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REVIEW

Ultrasound of pediatric breast masses: what to do with lumps and bumps

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Abstract The approach to breast masses in children differs from that in adults in many ways, including the differential diagnostic considerations, imaging algorithm and appropriateness of biopsy as a means of further characterization. Most pediatric breast masses are benign, either related to breast development or benign neoplastic processes. Biopsy is rarely needed and can damage the developing breast; thus radiologists must be familiar with the imaging appearance of common entities so that biopsies are judiciously recommended. The purpose of this article is to describe the imaging appearances of the normally developing pediatric breast as well as illustrate the imaging findings of a spectrum of diseases, including those that are benign (fibroadenoma, juvenile papillomatosis, pseudoangiomatous stromal hyperplasia, gynecomastia, abscess and fat necrosis), malignant (breast carcinoma and metastases), and have variable malignant potential (phyllodes tumor).

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Introduction

Breast masses in the pediatric population can present a diagnostic challenge to radiologists because they are relatively infrequently encountered and can cause great consternation to patients and their health care providers. The differential diagnosis differs substantially from that in the adult, and most findings are benign and relate to normal anatomical structures, physiological change or benign masses. In adults, the leading concern is primary breast cancer, yet this is decidedly rare in children, and most malignant breast masses are metastases from non-breast neoplasms. Many radiologists lack familiarity with the characteristic imaging features of pediatric breast masses that often can guide diagnosis and management, leading to increased anxiety for both radiologists and their patients.

Contrary to breast imaging evaluation in adults, mammography should rarely be used in children given the particularly high sensitivity of the developing breast to radiation. Further, the high proportion of fibroglandular tissue to fat hinders detection of masses, markedly decreasing the sensitivity of mammography in children [1, 2]. Given its lack of ionizing radiation and higher sensitivity in dense breast tissue, ultrasonography is the appropriate initial imaging modality in children [1, 3], with mammography reserved to assess for the presence and extent of microcalcifications in highly suspicious masses [3]. CT has no role in the workup of clinically evident breast masses, but lesions may be incidentally detected on CTs obtained for other purposes [3]. MR breast imaging is not widely used in the pediatric population but might be helpful for surgical planning or in the case of vascular and

lymphatic malformations that frequently involve multiple anatomical compartments [1, 3].

Finally, the management of breast lesions differs between the adult and pediatric populations. Biopsy of the immature breast can injure the developing breast bud and impair or prevent growth [1]. Although a mass in an adult has a considerable risk of malignancy, this is not true in children, thus management is typically conservative, consisting of US follow-up in most cases, with biopsy reserved for a few select cases [3].

Normal breast development

The female breast develops in two phases. The initial phase of differentiation and growth begins during fetal life, and the final phase occurs during puberty [4]. The initial phase occurs in both females and males in the 5–6th weeks of fetal development, as epidermal cells invaginate and form the primary mammary ridges, extending bilaterally from the axilla to the groin [4]. These ridges regress, except at the fourth intercostal space, forming a rudimentary breast composed of a simple network of ducts and supportive stroma [3, 5]. Commonly newborns are found to have bilateral subareolar nodules; this is because this tissue can physiologically enlarge under the influence of maternal hormones. This finding is temporary, with regression seen by 12 months of age [3, 6].

The second phase, also known as thelarche, occurs in girls as the breast bud develops during puberty. Estrogen promotes ductal elongation and differentiation, while progesterone promotes terminal lobular development [5]. The mean age of thelarche onset is 9.8 years, and it is considered premature if it occurs prior to 8 years and delayed if after 13 years of age [5].

Ultrasound evaluation of the breast and avoiding pitfalls

As with breast ultrasonography in adults, breast US findings in children must be interpreted in the context of the patient's family and background history, ethnicity and age. It is incumbent upon the radiologist to gather these pertinent pieces of information from the patient, parents and referring clinician prior to diagnostic imaging. Attention to patient comfort in the pediatric population may include distraction using movies or electronic games and attention from a Child Life Specialist during the examination. Certainly, simple measures such as patient privacy and warmth with appropriate draping are of utmost importance in school-age girls and adolescents.

US evaluation should be performed with a 15- to 7-MHz linear transducer, although curved-array transducers with lower frequencies may be required depending on depth of breast tissue [5, 6]. For interrogation of superficial structures, a standoff pad or large mound of coupling gel is helpful [5]. A useful landmark for defining the posterior boundary of the breast is the pectoralis muscle, characterized by its hypoechoic fibrillar appearance [3]. A common pitfall in the breast evaluation is misinterpretation of a rib, which appears as a hypoechoic nodule in the transverse plane, as a pathological lesion (Fig. 1). A rib's location deep to the pectoralis muscle, strong posterior acoustic shadowing, and elongated appearance in the longitudinal plane are features that distinguish it from a breast mass [5, 7]. Similarly, fat lobules in cross-section can appear to be isoechoic masses, and upon turning the transducer in a longitudinal orientation, the elongated morphology of a normal fat lobule becomes apparent [8].

The nipple creates strong posterior shadowing because of its dense whirled smooth muscle, and this shadowing is eliminated using angulation of the beam beneath the nipple to satisfactorily evaluate the subareolar region [8]. During scanning, the nipple can invert and project beneath the skin surface as a hypoechoic nodule. When recognized at the time of scanning, this is simply corrected with reducing compression by the transducer, but can be confusing on static images. Knowledge of transducer position relative to the nipple allows recognition of this normal structure [8].

Finally, Cooper's suspensory ligaments can cause posterior acoustic shadowing that is typically thin and linear but

