

Breast Disorders in Adolescence: A Review of the Literature

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Keywords

Adolescence · Breast disorders · Breast development · Fibroadenoma · Mastitis · Mastodynia · Breast cancer

Abstract

Background: Adolescence is accompanied by a variety of changes in young breast development, which greatly affects the adolescent's psychology and socialization. **Summary:** PubMed, EMBASE, and the Cochrane Library were searched for studies relative to epidemiology, clinical characteristics, diagnosis, and management of all breast disorders in adolescence and their consequences. Development disorders are breast asymmetry, breast atrophy, breast hypoplasia, hypomastia, juvenile breast hypertrophy, and tuberous breast. Breast congenital abnormalities include athelia, amastia, accessory breast tissue, polymastia, polythelia, and congenital disorders of nipples. Breast infections are commonly caused from Gram-positive coccus rather than Gram-negative bacteria. Breast abscess occurs when breast infections are not promptly treated. Nipple discharge is caused by a variety of conditions and should be managed carefully. Fibrocystic changes, cysts, and fibroadenomas are the most common benign masses in adolescence. Primary, secondary, or metastatic breast cancer is extremely rare in adolescence. However, clinicians should include breast cancer in the differential diagnosis of a breast mass in adolescence. **Key Message:**

es: Clinicians should be aware of all breast disorders that may occur in adolescence. Early diagnosis and treatment will result in the reassurance of adolescents and their families without any detrimental effect on their psychology, sexual behavior, and socialization. Adolescents with breast disorders may require a multidisciplinary approach by a pediatrician, a gynecologist specializing in pediatric-adolescent gynecology, a plastic surgeon, and a psychologist for the best management of breast disorders. © 2020 S. Karger AG, Basel

Introduction

Breast development begins in the 5th week of embryonic life. Breasts originate from the ectoderm and mesenchyme. Milky lines appear in the 6th week of embryonic life and extend from the axilla to inguinal region. In the 10th fetal week atrophy of the proximal and distal part of the milk lines occur and the middle part is responsible for the genesis of the breast. Development of the areola and 15–20 solid cords occurs in the 5th fetal month, while breast nipples appear in the 8th fetal month and lactiferous ducts and mammary glands are developed from milky lines. Later in childhood and puberty, under the influence of steroid hormones (estrogens, progesterone) the breast buds enlarge and glandular elements appear [1].

In adolescence adipose tissue and lactiferous ducts grow in response to estrogen while progesterone induces lobular growth and alveolar budding. Breast development in adolescence is described according to the Tanner stages. Thelarche is the onset of secondary breast development in adolescence. It occurs between 8 and 13 years of age (average age 10.3 years) and often represents the beginning of puberty. Breast development is completed between 2 and 4 years after thelarche.

Breast disorders in puberty are rare and mostly benign. However, they can significantly affect the daily life and quality of life of teenagers. Such disorders are various congenital abnormalities of the breasts, disorders in their development, infections and abscesses of the breast, mastodynia, nipple discharge, and various benign diseases occurring in the form of breast masses as well as breast malignancies [2].

Materials and Methods

PubMed, EMBASE, and the Cochrane Library were searched for studies relative to the epidemiology, clinical characteristics, diagnosis, and management of all breast disorders in adolescence and their consequences.

Results

Congenital Breast Abnormalities

Congenital abnormalities include disorders such as accessory breast tissue, amastia, athelia, and hypomastia. Other disorders are polymastia, polythelia, and disorders of the nipples, such as inverted nipples.

Accessory Breast Tissue, Polymastia

Accessory breast tissue is a rare condition, with an incidence of 0.4–0.6% among women, which is present at the time of birth [3]. Polymastia refers to the presence of any accessory breast tissue. Accessory breast is often located in the axilla and is influenced by estrogen and progesterone. It usually presents as an asymptomatic mass during pregnancy. It can undergo the same pathological problems as the normal breast, such as infections, fibrocystic changes, and carcinoma. It sometimes causes diagnostic problems, especially when it is unilateral and large [4]. The possibility of removing the accessory breast tissue should be discussed both for aesthetic reasons and for the prevention of pathology that may develop there.

