Disorders of the Breast

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Abstract
This chapter summarizes the current knowledge of congenital deformities of the breast, which can be categorized in hyperplastic, hypoplastic, and deformational anomalies. The embryological and anatomical background is introduced to understand the diversity of deformations before details of frequent anomalies are discussed. Finally, general approaches of surgical correction with careful timing for treatment as well as best cosmetic and functional outcome are described.

Keywords
Polythelia · Polymastia · Athelia · Amastia · Poland’s syndrome · Gynecomastia · Breast

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Introduction

Anomalies of the breast are usually benign alterations of normal breast development. The knowledge of the underlying embryology and the characteristics of common breast disorders in the pediatric population are important to establish the correct diagnosis and management. Deformities of the breast vary widely but can generally be classified as hyperplastic, hypoplastic, and deformational breast anomalies (Sadove and van Aalst 2005). Pediatric breast disorders can afflict both, patients and families particularly during puberty and adolescence, causing social embarrassment, depression, peer rejection, as well as low self-confidence, and sexual dysfunction (Latham et al. 2006; Kulkarni and Dixon 2012). Surgical correction can improve self-esteem and health-related quality of life (Sadove and van Aalst 2005).

Some degree of breast asymmetry is normal with the left breast being commonly larger than the right one. But even this natural asymmetry may hamper a child’s well-being, thus bearing the desire for surgical correction (Dixon and Mansel 1994; Holcomb et al. 2014). Besides congenital anomalies, iatrogenic alterations like biopsies of the pre-pubertal breast, thoracotomy, chest tube as well as central venous catheter placement, or abscess drainage may irreversibly cause disruption of breast development (Dixon and Mansel 1994; Jatoi and Rody 2016).

In general, functional deficits induced by breast deformities that require surgical repair in young infants like in severe Poland’s syndrome are rare, but may result in malfunctioning of lactation and breastfeeding in later life (Kulkarni and Dixon 2012). Cosmetic repairs should be delayed until breast maturation and development is complete to achieve the maximum possible symmetry (Latham et al. 2006). Thus, the pediatric surgeon needs to accompany families and patients during childhood and adolescence until surgical repair. Moreover, the contour of the breast changes during life and might require additional surgical procedures later. Successful transition of these patients to adult plastic surgical treatment is therefore mandatory for a pediatric surgeon.

Embryology

During the fourth to fifth week of gestation, the ectodermal milk line or mammary ridges form bilaterally on both sides of the ventral body wall from the axilla to the groin. Subsequently, the proximal and distal parts of the milk lines disappear, while the pectoral mammary anlage forms the mammary primordium (Skandalakis 2009). The mammary primordium invaginates into the underlying mesenchyme during week 10–14, which builds the superficial fascial system and suspensory ligaments of Cooper of the breast (Pryor et al. 2009). Epithelial tissue forms buds that divide into 15–25 branches with primitive breast alveoli by week 16 of gestation. In the last trimester, hormones from the maternal-placental-fetal unit mediate the canalization of the epithelial branches forming the primitive mammary ducts. Finally, breast parenchyma differentiates into lobules (Latham et al. 2006). The fibrous stroma and fat develop out of the surrounding mesenchyme (Jatoi and Rody 2016). The nipple-alveolar complex (NAC) forms late in gestation from mesenchymal cells, and a pigmented areola is first seen at 20–24 weeks (Holcomb et al. 2014). The superficial NAC is built onto a small depression of the epidermis on which the lactiferous ducts open (Jatoi and Rody 2016).

Physiology

At birth, breast enlargement occurs in both genders due to relatively high levels of placental estrogens in the perinatal period, followed by a surge in hypothalamic-pituitary-gonadal axis activity causing a mini puberty within the first months of life (Holcomb et al. 2014). When estrogen levels drop after birth paralleled by prolactin and oxytocin secretion, mammary tissue may produce colostrum, the so-called witch’s milk.

