pubertal infection, trauma, burns, biopsy of a breast bud, chest tube insertion, or radiation damage. A unilateral breast mass can give the appearance of breast asymmetry; pseudo-asymmetry may also arise from scoliosis associated with rib cage abnormality.

Transient or permanent breast asymmetry can be cause for considerable distress and anxiety for the adolescent. Surgical treatment should be considered during late adolescent or early adult years allowing full potential breast development. In addition, the adolescent or young adult is in a better position to understand the risks and benefits of the procedure. It is important to note that for the adolescent, sometimes, it is not the breast volume that is of concern, but the breast shape that requires a breast lift or mastopexy.

Tuberous breasts

Tuberous breasts have an abnormal breast appearance in which there is a small breast volume and the appearance of a protuberant, over-developed areola (1,2,8). In these cases, it may be difficult to establish a Tanner (SMR) stage as the nipple-areolar complex seems to be on a thickened stalk.

Two types are described, type 1 and 2. The more common, type 1, with small concentric breast base and a large nipple areola complex, represents herniation of breast tissue into the areola. The less common type, type 2, presents with a breast that is more deficient in its vertical than horizontal dimension and has a small breast base; and type 2, with a breast that is more deficient in its vertical

Table 2 Differential diagnosis of breast mass in adolescent female

Abscess
Adenocarcinoma
Cystosarcoma phyllodes
Fat necrosis
Fibroadenoma
Giant fibroadenoma
Infiltrating ductal adenocarcinoma
Intraductal breast papilloma
Juvenile hypertrophy
Juvenile papillomatosis
Lipoma
Mammary duct ectasia
Metastatic cancer
Neuroblastoma
Non-Hodgkin's lymphoma
Papillary duct hyperplasia
Rhabdomyosarcoma

than horizontal dimension and has a small breast base. Tuberous breasts can be a cause of significant psychological and emotional distress for the adolescent. Although, less severe cases may not require corrective surgery, most other cases would need consideration for surgical correction.

Mammary hyperplasia

Mammary hyperplasia (juvenile or virginal breast hypertrophy) is characterized by explosive breast growth, typically shortly post-thelarche probably due to tissue sensitivity to estrogen or endogenous (intracellular) hormone production (9,10). It can be familial, either unilateral or bilateral. The explosive growth of breasts may be associated with breast pain (mastalgia, mastodynia), and areolar stretching with tissue necrosis (as well as dermatitis and skin breakdown). Other complications may include neck strain, headaches, back strain (kyphotic posture), respiratory distress, spinal curvature in severe situation, and psychological distress that can include depression and anxiety.

In a unilateral breast hyperplasia, one must consider a breast mass such as a giant fibroadenoma or abscess; a biopsy may be indicated for definitive diagnosis. Treatment is individualized and ranges from reassurance that the breast tissue is normal (with firm bra support), to surgery in order to reduce the breast size (9). Although, there may be some regression of the hyperplasia later in adolescence, this is typically minimal. Surgery is considered after breasts have matured and adolescent or young adult is able to comprehend the implications of surgical options.

Breast atrophy

Significant weight loss can lead to decreased breast adipose tissue with decreased size of previously developed breasts (usually bilateral) (1,2,4). A careful history is essential to identify the cause of breast atrophy; for example, there can be severe dieting due to anorexia nervosa but other causes include hypo-estrogenism (premature ovarian failure), virilization syndromes, or systemic diseases (with weight loss and hypoestrogenic states). In scleroderma, there can be localized changes with secondary breast atrophy.

Bilateral breast hypoplasia may occur due to ovarian dysfunction, is typically seen with primary amenorrhea, and poorly developed nipples. Gonadal dysgenesis (Turner syndrome), congenital adrenal hyperplasia, pre-adolescent hypothyroidism, androgen-producing tumor, pituitary hypogonadism, radiation effects and bilateral oophorectomy should be considered in the differential diagnosis.