Polythelia

Polythelia is a condition that occurs in about 1% of women. A supernumerary nipple grows along the milky line and can be visible at birth or later. Polythelia may be

associated with congenital abnormalities in the urinary tract. It is therefore recommended to perform a renal ultrasound when a supernumerary nipple is found. Surgical removal of the nipple can be carried out for aesthetic reasons.

Amastia, Athelia

Amastia is the complete lack of breast tissue whereas athelia is the absence of nipples. These situations are due to a developmental failure or total disappearance of the milky lines. When amastia is bilateral, other congenital abnormalities are likely to occur [5]. Poland syndrome consists of unilateral breast aplasia or hypoplasia, aplasia or hypoplasia of the pectoralis muscle, and a variable degree of ipsilateral hand and digit anomalies. Surgical treatment with breast augmentation may be indicated for these situations [6].

Disorders of the Nipples

The most common congenital nipple disorder is the inverted nipple. It is a benign, often familial condition that is a normal variation of the nipple shape. As an abnormal finding, when it did not exist from birth, it may indicate inflammation or even malignancy. No treatment is required, unless the woman wishes surgical correction for aesthetic reasons [7]. For a teenager who has not completed breast development yet, cosmetic surgery should be refrained from until breast development is complete.

Development Disorders

Breast Asymmetry

Breast asymmetry is a common finding in about 25% of adult women. It is considered a normal variant of breast development rather than a disease entity. Usually, the smaller breast is on the opposite site from the dominant hand. Teenage patients should be reassured and informed that their breast development is not yet complete. In the case of a large asymmetry that affects the quality of life of a woman, besides the use of special brassieres, surgical correction from a plastic surgeon is possible.

Other causes that may give the breasts an asymmetrical image are mastitis and abscesses in the largest breast, disorders of the thoracic cavity after thoracotomy or thoracostomy, conditions after injuries and burns to the breasts and generally in the chest, radiation of the chest for the treatment of benign or malignant conditions, and excision of breast tumors during childhood.

Breast Atrophy, Hypoplasia, Hypomastia

Hypomastia and breast hypoplasia are conditions that are often difficult to separate from idiopathic small breasts. Bilateral breast hypoplasia is due to either decreased estrogen secretion or inability of the target tissue

(breast tissue) to respond to the circulating estrogens. Possible causes of breast hypoplasia include gonadal dysgenesis in the context of Turner syndrome, various tumors producing androgens, pre-adolescent hypothyroidism, and pituitary hypogonadism. Unilateral hypoplasia has been described in association with the Poland syndrome and anterior thoracic hypoplasia [8].

Breast atrophy is usually acquired and is due to significant weight loss resulting in significant loss of adipose tissue of the breast. Causes of breast atrophy can be anorexia nervosa, weight loss because of chronic illness, and postpartum depression. Also, other causes of acquired breast atrophy may be scleroderma and early ovarian failure resulting in a premature decrease in circulating estrogen levels.

In order to find the cause of these conditions it is necessary to obtain a detailed history and conduct a detailed clinical examination of the patient for the development of both breasts and other secondary characteristics of the sex, as well as carrying out hormonal examinations. If the severity of the condition affects the patient's socialization and quality of life, surgical correction with breast augmentation is necessary [6].

Juvenile Breast Hypertrophy

Juvenile, virginal, or idiopathic breast hypertrophy is characterized by a massive rapid development of one or both breasts despite normal levels of circulating estrogens. It is a rare condition, mostly sporadic rather than familiar, which occurs often 1–2 years before menarche. It is considered a result of high sensitivity of estrogen receptors in the breast or a result of an abnormal ratio between estrogens and progesterone. Breast weight can even reach 10–22 kg. This can lead to a significant limitation of the woman's daily routine, resulting in psychological problems. Other entities, which must be differentiated from juvenile breast hypertrophy, are breast masses and idiopathic obesity [9, 10].