During puberty, ovarian follicles produce estrogen that induces ductal development and site-specific adipose deposition in the breast (Holcomb et al. 2014; Karaayvaz 2019). The initiation of breast growth and maturation is called thelarche and starts at the age of 10.3 years (range: 8–13 years), typically preceding menarche by two years (De Silva 2018). Thelarche usually
starts unilaterally, presenting with a firm disk-like area that must not indicate a biopsy as this may hamper breast development (De Silva and Brandt 2006). The five stages of breast development have been defined by Tanner for boys and girls (Marshall and Tanner 1969, 1970). Breast expansion normally lasts until the age of 25 (Jatoi and Rody 2016).

Of note, hemangiomas and lymphangiomas can impede the developing breast by compression of the mammary bud during rapid growth with subsequent deformity (Brandt 2006). Therefore, therapeutic options including propranolol therapy for hemangiomas or surgery have to be weighed against iatrogenic disturbance of the developing breast.

**Anatomy**

The breast consists of glandular tissue of lobules and ducts, as well as stroma of fibrous and fatty tissue. Terminal ducts drain via branching ducts into the nipple. The adult breast is typically located between the second and the sixth rib, as well as the sternal edge and the midaxillary line, fixed between the superficial and deep pectoral fascia. The nipple is found over the fourth intercostal space, with an oval-shaped NAC in 91%, with a mean diameter of 2.3 cm and a 2.7–2.0 horizontal-to-vertical-width ratio (Beer et al. 2001). The breast parenchyma is arranged in 15–20 segments radially around the NAC. Each segment consists of several lobes, each of which summarizes 20–40 lobules that are made up of alveoli (Latham et al. 2006). The segments drain into collecting ducts that form lactiferous sinuses, which run into up to ten milk ducts per breast. The internal mammary and lateral thoracic vessels mainly supply the breast tissue. Sensory innervation comes from T3 to T5 nerve roots (Harris et al. 2014).

**Hyperplastic Anomalies**

**Polythelia**

Supernumerary nipples (Fig. 1) or NAC occur, both sporadically or familiarly, in 0.2–5.6% of the population in males and females, along the milk lines from the axilla to the inguinal region (Brown and Schwartz 2003). They are typically located caudal to the true nipples, bilaterally in up to 50% of patients (Latham et al. 2006; Pryor et al. 2009).

Of note, different associations with renal anomalies such as renal duplication, obstruction, agenesis, and malignancy require a detailed workup including renal ultrasound (Sadove and van Aalst 2005). Moreover, vertebral anomalies, cardiovascular system disorders, central nervous system problems, chromosomal abnormalities, genetic syndromes, gastrointestinal disease, skeletal disease, spina bifida occulta, and cutaneous disorders have been linked to polythelia (Lewis et al. 1997; Panigrahi et al. 2008). Therefore, a detailed clinical examination and additional diagnostics if necessary should be warranted. The treatment of choice, if requested by the patient, is a surgical resection along the lines of Langer for cosmetic reasons or discomfort.

**Polymastia**

Supernumerary breast tissue, with or without a NAC, originates from residual tissue of the mammary ridge (De Silva and Brandt 2006). This can be seen in 1–2% of the population, predominantly in females, and is typically located in the lower axilla (Dixon and Mansel 1994). It is associated with chromosomal aberrations as well as malignant neoplasms of the urogenital tract (Pryor et al. 2009).

Supernumerary breast tissue behaves like normal breast tissue and can cause discomfort during puberty, menstrual periods, pregnancy, and lactation (Jatoi and Rody 2016; De Silva and Brandt 2006). It is also susceptible to similar diseases as regular breast tissue including breast cancer, and must be evaluated in a similar manner (Kulkarni and Dixon 2012; Pryor et al. 2009). Therefore, excision is the obvious choice for discomfort or cosmesis. Conversely, others report high rates of postoperative complications such as seroma, infection, incomplete excision, nerve damage, painful scars, as well as deformity, and suggest to avoid surgery if possible (Kulkarni and Dixon 2012; Pryor et al. 2009). These considerations need to be discussed with
the families involved. Preferentially, polymastia is diagnosed and resected elliptically prior to the onset of puberty to avoid possible glandular development (Sadove and van Aalst 2005).