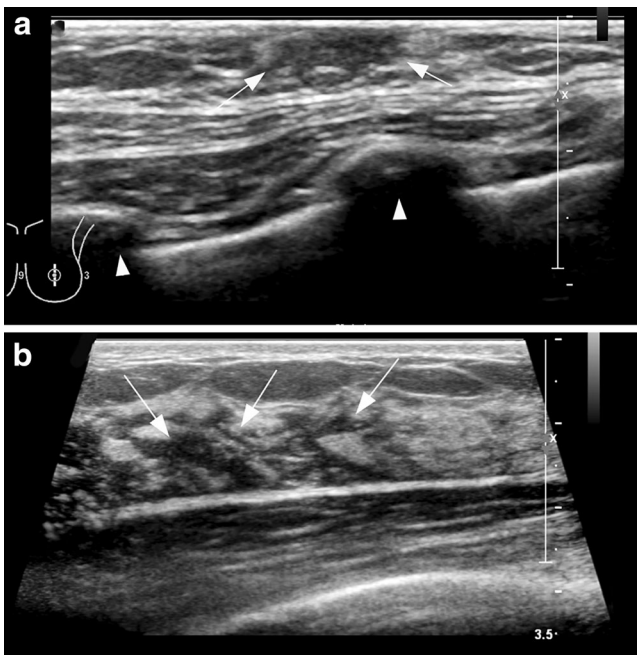

Fig. 1 Potentially confusing pitfalls in breast ultrasonography. **a** Single sonographic image of breast in an 8-year-old girl shows normal hypoechoic appearance of the subareolar breast bud (*arrows*). Note posterior acoustic shadowing of ribs (*arrowheads*), deep to the linear striations of chest wall musculature. **b** Cooper's ligaments cast posterior acoustic shadowing (*arrows*) as shown in this single sonographic image of breast tissue in a 13-year-old girl

occasionally simulates a mass (Fig. 1). Modification of technique by changing pressure or angle can resolve this shadowing mimic [8].

Ultrasound findings during breast development

Pubertal development in both boys and girls is conventionally summarized using the Tanner staging system, first described in 1962 [9, 10]. Breast development is clinically divided into five Tanner stages based on the physical exam (Table 1). Five characteristic sonographic depictions of breast morphological development have been described in the literature as reflecting the five Tanner stages of breast development [3, 5]; however, considerable overlap has been reported between the sonographic appearances of breast development and the clinical Tanner breast stages 2 through 4 [11]. Nevertheless, it is generally accepted that rising estrogen levels correlate with the maturation of breast tissue, as observed sonographically [3, 5, 6, 11]. Knowledge of this range of appearances is useful for accurate interpretation and is summarized in Table 1 and illustrated in Fig. 2. It is important to note that the breast bud can initially appear asymmetrical in size, and the normal breast bud may be mistaken for a mass on clinical exam.

In addition to the morphological descriptions summarized in Table 1, volume of breast tissue observed sonographically can also be helpful in the evaluation of girls with premature thelarche: breast volume (as calculated by measuring glandular tissue according to the formula $D1 \times D2 \times D3 \times 0.523) \geq 0.85\ cm^3$ was significantly associated with rapidly progressive central precocious puberty in one study (Fig. 3) [11].

Congenital anomalies and anatomical variants

Polythelia (an accessory nipple) and polymastia (an accessory breast gland) are congenital variants caused by incomplete regression of the mammary ridge. They are usually encountered in the axilla or infra-mammary fold (Fig. 4) [3, 12] but can occur anywhere along the embryonic milk line. Polythelia is the more common entity, found in 1–2% of the population and often clinically mistaken for a nevus given its small size and pigmentation [3, 12]. Polymastia can lead to a clinically evident mound and can cause cyclical breast pain or breast masses [13].

Hypoplasia or amastia (absence of the breast and nipple) are rare and most commonly encountered in the setting of Poland syndrome [3, 14]. Most abnormalities of the pectoralis muscle do not disturb breast development, though. Amazia is the presence of a nipple with lack of underlying breast tissue. The most common cause is iatrogenic, from biopsy of the immature breast or excision of the breast bud [14]. Radiation therapy prior to puberty has also been reported as a cause of amazia [14].

Developmental abnormalities

Gynecomastia is the development of excessive breast tissue in boys [3]. There is a trimodal distribution, occurring in the neonate (under the influence of maternal hormones), in adolescents and in elderly men [5]. Of these age groups, gynecomastia is most commonly encountered in adolescence, 1–2 years after the onset of puberty, and may be present in 60–

Table 1 Summary of clinical and US findings at each stage of breast development

Breast stage	Clinical findings	US findings
Stage 1 (Pre-thelarche)	TS 1: Elevation of the papilla only	• Small focus of subareolar echogenic tissue • Absence of the breast bud
Stage 2 (Breast bud stage)	TS 2: Elevation of both breast and papilla, with a small mound and enlargement of areolar diameter. Clinically palpable subareolar nodule	• Subareolar hypoechoic nodule appears (the breast bud), within echogenic adipose and loose connective breast tissue
Stage 3	TS 3: Further enlargement of breast and areola without separation of their contours	Enlargement of the hypoechoic breast bud that: • Overall maintains a rounded morphology • Displays linear projections and a spider-like shape as ducts elongate
Stage 4	TS 4: Projection of areola and papilla to form a secondary mound above the level of the breast	• Echogenic tissue fans out • Hypoechoic breast bud becomes more widely elongated, losing the rounded appearance • Subcutaneous fat may be present
Stage 5	TS 5: Projection of papilla only, due to recession of areola to the general contour of the breast	• Loss of the hypoechoic breast bud • Mature breast tissue composed of hypoechoic fat lobules intermixed with echogenic glandular tissue and stromal tissue • Superficial subcutaneous fat