Treatment of juvenile breast hypertrophy includes surgical breast reduction because no medications are acceptable for use in adolescents. However, breast reduction is often associated with high recurrence rates [11].

Tuberous Breast

Tuberous breast deformity is a common congenital condition in which the base of the breast is underdeveloped, and the nipple and areola are overdeveloped. The etiology of this entity is unknown. Tuberous breast deformity in adolescence can cause severe psychosexual problems due to the unusual shape of the breast. Surgical correction can lead to notable improvements in self-esteem to the level where the person engages in normal social activities [6, 12].

Infections and Breast Abscess in Adolescence

Mastitis and breast abscesses are less common in adolescents and non-lactating women than in adults and lactating women. Mastitis is caused by the presence of bacteria in the ductal system of the breast. The most common bacteria are *Staphylococcus aureus*, *Enterococcus*, *Streptococcus pyogenes*, *Pseudomonas*, and other Gram-negative bacteria. Actinomycosis can cause mastitis in patients with nipple piercings. Patients with a weak immune system, such as patients with diabetes mellitus, rheumatoid arthritis, glucocorticoid therapy, and severe obesity are more likely to develop breast infections and abscesses. Common causes of breast infections are superficial injury of the breast, obesity, mammary duct ectasia, epidermoid cysts, hidradenitis suppurativa, and local skin infection. Clinical features of mastitis consist of erythema, swelling, warmth, and tenderness. In the case of a breast abscess there is also fluctuance and maybe purulent discharge of the nipple. Diagnosis of mastitis or abscess is usually possible only from clinical examination. Other examinations include Gram stain and culture of the nipple discharge. Ultrasound can help for guided aspiration in patients with a breast abscess. Differential diagnosis includes breast trauma, lymphangiomas, mammary duct ectasia, superficial thrombophlebitis of the thoracoepigastric vein (Mondor disease), and breast carcinoma. Management of mastitis includes supportive care with a warm compresses and antibiotic therapy with an antibiotic in accordance with the result of the Gram stain and culture, or if it is not available with empiric coverage for *S. aureus* and Gram-positive coccus for 7–10 days. In the case of a breast abscess, an ultrasound-guided aspiration or an incision and drainage is required if there is no response to antimicrobial therapy. Patients with mastitis caused by *S. aureus* are at risk of subsequent infections at other sites [5, 13, 14].

Mastodynia

Breast pain (mastalgia, mastodynia) is one of the most commonly reported symptoms to gynecologists. It has been associated with pregnancy, exercise, contraceptives (oral and implant), and the period directly before menstruation. The exact cause of breast pain can be identified with appropriate information from the patient's history. When the pain is cyclic premenstrually and without other findings, it can be attributed to normal breast swelling. Hence, a supportive brassiere and analgesia should be included in the treatment. For adolescents, ibuprofen should be administered because other analgesics have been studied only in adults. Ibuprofen could also be combined with oral contraceptives, as they appear to improve symptoms in many women [15]. Moreover, the effect of caffeine in breast pain is controversial [16]. However, if mastodynia is more intense with caffeine consumption,

its intake should be avoided. Furthermore, adolescents could have breast pain if they are very physically active and have large breasts. Significant relief could be achieved in such cases with a sports brassiere. In addition, the distinction between localized and generalized mastodynia is important. The first is associated mostly with cysts, poorly fitting brassieres, and periductal masses, while the second is associated with cyclic pain. A recent onset of oral contraceptives and the existence of a contraceptive implant could also be responsible for breast pain. Finally, the administration of certain drugs (e.g., hormones, phenothiazines) and illegal substances (e.g., marijuana) should be controlled, because each of them could be the cause of breast pain.

A clinical examination of the breasts is a crucial procedure and should never be omitted. A breast inflammation is easily identified by any physician. Additionally, a variety of masses could be detected with palpation, such as cysts, abscesses, and regional lymph nodes. Ultrasonography may be necessary for every detected mass to evaluate its features and define its consistency (cystic or solid). Nevertheless, extramammary causes of chest pain are common and could be revealed during the clinical examination. The most frequent are pneumonia and gallstones. Finally, in every woman of reproductive age a pregnancy test should be performed.