Benign breast masses or tumors

Fibroadenoma

Most breast masses found in the female adolescent are fibroadenomas that are usually found in the upper, outer breast quadrant. Fibroadenoma is the most common breast tumor in adolescent females, noted in 70% to 95% of breast biopsies in this age group; it is the most common cause of a solid breast mass in females from puberty to age 30.

The fibroadenoma is usually painless, slow-growing, firm (rubbery), and typically under 5 cm at initial finding (19,20). It is an estrogen-sensitive lesion that may or may not change with the menstrual cycle. In 10% to 20% of cases, the lesions are multiple and/or bilateral and this is termed fibroadenomatosis. Other considerations for a breast mass (es) include giant (juvenile) fibroadenoma, benign breast cyst (s), cystosarcoma phylloides, adenocarcinoma, and many other conditions (*Table 2*) (19-35). Mammography is often not helpful in differentiating breast lesions in adolescent females because of the typical density of this breast tissue.

Investigation of breast lesion(s) includes use of such techniques as fine-needle aspiration (FNA), a core needle biopsy (CNB), or an excisional biopsy. A breast ultrasound may be used to differentiate cystic from solid mass; while a CT/MRI is used to differentiate a breast lesion from a rib lesion or other lesions in the chest wall (22,23).

A variant of a fibroadenoma, the giant or juvenile fibroadenoma is larger than 5 cm in diameter, sometimes doubling in size within 3 to 6 months, up to 15 or 20 cm; it may compress or replace normal breast tissue Surgical excision is indicated for the faster-growing lesions and/or if there is a concern about potential malignancy (1,2). Fibroadenoma may enlarge late in a menstrual cycle and especially during pregnancy; spontaneous regression may occur, but is uncommon. Malignancy is often the concern of the adolescent and her parents; however, no link has been established between fibroadenoma and malignancy. It is not possible to predict the growth of a fibroadenoma; some spontaneously involute over several months, some grow slowly, and some remain dormant for many years. Discrete breast masses should almost always be removed in boys and postpubertal girls. A small and slow-growing lesion in an adolescent female that is rubbery and non-tender may be observed over 2 to 4 months; however, longer periods of delay should be avoided to optimize surgical treatment outcomes.

Fibrocystic change

The previous term for this condition was fibrocystic/proliferative breast disease (1,2). Diffuse cord-like thickenings and lumps may develop over time, while some patients present with vague lumps or nodules (1,2,9,22). The second most common breast lesion in adolescents after the fibroadenoma is fibrocystic change). The etiology is unclear and often linked to estrogen and progesterone imbalances. It typically is seen in females in the third-fourth decade in which there are breast lesions that have nodularity and tenderness that can change during the menstrual cycles. The differential diagnosis includes benign breast disease, normal breast tissue, post-partum galactocele and traumatic necrosis. Diagnosis is aided with ultrasound and a FNA with cytologic evaluation.

Treatment depends on the severity of the condition. Treatment options include reassurance of its benign nature, use of a well-fitting (sports) brassiere to prevent inflammation as well as stretching of breast ligaments, cold compresses, a trial of analgesics, and use of oral combined contraceptive pills.

Benign breast disease

This term applies to a large number of breast lesions that are benign, especially in the adult female (35-40). It can include normal, physiologic changes in the size of breast tissue in adolescents; also, it can refer to pseudolumps and benign cysts that are not fixed to breasts tissue. Variation over menstrual cycles is typical of benign breast disease. The medical practitioner needs to consider such diagnoses as fibrocystic change, normally developing breast tissue, postpartum galactocele and traumatic necrosis. A fine needle aspiration with cytologic evaluation and ultrasound may be indicated for definitive diagnosis.

Breast cancer

Cystosarcoma phyllodes

Though rare, it is the most common malignant breast tumor in the adolescent female—though it is often benign. Cystosarcoma phyllodes usually presents as a painless, slow growing breast tumor that is typically 8 cm to 10 cm when found. It can present as a rapid or slow-growing lesion with bloody nipple discharge, overlying skin retraction as well as necrosis (24-31). As a malignant lesion, it can spread to the lungs. The evaluation includes an ultrasound, fine-needle biopsy, core-needle biopsy and/or excisional biopsy.