TS Tanner stage

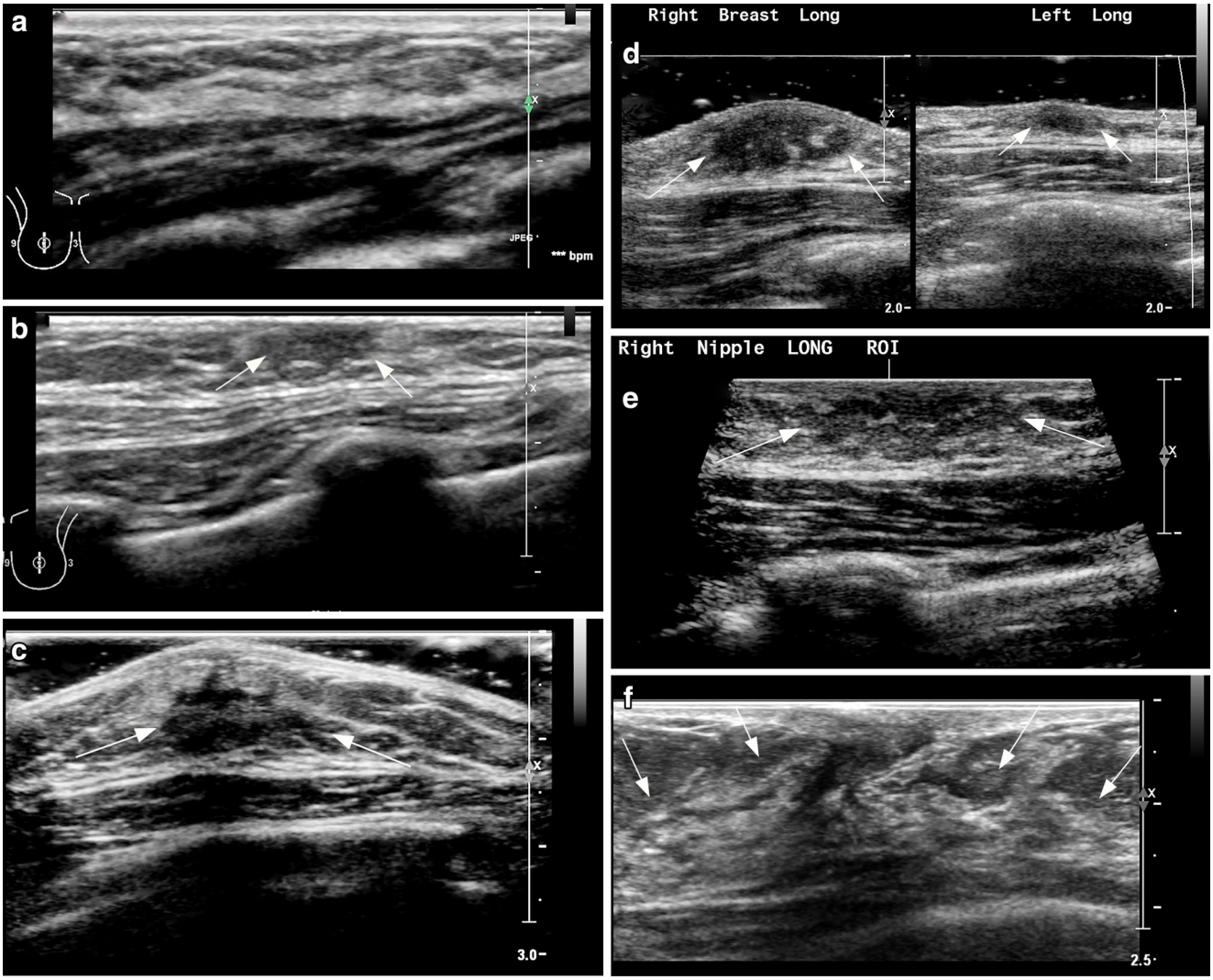

Fig. 2 Five stages of breast development as seen on sonographic images. **a** Stage 1 in a 4-year-old girl shows absence of breast tissue. **b** Stage 2 in an 8-year-old girl shows a hypoechoic nodular breast bud (*arrows*). **c** Stage 3 in an 11-year-old girl shows increasing volume of hypoechoic nodular subareolar glandular tissue (*arrows*), maintaining a rounded shape but showing marginal linear projections extending outward into the adipose-connective tissue. **d** Asymmetrical breast development in a 9-year-old girl at stage 3 on the right and stage 2 on the left (*arrows* indicate glandular tissue). **e** Stage 4 in a 10-year-old girl shows elongating glandular tissue extending outward (*arrows*) into fibrofatty tissues. **f** Stage 5 in a 16-year-old girl shows mature breast tissue with a mixture of echogenic and hypoechoic tissues, reflecting a combination of glandular tissue integrated with background fibrofatty tissues (*arrows*)

75% of normal boys [5, 6, 15]. Gynecomastia can be unilateral or asymmetrical [3]. An imbalance of estrogen and testosterone may be the primary cause, although data are emerging regarding the role of leptin, an enzyme in adipose and breast tissue that increases estrogen, in the development of gynecomastia [1]. Many drugs have also been implicated, including anabolic steroids, tricyclic antidepressants, spironolactone, cimetidine, marijuana, some antibiotics including ketoconazole and metronidazole and even some chemotherapy regimens such as methotrexate and alkylating agents [16]. The neonatal and adolescent cases typically resolve within 2 years, and reassurance is all that is necessary [3]. Extreme or prepubertal gynecomastia should prompt a medical workup. Possible etiologies include hormone-producing tumors (Sertoli–Leydig testicular tumors, functional adrenal cortical tumors, hepatoblastoma and fibrolamellar carcinoma), liver disease and Klinefelter syndrome [1, 3].

Clinical exam reveals a tender, subareolar mass. The main role of US is to demonstrate normal-appearing breast tissue and exclude a mass lesion [1]. US may demonstrate a range of appearances, including nodular, poorly defined, and triangular, flame-shaped mass, all of which are generally hypoechoic (Fig. 5). Spiculated margins or dendritic projections may be present, with variable vascularity [17]. Location is critical and should be subareolar. Eccentric masses must be scrutinized, because carcinomas tend to be eccentric with sparing of the subareolar region [18]. The margins of carcinoma may be microlobular, and axillary lymphadenopathy or skin changes

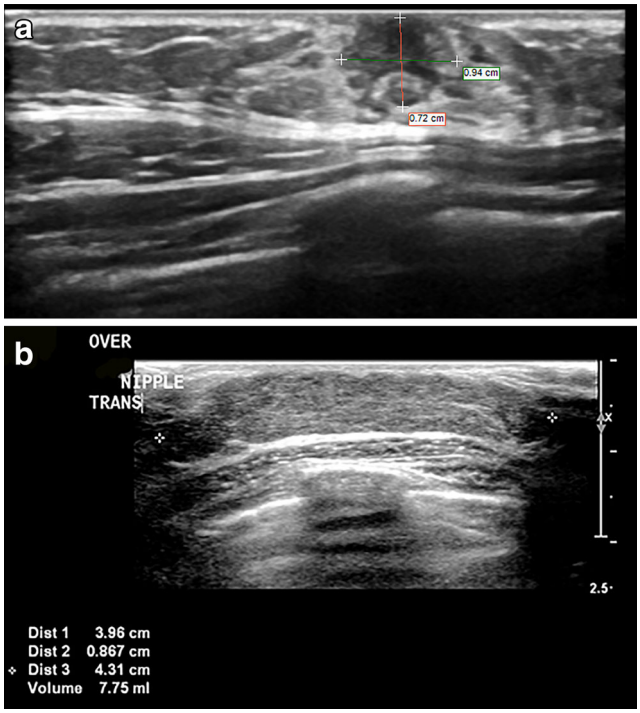

Fig. 3 Examples of breast volume calculation in evaluation of premature thelarche. **a** US shows normal breast volume in a 7-year-old with thelarche and morphological stage 3 breast development, calculated by US as 0.38 cm^3. Remaining evaluation for premature onset of puberty was negative. **b** Abnormally generous glandular tissue measures 7.7 cm^3 in a 3-year-old girl with central precocious puberty

may be present, although these findings would be observed in boys extremely rarely because the typical age group affected is middle-age men [18, 19]. Finally, gynecomastia is often bilateral, unlike carcinoma [18]. Pseudogynecomastia occurs in the setting of general obesity, in which subareolar adipose tissue accumulates, rather than breast tissue [6]. In these