Nipple Discharge

Any release of fluid from the nipples is identified as nipple discharge. This symptom is not usual in adolescents. Although it is rarely associated with malignancy, a clinical examination is crucial when it is mentioned. The appearance of the fluid (e.g., serous, bloody, and milky) contributes to the differential diagnosis. Moreover, it is important to recognize whether the discharge is excreted unilaterally or bilaterally and if it is provoked or spontaneous. The most common causes of nipple discharge are galactorrhea, pregnancy, endocrinological disorders, use of specific drugs (such as antipsychotics), and breast cancer. Milky discharge is associated with lactation, pregnancy, endocrinological disorders, and prolactin-secreting tumors. Multicolored and sticky discharge is associated with mammary duct ectasia, while purulent discharge is common in infections of the breast and breast abscess. Serous or serosanguineous nipple discharge is associated with Montgomery tubercles, while bloody discharge, which is rare in adolescents, is associated with mammary duct ectasia, intraductal papilloma, trauma, mastitis, and breast cancer. A clinical examination and galactography are useful in the differential diagnosis of nipple discharge. Surgical excision of the involved duct may be indicated for the definite diagnosis and treatment of nipple discharge [17, 18].

Breast Masses in Adolescence

Finding a mass in an adolescent breast causes stress in both the girl and her family. However, in adolescence most masses are benign. It is reported in the literature that only 2.5% of masses in women under 30 years of age are malignant, and only 0.5% of masses in women under the age of 20 are malignant [19]. Investigating a mass involves taking a detailed history, clinical examination by palpation of the breast, and often performing an ultrasound, which is the most appropriate screening test for the assessment of a mass in adolescence. Women with an increased risk of breast cancer may require magnetic resonance imaging. Most of the masses in young women are self-limiting and rarely need biopsy and surgical excision. However, although rare, the possibility of breast cancer should be ruled out.

Juvenile Fibroadenoma

Fibroadenoma of the breast refers to a benign tumor formed of fibrous and glandular tissue. It occurs not only in adult women, but also in adolescents. At such ages the fibroadenoma is called juvenile and it is the most common breast disorder. It is reported that juvenile fibroadenomas constitute 30–50% of breast masses. The clinical presentation of fibroadenomas is not clear because they are usually asymptomatic. Hence, the differential diagnosis could be aided by specific findings during the clinical examination. Fibroadenoma is a well-circumscribed, unilateral breast mass (2–3 cm) accompanied by elasticity and mobility. Moreover, no evidence of infection is present and the majority of fibroadenomas originate in the upper, outer quadrant. The probability of a breast malignancy is diminished significantly with these clinical features. If it is not feasible to establish the diagnosis of juvenile fibroadenoma clinically, further investigation is necessary with ultrasonography and fine-needle aspiration. However, it should be noted that difficulties have sometimes been encountered in the distinction between a phyllodes tumor and a fibroadenoma with fine-needle aspiration. The accuracy of mammography is reduced because of the high density of glandular tissue in an adolescent's breasts. Consequently, it should not be performed in every adolescent, also taking into consideration the high radiation dose [17, 19].

Regular surveillance and surgical incision are included in the management of fibroadenomas. Surveillance should initially be intense and is preferred especially when the size is less than 5 cm. It is important to recognize whether an increasing or decreasing tendency exists. In adolescents the disappearance of a fibroadenoma after a few months is common, although the reported incidence of recurrence varies from 10 to 25%. However, a surgical excision should be considered for patients with a high risk of breast cancer based on a history of breast cancer, age,

and anxiety. Finally, surgery is recommended for adolescents when a fibroadenoma is greater than 5 cm, has an increasing tendency, or has remained until early adulthood [20].

Giant Fibroadenoma

A giant fibroadenoma is larger than 5 cm and is characterized by a rapid massive growth. Consequently, a breast compression and distortion are often observed. The differential diagnosis between a giant fibroadenoma and phyllodes tumor is difficult. Surgical treatment should always be recommended for the definite diagnosis and because of the aggressiveness of phyllodes tumor [21].