**Virginal Hypertrophy**

A usually bilateral, rapid, and disproportional enlargement of the breast is called virginal hypertrophy or gigantomastia, if more than 1800 g per side needs to be resected (Pryor et al. 2009). It sporadically affects girls at the age of 11–16 years with an unknown incidence (Latham et al. 2006). The fatty and fibrous elements, but not the glandular tissue of the breast, is abnormally sensitive to normal levels of circulating estrogen, occurring during puberty or pregnancy but independent from obesity (Dixon and Mansel 1994).

Due to the rapid growth of several centimeters per month, which is disproportional to the growth of the child, patients often suffer from painful, large, and tender breasts associated with skin changes like striae, thin skin, or dilated veins (Latham et al. 2006). Surgical breast reduction via reduction mammoplasty or mastectomy is the treatment of choice and should be postponed, if tolerable, until breast size is static for one year (Pryor et al. 2009). However, recurrences with the need for reoperation or mastectomy followed by implant reconstruction have been reported as the breast may continue to grow, which needs to be discussed with the families (Pryor et al. 2009; Baker et al. 2001). Anti-estrogenic medical treatment with bromocriptine, tamoxifen, medroxyprogesterone acetate, or dydrogesterone can alter growth and prevent recurrence (Latham et al. 2006). A combination treatment of breast reduction surgery and tamoxifen has been suggested to eliminate the need for repeated surgeries for girls with virginal breast hypertrophy (Karagüzel et al. 2016). However, adverse effects of tamoxifen preclude its administration in young patients (Pryor et al. 2009).

**Gynecomastia**

Gynecomastia (Fig. 2) is an often bilateral but typically asymmetric enlargement of glandular tissue in the male breast that typically occurs in neonates, pubertal boys, and elderly men (Nordt and DiVasta 2008). Gynecomastia of infancy is a common condition that usually resolves spontaneously, typically within the first year of life (Kanakis et al. 2019). Pubertal gynecomastia can be found in 65% of boys at 14 years of age, at least 6 months after the onset of male secondary sex characteristics. It is familiar in 50% of patients and more common in boys with varicocele (Kumanov et al. 2007). It is characterized by fibroblastic stromal as well as ductal proliferation due to an imbalance between estrogens and androgens, or an increased sensitivity to normal male estrogen concentrations (Nordt and DiVasta 2008; Mathur and Braunstein 1997; Ersöz et al. 2002). It usually resolves spontaneously within 1–2 years. However, after one year, fibrosis and hyalinization can occur with regression of epithelial proliferation and persistence of the enlarged fibrotic and inactive breast tissue (van Aalst et al. 2009).

True puberty gynecomastia has to be distinguished from pseudogynecomastia, the enlargement of adipose tissue in obese men, and secondary gynecomastia due to altered estrogen or decreased androgen concentrations or their metabolism (Nordt and DiVasta 2008). This broad spectrum includes testicular tumors, malnutrition, liver diseases, hyperthyroidism, androgen insensitivity syndrome, Klinefelter’s syndrome, secondary hypogonadism, and defects in
testicular enzymes. Finally, a large number of medications like corticosteroids or cimetidine, and substances like marijuana, alcohol, heroin, methadone, or amphetamines as well as anabolic steroids and herbal remedies can be responsible for reversible gynecomastia (Nordt and DiVasta 2008). These issues need to be addressed in a detailed medical history followed by a thorough physical examination with regard to indicators of more serious diseases, which may impede additional assessments. Secondary causes for gynecomastia including drug abuse and medication, need to be addressed. Pubertal gynecomastia is usually a self-limited condition with spontaneous regression in 75 to 95% (Nydick et al. 1961). Surgical management of pubertal gynecomastia may be considered in non-obese male adolescents who present with persistent breast enlargement after a period of observation of at least 12 months, breast pain or tenderness, and/or significant psychosocial distress (Soliman et al. 2017). Surgical treatment includes central glandular resection, with or without liposuction for contouring the peripheral areas (Fig. 2). Postoperative complications like hematoma, seroma, and scarring, as well as technical errors including asymmetry and contour irregularities are common (20%) (Wiesman et al. 2004). Therefore, ultrasound-guided liposuction has been suggested as an alternative (Hodgson et al. 2005). Recently, microdebrider excision and liposuction technique has been used to treat gynecomastia with good results (Sim et al. 2020). Finally, medical treatment including estrogen receptor modulators, antiestrogens, and aromatase inhibitors have been tested especially in the early period of pubertal gynecomastia before fibrous remodeling takes place (Nordt and DiVasta 2008). However, due to the paucity of data on risks and benefits, pharmacological treatment is not recommended for adolescents (Lemaine et al. 2013).