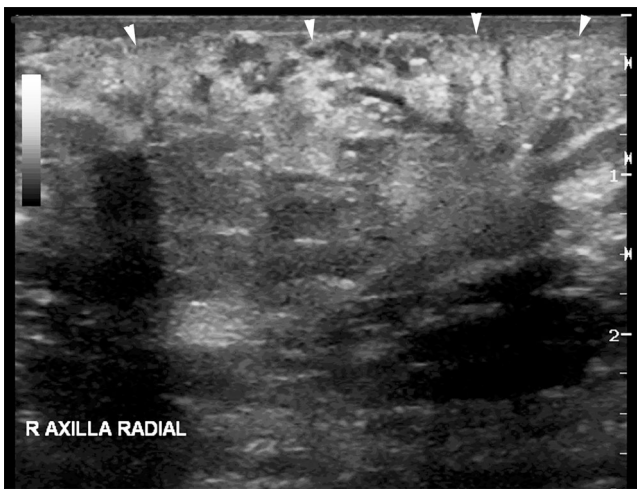

Fig. 4 Accessory breast tissue. Single sonographic image in a 16-year-old girl evaluated for a painful lump in the right axilla shows accessory breast tissue (*arrowheads*) at the site of tenderness

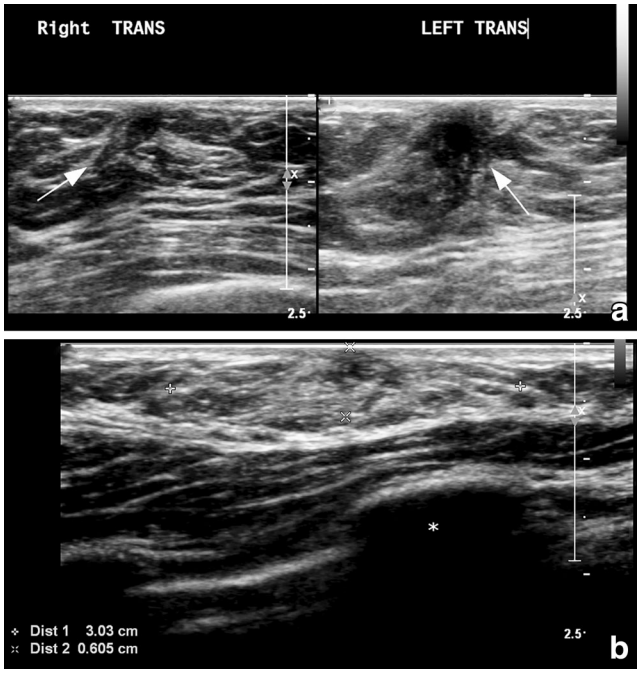

Fig. 5 Gynecomastia on breast US. **a** Bilateral subareolar breast tissue is identified in a 14-year-old boy. **b** Asymmetrical subareolar glandular breast tissue is seen in a 12-year-old boy (calipers outline glandular breast tissue). Note acoustic shadowing of ribs (*)

cases US shows only adipose tissue, without glandular breast tissue [1, 17].

Benign cystic masses

Simple cyst

Simple cysts are most commonly seen in women ages 30–50 years but can be present at any age [5]. In adults, obstruction of the duct or discrepancy between fluid secretion and absorption lead to dilation of the lobular acini [5]. In adolescents, cysts tend to occur near the nipple, representing obstructed glands of Montgomery located at the edge of the areola [3, 6]. Two-thirds present with signs of inflammation and nipple discharge, while the remainder present with a painless mass (Fig. 6) [3, 12].

Obstructed glands of Montgomery typically appear as retroareolar cysts less than 2 cm [3]. They usually resolve with conservative treatment [3, 12]. US is a useful tool to distinguish solid and cystic masses, revealing a cyst as a round or oval, well-circumscribed anechoic mass with a thin wall, posterior acoustic enhancement, and no internal blood flow appreciable on color Doppler [5, 20]. It is important to keep in mind that not all entities that contain fluid are cysts, because fluid can also be seen in fibroadenomas and abscesses [20]. Further, posterior acoustic enhancement and avascularity are common features of fibroadenomas [6, 20]. Clinical history

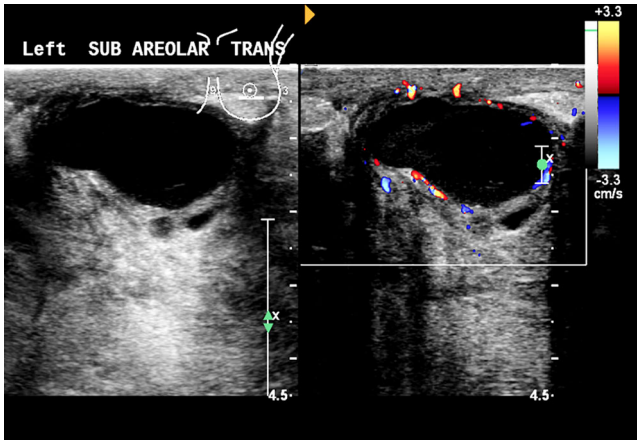

Fig. 6 Simple cyst. Breast US in an 11-year-old girl with cellulitis shows a large anechoic avascular structure consistent with a cyst. The large size of this cyst (greater than 2 cm) implies this is not an obstructed gland of Montgomery and may not spontaneously resolve. Color Doppler shows peripheral vascularity, suggesting the cyst is complicated by infection, given the background of cellulitis. A separate small cyst is adjacent to the dominant cyst at the posterior right margin

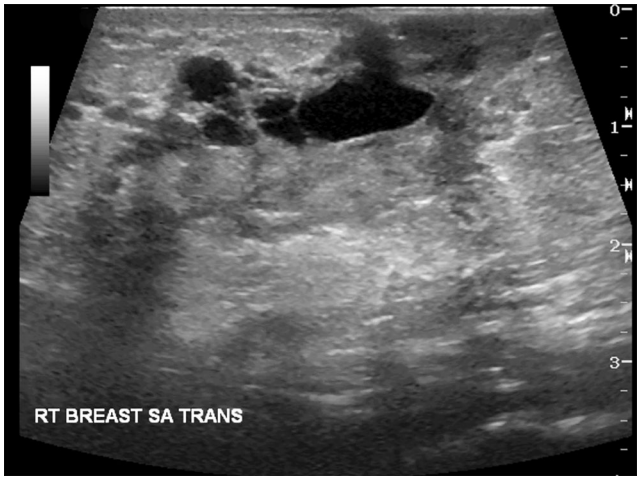

Fig. 7 Duct ectasia. Right breast US performed in a 12-year-old girl shows bilateral subareolar tubular anechoic structures consistent with dilated ducts

and aspiration may be helpful to guide diagnosis [20]. When complicated by hemorrhage or infection, cysts may contain fluid-fluid levels, echogenic debris and internal septa and may show peripheral vascularity [6].