Cystic Breast Disease

The adolescent breast undergoes a variant of physiological changes during menstruation, including changes in breast size, tenderness, swelling, nodularity, mastodynia, and various breast cysts. Breast cysts may be single or multiple and they are not fixed to breast tissue. They often contain fluid that is clear, serous, brown, or bloody. Sometimes a fine-needle aspiration is essential, both for the diagnosis through a cytological exam and for the treatment. In most cases examination with ultrasound after 2–3 months shows no recurrence of the cyst. When there is recurrence of a breast cyst or its characteristics are suspicious for breast carcinoma, an excision and an open biopsy are needed [22].

Fibrocystic Changes

Fibrocystic changes are common in adolescence [23]. They consist of firm, movable nodularities, which originate diffusely in the breast tissue. They are characterized by cyclic changes in breast size during menstruation and mastodynia and breast tenderness premenstrually. A breast ultrasound is often obtained for the evaluation and the differential diagnosis of the disease [17]. Sometimes a fine-needle aspiration or a core biopsy is essential for the diagnosis. Management of fibrocystic changes include good brassiere support, heat, analgesics, especially ibuprofen, and oral contraceptives. Some studies support vitamin E administration (600 IU/day) for symptom relief. Avoidance of methylxanthine (caffeine) consumption is supported by many studies, although the data are controversial [15, 16]. Administration of bromocriptine, danazol, and tamoxifen is not recommended in adolescence.

Cysts of Montgomery

The glands of Montgomery originate from the edge of the areola. Cyst of Montgomery or retroareolar cyst is called a benign subareolar mass, usually found in adolescents, which is caused by an obstruction of the Montgomery glands. It could be accompanied by acute inflammation and clear to brownish nipple discharge. The diagno-

sis is usually set by the clinical examination. However, in some cases a confirmation with ultrasound is required. The treatment of a cyst of Montgomery varies according to the accompanying symptoms. Spontaneous resolution is common (80%) in these patients. Consequently, regular ultrasound examination should be performed for up to 2 years. Nevertheless, if inflammation coexists locally, a treatment for mastitis is necessary. Finally, surgical treatment could be considered when the diagnosis is not determined or the cyst persists [17, 24].

Intraductal Papilloma

The prevalence of intraductal papilloma of the breast is 2–3% [25]. It can be classified as central or peripheral, when located near the nipple or in peripheral breast tissue, respectively. The central intraductal papilloma is solitary and mostly affects older women near menopause, while the peripheral papilloma is multiple and is found commonly in younger women. The latter is characterized with higher risk of malignancy. The clinical presentation is not clear because this type of papilloma is usually a small impalpable mass. However, a bloody nipple discharge is often associated with this disorder. Mammography is not indicated for the diagnosis because of the papilloma's small size [25, 26]. Although ultrasound could sometimes be useful, a galactogram represents the gold standard to define the diagnosis. Finally, the optimal treatment is to surgically remove the abnormal breast duct (microdochectomy) [27, 28].

Mammary Duct Ectasia

Mammary duct ectasia concerns mostly perimenopausal and postmenopausal women and refers to an obstruction that interrupts the flow of the lactiferous duct. Consequently, the duct is widened, and a local infection can develop with every characteristic sign. This situation is usually accompanied by fibrosis and a multicolored (green-brown) nipple discharge. A common finding is a blue mass under the nipple that occurs when dark fluid collects in the mammary duct. If the duct ectasia is bilateral, it may be associated with systematic disease. The diagnosis can be accomplished by ultrasound [29]. Although a spontaneous resolution can occur leaving behind a benign nodule, sometimes the infection can lead to mastitis or a breast abscess. Surgical treatment should be considered necessary whether the symptoms remain stable or a recurrence is noticed. Finally, it should be noted that mammary duct ectasia requires attention in its management because it can mimic breast cancer [30].