Hypoplastic Anomalies

Athelia, Amazia, and Amastia

Athelia is defined as an absence of the NAC, amazia describes the lack of breast tissue, and amastia means the absence of both, breast tissue and NAC. Hypoplastic anomalies arise from an abnormal involution of the mammary ridge. They are typically rare, familiar or sporadic, and are often associated with other anomalies and syndromes including Poland’s syndrome, choanal-atriesia-athelia syndrome, scalp-ear-nipple syndrome, Al-Awadi/Raas-Rothschild syndrome, Mayer-Rokitansky-Kuster-Hauser syndrome, dermoid cysts, anomalies of the plate and upper extremities, and ectodermal dysplasia (Latham et al. 2006; Trier 1965; Amesse et al. 1999; Mollica et al. 1995).

In general, patients can present with bilateral amastia secondary to ectodermal defects, with unilateral amastia including Poland’s syndrome, or with bilateral amastia only (Lin et al. 2000). Significant hypoplasia may also be related to
connective tissue disorders, mitral valve prolapse, or genitourinary tract abnormalities (Brandt 2006; Trier 1965). Hypoplasia accompanied by abnormal pubertal development requires endocrinologic evaluation including ovarian dysfunction, hypothyroidism, or androgen-producing tumors (Brandt 2006). Thus, a thorough workup is obligatory.

Surgical reconstruction of the breast and/or nipple is best delayed until breast development has been completed to achieve an optimal symmetry, and may be accomplished by tissue expansion and subsequent implant placement with respect to possible blood supply aberrancies (Lin et al. 2000; Taylor 1979). In bilateral absence of the NAC, its size can be calculated based on reproducing two dimensions of the normal chest (Beer et al. 2001). For breast asymmetry, mostly bilateral procedures with reduction of the larger and enlargement of the smaller breast are performed (Pryor et al. 2009).

**Poland’s Syndrome**

Poland’s syndrome is a rare congenital anomaly found in 1:20–30,000 live births and outlines a combination of absence of the pectoralis muscle, abnormalities of the chest wall and breast, as well as hand and arm anomalies (Sadove and van Aalst 2005; Poland 1841; Romanini et al. 2018). It preferentially occurs unilaterally and mostly right-sided. Poland’s syndrome is often a sporadic mutation that is more commonly found in boys (3:1) and can be associated with other syndromes like Möbius, Klippel-Feil, or Sprengel’s deformity (Fokin and Robicsek 2002; Moir and Johnson 2008). Maternal smoking has been found to double the risk for the disease, which has a yet unknown etiology (Martínez-Frías et al. 1999). Vitally important, Poland’s syndrome has also been linked to other abnormalities like renal diseases as well as thoracic tumors or leukemia (Moir and Johnson 2008).

It has been postulated that either a regional disturbance in blood supply of the subclavian vessels and their branches or a defective attachment of the primitive limb bud to the upper rib cage and sternum impedes the normal development of the chest wall and upper limb (Holcomb et al. 2014). Presentation varies widely depending on the extent of the associated anomalies. The second to fifth ribs may be missing or deformed, and the hemithorax is often narrower with elevation of the shoulder and scapula (Pryor et al. 2009; Caouette-Laberge and Borsuk 2013). The costosternal portion of the pectoralis major is always absent, resulting in an absence of the anterior axillary fold and webbing of the axilla (Caouette-Laberge and Borsuk 2013). The pectoralis minor is absent in 75% of cases, and serratus anterior, latissimus dorsi, trapezius, or external abdominal oblique muscle can be absent or hypoplastic as well (Pryor et al. 2009; Moir and Johnson 2008). The skin is thinner with a hypoplastic nipple and alopecia of the axilla and the anterior chest wall with a smaller, higher-located breast than on the contralateral side. The majority of patients also present with a shorter upper limb and syndactyly, or less frequent brachydactyly, typically of the three middle fingers (Shamberger et al. 1989). Interestingly, up to 10% of patients with a syndactyly will have Poland’s syndrome (Al-Qattan 2001). Of note, vascular anomalies can occur and may hamper the surgical outcome.