Cysts require no action. If they are symptomatic, they can be aspirated for short-term relief, but one should counsel patients that they can recur. Occasionally, a cyst that is complicated (for instance, contains debris from protein or blood) may not be easily distinguished from a solid mass. Such cases can be managed using either short-interval imaging follow-up (6 months) or aspiration to confirm a cystic nature.

Duct ectasia

Duct ectasia is a rare entity of unknown etiology that occurs in infancy and early childhood [15]. The retroareolar ducts are most commonly affected [15]. Patients typically present with bloody nipple discharge, but a palpable tender mass is sometimes present in advanced cases [3, 15]. Stasis of secretions predisposes to infection by *Staphylococcus aureus* and bacteroides species [3]. US shows retroareolar, dilated, anechoic tubular structures, possibly with echogenic debris (Fig. 7) [3]. Maternal hormones are thought to play a role, and treatment of affected infants is typically conservative with antibiotics and cessation of breast-feeding. Refractory cases may require surgery [3].

Mastitis and abscess

Mastitis typically occurs in the puerperal period but can occur in children with a bimodal distribution; it is seen in neonates younger than 2 months and children 8–17 years old [1, 5]. Neonatal mastitis is rare and is thought to be secondary to maternal hormone-induced ductal ectasia, which facilitates pathogen entry, as mentioned above [1]. More commonly, mastitis occurs in the older pediatric group, secondary to breaks in the skin from infection, piercing and lactation [1, 5]. The most common pathogens are staphylococci and streptococci species [5, 18]. Common signs are warmth, erythema, tenderness and a fluctuant mass in the case of superimposed abscess [1, 2].

In the case of uncomplicated mastitis, US reveals heterogeneously increased echogenicity and vascularity of the breast parenchyma (Fig. 8). Focal decreased echogenicity is suggestive of phlegmon [1, 7]. Mastitis is a clinical diagnosis, but US should be considered to exclude an underlying fluid collection and guide therapeutic and diagnostic aspiration if an abscess is present [5, 15]. At US, abscesses have an irregular shape with ill-defined margins, a complex hypoechoic center and thick echogenic wall (Fig. 8) [12]. Doppler US often demonstrates increased peripheral vascularity, with little to no internal flow [6, 18]. In the setting of both mastitis and abscess, reactive axillary lymphadenopathy may be present [12]. The differential diagnosis for these findings includes cystic breast disease, duct ectasia and fat necrosis; confusing cases with a mass complex enough to appear solid may warrant consideration of invasive breast carcinoma [12]. Treatment includes oral antibiotics, with fine-needle aspiration or incision and drainage for larger collections [2]. Follow-up imaging could be considered to ensure resolution [12].

Galactocele

Galactoceles are thin-walled, milk-containing cysts lined by secretory epithelium [15]. Most cases occur during lactation as a result of an obstructed duct. Rarely, galactoceles develop in infants or adolescent boys and present as painless enlargement of the breast [3, 15]. Causative factors in children are thought

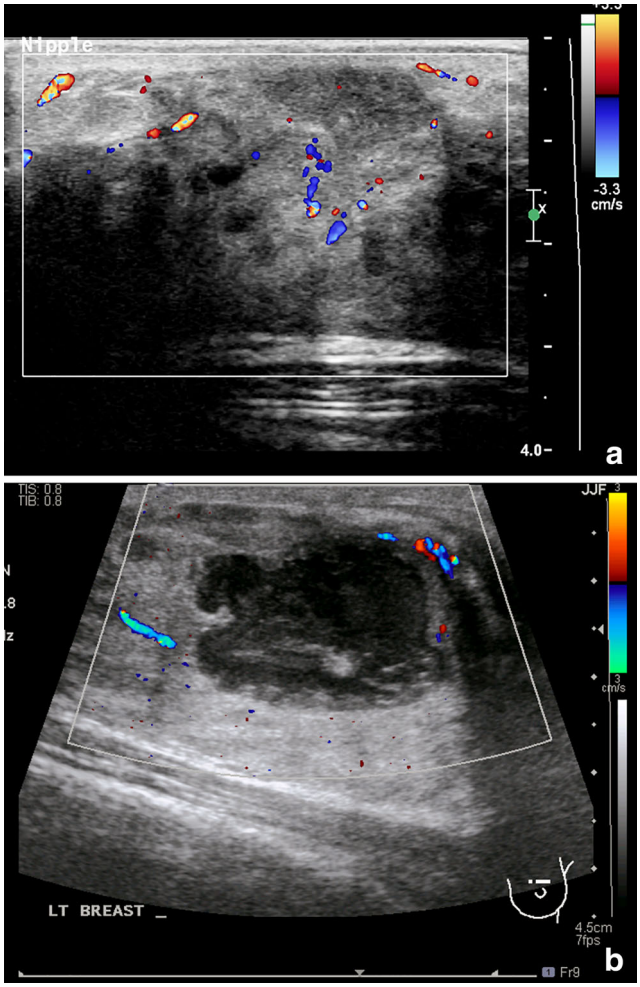

Fig. 8 Mastitis and breast abscess. **a** Breast color Doppler US in a 12-year-old girl with breast pain, swelling and redness and a fever shows diffuse echogenic breast tissue with scant hyperemia. **b** Breast color Doppler US in a 13-year-old girl shows a complex fluid collection within the breast tissue, consistent with breast abscess