Phyllodes Tumor

Phyllodes tumor (cystosarcoma phyllodes) is a rare breast neoplasm (<1%). A breast mass is suspicious for phyllodes tumor if it is large and has a rapid growth rate.

This tumor originates from the periductal stromal cells of the breast and occurs mainly in adult women. The highest incidence of phyllodes tumor is observed prior to menopause. However, a few cases have also been reported in adolescents. Although histopathologic examination can classify phyllodes tumors into benign, borderline, and malignant grade categories, all of them are managed as malignant because these are aggressive and can develop distant metastases [31]. The incidence of a malignant phyllodes tumor is associated with age. Hence, it rarely presents in young women. Surgical treatment with wide excision is indicated for phyllodes tumor. The histologic grade of the tumor defines the risk of recurrence or metastasis. Finally, the incidence of recurrence can be decreased by radiation therapy after successful breast-conserving surgery [32].

Primary Breast Carcinoma

Primary breast cancer is extremely rare in childhood and adolescence. It has an incidence only 0.1/100,000 in children and young women aged 15–19 years [33]. The most common way in which breast cancer occurs is in the form of a painless, hard, irregular palpable mass. This mass may be fixed or not with the underlying breast tissue. Usually the mass is located in the upper-outer quadrants of the breast and may be accompanied by nipple inversion, change in color or texture of the overlying skin, nipple discharge, and lymphadenopathy. Histologically, the most common types are juvenile secretory carcinoma (>80%) followed by ductal carcinoma. Rarely occurring tumors are rhabdomyosarcoma and lymphoma. Risk factors for primary breast cancer are a personal cancer history, familiar breast cancer history, radiation exposure in childhood, smoking, and increased alcohol consumption [34]. For breast cancer diagnosis it is particularly useful to obtain a detailed history of the time of mass appearance, changes in size, previous cancer history, or irradiation exposure of the area, and also of family history. A clinical examination is particularly important. During the clinical examination information on the location, composition, size, and mobility of the mass is obtained. It is also checked for tenderness, skin changes or nipple discharge, lymphadenopathy, and hepatosplenomegaly. Breast ultrasound is the examination of choice for the evaluation of breast masses in adolescence. By ultrasound, breast cysts can safely be separated from solid masses, facilitating their further management. Thus, asymptomatic cysts usually resolve alone after a few weeks or months. Solid masses <5 cm with benign characteristics, such as fibroadenomas, can be observed. In the case of a cyst that persists, it is possible to conduct fine-needle aspiration and cytological examination of the fluid. In suspicious solid masses as well as in non-resolved cysts a surgical resection and biopsy is recommended [30, 35].

Secondary and Metastatic Breast Carcinoma

Extremely rare cases of secondary breast cancer may develop in adolescence. Usually secondary cancer develops after exposure of the chest area to radiation for the treatment of a primary cancer, usually lymphoma [36]. Metastatic breast cancer represents the majority of breast cancers in adolescence [37]. Hodgkin or non-Hodgkin lymphoma, neuroblastoma, hepatocellular carcinoma, and rhabdomyosarcoma are the most common causes of metastatic breast cancer [38]. Treatment of breast cancer in adolescence includes surgical resection with lumpectomy and sentinel lymph node biopsy, and then radiation or, more rarely, modified radical mastectomy. As the disease tends to be more aggressive in young women, all young women with breast cancer are recommended for systemic adjuvant chemotherapy. There are no clear recommendations for hormone therapy in adolescents [39, 40].

Conclusion

Female adolescents experience significant changes in their body. Breast development is a very important fact in adolescent life because it significantly affects the psychology and self-esteem of girls. Therefore, they often visit a doctor to deal with commonly arising concerns. In addition, a periodic clinical examination of the breast each year from the onset of puberty should be recommended. Moreover, it is important for young patients to be instructed in self-examination from an early age. Although they should be informed that the chance of breast malignancy at this age is extremely low, a visit to a specialist is necessary if any palpable masses are discovered.

Conflict of Interest Statement

All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria, educational grants, participation in speakers' bureaus, membership, employment, consultancies, stock ownership, or other equity interests, and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this article.

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