Surgical correction was spurred by Mark Ravitch in 1952 and includes the correction of the chest wall component, tissue implants, and myocutaneous flaps; it is ideally done as a single stage repair in multiple layers after completion of growth (Moir and Johnson 2008). In particular cases, when early surgical procedures on the chest wall are necessary to protect mediastinal structures, soft tissue reconstructions are postponed in favor of contralateral matching and prevention of recurrence (Moir and Johnson 2008; Delay et al. 2016).

**Deformational Anomalies**

**Tuberous Breast Deformity**

This often bilateral, asymmetric deformity of an unknown incidence also known as “Snoopy deformity” describes herniated breast tissue
through a constricting fascial ring beneath the areola with a constricted mammary base (Teimourian and Adham 1983; Rees and Aston 1976). It has been suggested that the growth of the breast is restricted into a tuberous plant root shape either by an adherent superficial fascia to the dermis and muscular plane, or by a constrictive ring at its base (Latham et al. 2006). Thus, classical features may include a lack of breast skin, breast hypoplasia and asymmetry, conical breasts, herniated NAC, large areola, and a constricted breast base (Kulkarni and Dixon 2012; Rees and Aston 1976).

Surgical correction usually requires several steps like placement of an implant, reduction or augmentation mammaplasty, a release of breast tissue to broaden its base, and lowering of the inframammary fold (Rees and Aston 1976). Various techniques have been described addressing the challenging surgical repair that should be performed by experienced hands (Latham et al. 2006; Kulkarni and Dixon 2012; Pryor et al. 2009; van Aalst et al. 2009).

Acquired Anomalies

Of note, some of the breast deformities that pediatric surgeons will be confronted with are of an iatrogenic nature. The breast bud becomes palpable at week 34 of gestation and is 3 mm in size at 36 weeks (Jatoi and Rody 2016; Duflos et al. 2012). In the term neonate, it is a firm nodule up to 1 cm in diameter that involutes only late in infancy, with minimal breast tissue and a nearly flush nipple throughout prepuberty (Holcomb et al. 2014). Premature infants lack the firm breast nodule, being particularly vulnerable to damage by an ill-placed surgical incision (Holcomb et al. 2014).

Iatrogenic breast bud damage has been reported after thoracotomy, chest tube as well as central venous catheter placement, or abscess drainage (Holcomb et al. 2014; Pryor et al. 2009). After anterolateral thoracotomy for chest tube placement, scarring or tethering of the breast to the chest wall with contour deformity and restricted growth can occur (Sadove and van Aalst 2005). An anterolateral or posterolateral thoracotomy through the fourth intercostal space can cause direct damage to the breast bud or tethering of breast tissue to the chest wall, thus interfering with breast and pectoral muscle development (Cherup et al. 1986). A horizontal thoracotomy at the level of the inframammary fold results in cosmetically acceptable scar formation and does not harm breast development or lactation, but causes areola hyposensitivity in one third of patients (Deutinger and Domanig 1992). Breast hypoplasia or aplasia has also been reported after placement or removal of Broviac and Hickman catheters, especially in females less than 30 weeks gestational age and/or 1000 g body weight (van Aalst et al. 2009).

Thus, thoracic surgical procedures especially in young female infants should always take the location and development of the breast into consideration. Injudicious injury to the breast bud for a benign process is unacceptable (Pryor et al. 2009).

Conclusions and Future Directions

Breast disorders comprise a broad spectrum of congenital as well as acquired anomalies. Prepubertal surgery may bear the risk of iatrogenic disruption of breast development. Conversely, deformities such as virginal breast hypertrophy and gynecomastia can have a significant negative impact on one’s self esteem, especially in adolescence. Future studies are needed to determine true incidences and prevalences, and to further investigate short- and long-term physical and emotional effects of breast anomalies in children and adolescents.

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