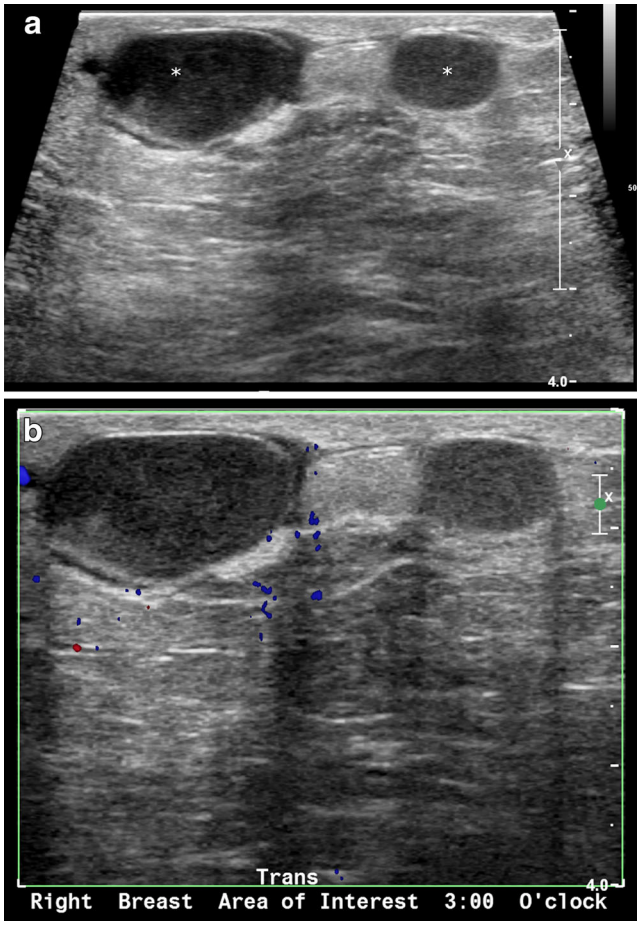

Fig. 9 Galactocele. Right breast US using (**a**) gray-scale and (**b**) color Doppler in a 15-year-old lactating girl with a palpable breast lump and absence of breast pain or redness and no fever shows two adjacent round, hypoechoic avascular structures consistent with complex cysts (*). In the context of breastfeeding, this finding is consistent with galactocele. (Images courtesy of Dr. Stephen Simoneaux, Children's Healthcare of Atlanta at Egleston, Atlanta, GA)

to include prolactin stimulation, ductal obstruction and epithelial cell secretion following trauma [1, 15]. US appearance varies depending on the relative composition of fat and fluid, ranging from purely anechoic to a complex cyst [1, 3]. A potentially helpful feature is fluid of variable complexity layering non-dependently with fat, although this is not always seen (Fig. 9) [1, 3, 21]. Aspiration is both diagnostic and therapeutic, revealing milky fluid [3, 5].

Hematoma

Hematomas are usually post-traumatic and sport-related but are sometimes iatrogenic [3, 18]. At US, their appearance varies with the age of the hematoma, acutely appearing hyperechoic and ill-defined from reactive changes in the surrounding parenchyma. As the blood products are broken down, the hematoma becomes cystic with debris, septa and fluid-fluid levels [3, 18] (Fig. 10). History may aid in the diagnosis; however the inciting trauma may be minor and not recalled by the patient, especially if the patient is coagulopathic [18]. Aspiration can be both diagnostic and therapeutic, revealing blood at different phases of degradation [15, 20, 22]. The differential diagnoses include fat necrosis and abscess.

Fat necrosis

Fat necrosis is a benign consequence of trauma caused by the action of tissue lipases on released fat, a process known as fat saponification [23]. Clinically, fat necrosis can be non-palpable or a mobile or fixed mass, often near the skin or nipple — sites most susceptible to trauma [23]. The US appearance can range widely depending on the degree of inflammatory response. An anechoic oil cyst with posterior acoustic enhancement or shadowing occurs when there is little tissue reaction. In contrast, a complex cyst with mural nodules or a

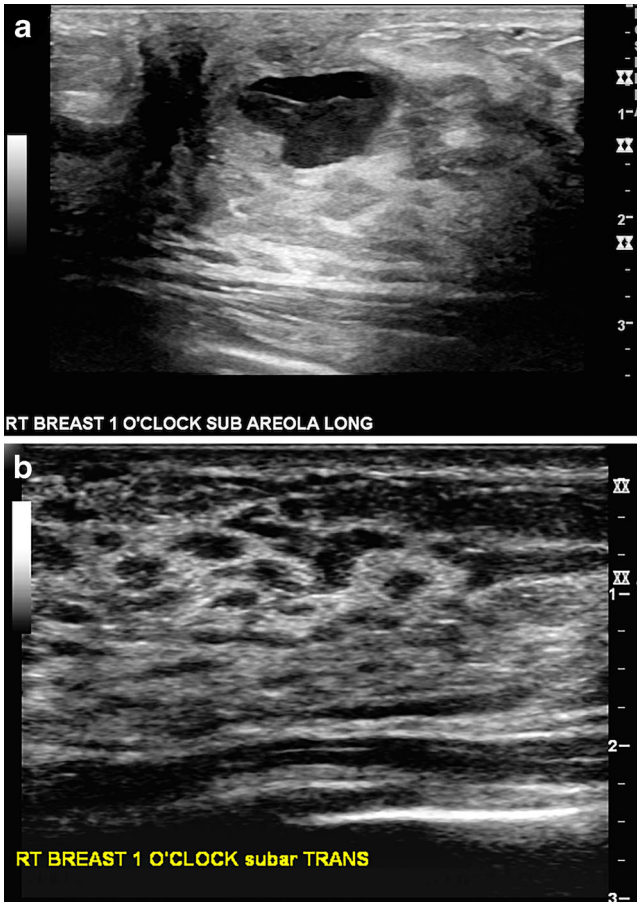

Fig. 10 Breast hematoma. **a** Right breast US in a 15-year-old girl with a history of breast trauma and a palpable mass shows a well-demarcated hypoechoic fluid collection with internal debris deep to the areola at the one o'clock position. **b** Follow-up US at 6 months shows normal breast tissue at the site of prior cystic finding, consistent with resolution of trauma-related hematoma

solid spiculated mass can manifest following inflammatory fibrotic reactions [22, 23]. The appearance of fat necrosis can change over time as the necrotic fat liquefies, leading to fat-fluid levels and internal debris [18]. In some cases the lesion becomes more solid; however, enlargement is not a typical feature [22]. Although a history of trauma is helpful, it is not always provided, and short-term US follow-up or aspiration is advised. If the lesion demonstrates an increase in size, it should be viewed upon with suspicion and biopsied [22].