Adenocarcinoma

This is a very rare cause of breast cancer in adolescent females. It presents as a hard, immobile mass with overlying skin changes (peau d'orange) and lymphadenopathy (axillary, supraclavicular) (32-34). There may be a positive family history with genetic markers that include BRCA-1 (chromosome 17) or BRCA-2 (chromosome 13).

Intraductal papilloma

The adolescent female presents with a unilateral mass under the areola that has a bloody nipple discharge (1,2). Fortunately, it is rare and typically benign. Its differential diagnosis is listed in the Table and the medical practitioner should also rule out the presence of galactorrhea. The work-up includes an ultrasound and a fine needle or core-needle biopsy.

Breast pain

Breast pain is a common symptom in adolescent females and may be due to rapidly growing breasts, cystic breast disease, or mastodynia (mastalgia) (1,2,41). Breast pain may be part of the premenstrual syndrome with various breast tissue nodularities as well as swelling on a cyclic basis often initiating 18 months after menarche. It can worsen with use of oral contraceptives. Mastitis (lactational or non-lactational) may also cause pain.

Breast pain may also occur with trauma as noted in jogger' nipple (due to abrasive injury from shirts, especially in males), breast contusion, breast abrasion, breast laceration, or even breast hematoma. Breast trauma may arise from sports activity as well as motor vehicle accidents and others (42-45). In nipple trauma termed Jogger's nipple (bicyclist's nipple) the nipple is injured in runners or bicycle riders due to the frictional injury of the bra on shirts (1,42-45). The nipple is the most prominent breast part and can be seen in males. There is a raw, bleeding nipple that can be a unilateral or bilateral issue. The differential diagnosis includes an intraductal papilloma.

The differential diagnosis of breast pain includes costochondritis, cervical spine disease, cardiac disease, and drug side effects (i.e., phenothiazines, others).

Galactorrhea

Galactorrhea refers to milk-like nipple discharge usually due to pregnancy but other causes can be seen such as drugs and neuroendocrine disorders (17,18). A careful work-up is needed if this is seen apart from pregnancy.

Mastitis

Mastitis is most common in lactating females but can be seen in non-breasting females as well (1,2,46,47). Precipitants for mastitis include breast trauma, including sexual and areolar hair plucking. In this condition there is a tender, warm breast induration with erythema and a breast abscess may develop. A breast abscess can be seen without overt mastitis. *Staphylococcus aureus* is the offending microbe in up to 90% of mastitis but other bacteria can be seen including streptococcus, pseudomonas, E coli, Micrococcus dyogenes and others.

A needle aspiration of the abscess with cultures and a breast ultrasound may be indicated for definitive diagnosis (1,2,48). Since there may be underlying pregnancy as a precipitant to the mastitis, a pregnancy test is done as well. Blood cultures may aid in identification of the offending bacteria as well. Treatment of mastitis in cases of milk stasis (with no associated infection) is by the use of warm compresses and continued breast feeding, as well as pumping out extra-produced milk, until normal balance is established between production and consumption. Antibiotics are used in cases of infection in order to cover the expected bacteria that are seen in such infections (1,2,4,5,9).

Approach to evaluation and treatment of adolescent breast conditions

In addition to history and examination, additional investigation may be indicated to differentiate various conditions and arrive at a definitive diagnosis. In the primary care medical practice, setting an early recognition of the broad category of presenting conditions is essential. For most conditions recognized initially in the primary care practice setting, further evaluation and treatment will require a surgical consultation. The timing of surgical intervention will be guided by the specific condition, the urgency of treatment and the ability of the adolescent to fully comprehend the risks and benefits of the procedure.

Conclusions

A number of breast concerns in female adolescents are considered in this discussion. Some may need referral to subspecialists for evaluation such as surgeons for breast reduction in mammary hyperplasia, surgical repair of tuberous breasts, surgery for polythelia or polymastia, breast mass removal or biopsy, endocrine evaluation for bilateral breast hypoplasia, and others. Most concerns, however, can be managed by the primary care medical practitioner.

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