Hemangioma

Vascular lesions in the pediatric breast are usually benign [1, 3]. The infantile hemangioma is the most common vascular mass arising in breast tissue, and this typically presents soon after birth. A cutaneous hemangioma (also called "strawberry nevus") may be present on the breast or elsewhere on the body. The hemangioma typically undergoes a rapid growth phase followed by slow involution. A wide range of sonographic appearances have been described, from solid masses

Fig. 11 Infantile hemangiomas of the breast. **a** Gray-scale and (**b**) color Doppler sonographic images of breast tissue in a 7-week-old girl show a solid, oval echogenic mass with a longitudinal parallel orientation with respect to the skin line, circumscribed margins and considerable internal vascularity. Follow-up US of the lesion (not shown) demonstrated diminished vascularity and gradual regression of soft-tissue abnormality. **c** Gray-scale and (**d**) color Doppler sonographic images of a different female infant with breast infantile hemangioma at age 11 weeks show more internal hypoechoic components, which can also be seen with this type of hypervascular tumor

to complex cystic structures [3, 17, 24]. However in our experience the infantile hemangioma in the breast is a vascular mass characterized by partly circumscribed margins, heterogeneous echogenicity, and obvious hypervascularity evident with application of color Doppler (Fig. 11).

Benign solid masses

Fibroadenoma

Most solid breast masses in the pediatric population are fibroadenomas, which comprise 54–94% of cases [2]. A fibroadenoma is a benign proliferation of fibroepithelial tissue [3, 20]. Most children present at age 15–17 years with a painless, slowly growing mass. On physical exam, the fibroadenoma is well-circumscribed, mobile and rubbery, most commonly in the upper outer quadrant of the breast. They can be multiple in 10–15% of cases and are more common in African Americans [2, 3, 6].

Classification is based on histology and size. Conventional fibroadenomas are the most common type, usually reaching 2–3 cm in size [25]. When a fibroadenoma reaches 5–10 cm it is considered a giant fibroadenoma [3]. The juvenile fibroadenoma is rare, accounting for 7–8% of cases, and differs histologically in that there is a larger stromal component than is seen in the conventional fibroadenoma. This subtype has the potential for rapid growth and is most common in African Americans [3, 25]. Complex fibroadenomas are very rare and have foci of sclerosis, adenosis, calcifications or papillary apocrine metaplasia. Complex fibroadenomas place the child at a slightly higher, albeit still low, risk of developing future breast cancer [25].

Findings at US are characteristic, but nonspecific, and are shared with phyllodes tumor and pseudoangiomatous stromal hyperplasia (PASH). Hypoechoic echotexture, round or oval shape, well-circumscribed margins with three or fewer macrolobulations, and a parallel orientation of the long axis with respect to the skin line are common findings (Fig. 12) [3, 5, 6, 25]. The mass might appear nearly anechoic, and color Doppler shows little to no internal vascularity [1, 3]. Posterior acoustic enhancement may be present [3, 24]. Unusual features would include angular margins and posterior shadowing, and these should be considered suspicious [25].

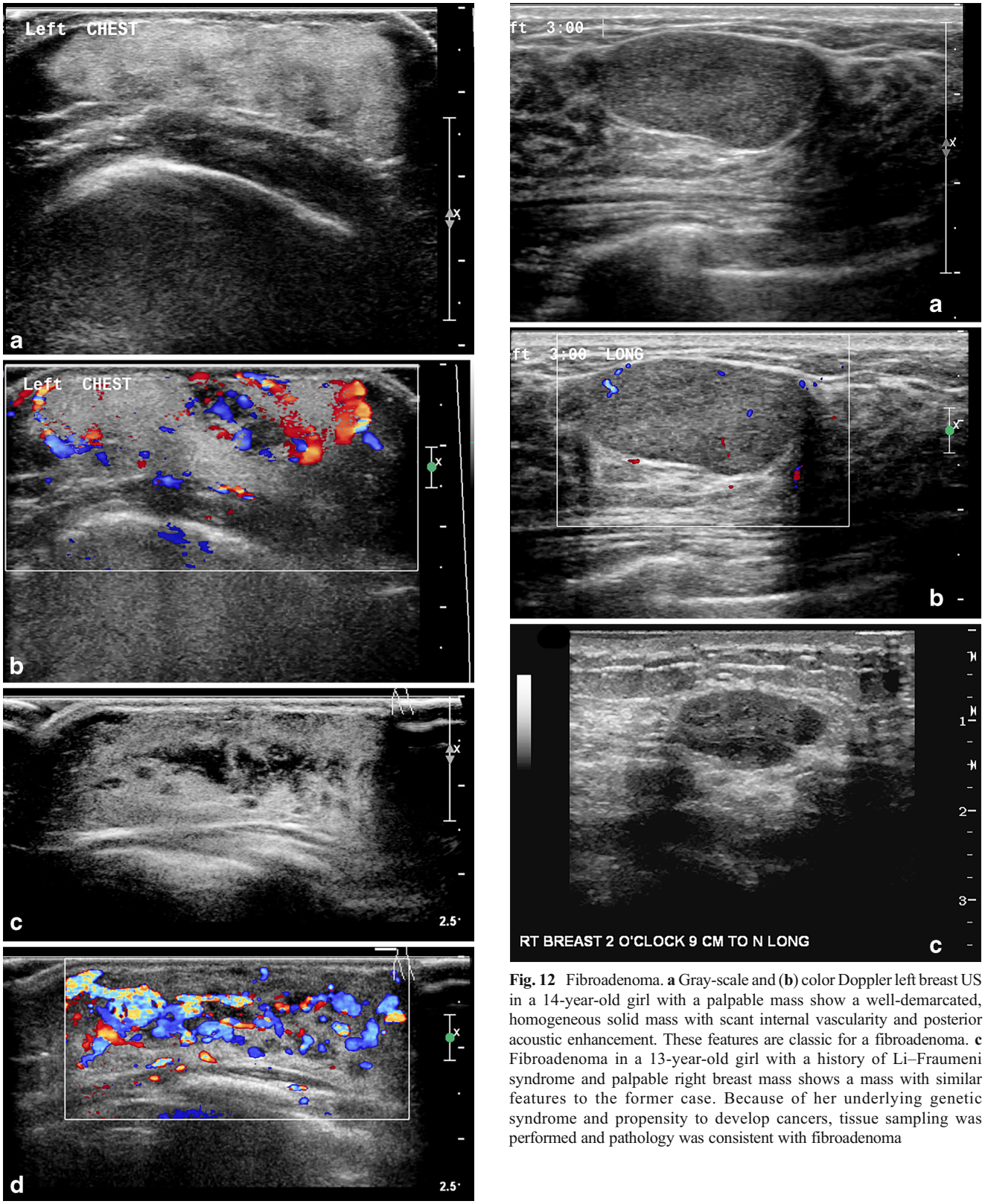

Fig. 12 Fibroadenoma. **a** Gray-scale and (**b**) color Doppler left breast US in a 14-year-old girl with a palpable mass show a well-demarcated, homogeneous solid mass with scant internal vascularity and posterior acoustic enhancement. These features are classic for a fibroadenoma. **c** Fibroadenoma in a 13-year-old girl with a history of Li–Fraumeni syndrome and palpable right breast mass shows a mass with similar features to the former case. Because of her underlying genetic syndrome and propensity to develop cancers, tissue sampling was performed and pathology was consistent with fibroadenoma

Treatment of a fibroadenoma varies depending on its size and associated symptoms (Table 2). For typical-appearing, asymptomatic fibroadenomas that are smaller than 5 cm, sonographic follow-up at 6 months, 1 year and 2 years is appropriate to document stability in size. For any detectable growth and for any symptoms such as pain, referral to general surgery for resection is appropriate.

Pseudoangiomatous stromal hyperplasia (PASH)

Pseudoangiomatous stromal hyperplasia is a relatively common proliferation of mesenchymal cells that occurs in response to hormonal stimulation [1, 3]. PASH is a histological finding commonly seen in the background of breast tissue in association with other breast pathology; however, it only rarely creates a mass in the pediatric breast. The name "pseudoangiomatous" derives from its histological appearance of interconnected empty, slit-like spaces resembling vascular structures [1]. This pathological appearance resembles that of a low-grade angiosarcoma, but in PASH, erythrocytes are absent and the channel-like spaces differ in histological staining patterns from an angiosarcoma [1, 11, 17]. PASH is often found incidentally in perimenopausal women as microscopic foci in normal tissue or associated with proliferative changes such as lobular hyperplasia or even gynecomastia in males [1, 17]. Interestingly, PASH has been rarely reported in children and has been associated with immunodeficient states and neurofibromatosis type I [17].

When PASH forms a mass, it can present similarly to fibroadenoma, both clinically and sonographically. If palpable, the mass is typically painless, mobile and rubbery [3]. Common US findings include a solid, hypoechoic, oval mass with the long-axis parallel orientation to the skin line (Fig. 13). The absence of well-circumscribed margins and posterior acoustic enhancement has been reported to suggest PASH [3], but these are nonspecific findings.

Imaging follow-up is often sufficient; however these lesions have a tendency to grow, sometimes rapidly in adolescents, prompting surgical excision in such cases. Some advocate for surgical resection if greater than 2 cm or with a strong family history of cancer [17]. A goal of 1- to 2-cm disease-free margins is desired to prevent recurrence, which occurs in 5–18% of cases [3, 17]. If recurrence does occur, a repeat biopsy to exclude an underlying cancer is suggested [17].

Juvenile papillomatosis

Juvenile papillomatosis is a rare benign focal proliferative disorder resulting in a fibrotic mass with many small cysts

Table 2 Summary of appropriate differential diagnoses and clinical recommendations for diagnosis of pediatric breast masses

Clinical situation	Differential diagnosis	Recommendation
Neonate or young child	• Physiological response to maternal hormones • Gynecomastia	• Do not biopsy, clinical follow-up is sufficient • If vascular, likely hemangioma
Simple cystic mass	• Must demonstrate the following features: unilocular, well-circumscribed, anechoic, posterior acoustic enhancement • If any internal debris or vascularity is present, refer to complex cystic mass	• Most commonly no treatment or follow-up is necessary. Aspiration could be pursued for significant pain or to confirm liquid contents if sonography is confused by internal debris/complexity
Duct ectasia		• Observe and culture nipple discharge. Likely to resolve spontaneously
Complex cystic mass	• Abscess • Hematoma/fat necrosis • Galactocele	• Aspiration, consider follow-up US
Adolescent with breast mass <5 cm, benign US features	• Most likely fibroadenoma • Less likely PASH, phyllodes tumor	• US follow-up • If stable for 2 years, clinical follow-up • If growing or painful→core biopsy and referral to breast surgeon
Adolescent with breast mass >5 cm, benign US features	• Giant fibroadenoma • Phyllodes tumor	• Surgical consultation for anticipated surgical excision. Lesions of this size cannot be distinguished by needle tissue sampling
Breast mass with irregular shape, angular margins, shadowing or in setting of personal cancer	• Malignancy • Abscess • PASH • Galactocele • Fat necrosis	• Tissue sampling or surgical excision
Any solid or complex cystic mass in setting of prior/known cancer or prior radiation therapy to breast tissue	• Metastasis is the primary concern	• Tissue sampling or surgical excision

PASH pseudoangiomatous stromal hyperplasia

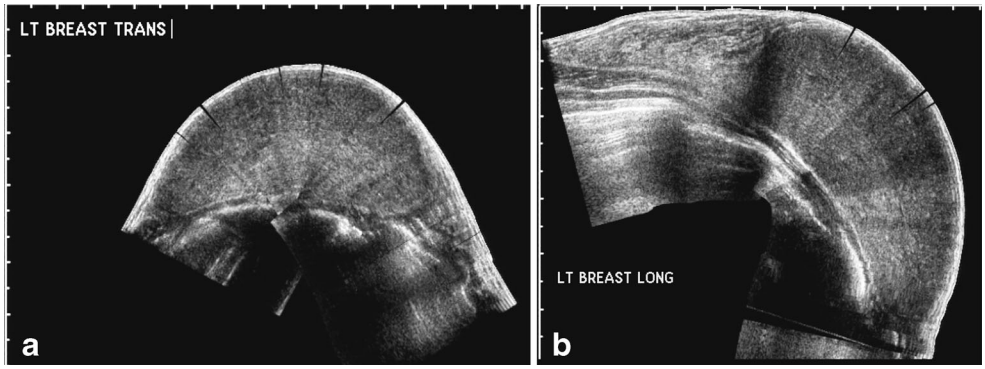

Fig. 13 Pseudoangiomatous stromal hyperplasia (PASH). Unilateral breast US in (**a**) transverse and (**b**) longitudinal projections in a 12-year-old girl with asymmetrical left breast enlargement and palpable mass show a homogeneous mass with a longitudinal parallel orientation and partly circumscribed margins. Main differential considerations are a giant fibroadenoma and phyllodes tumor. (Images courtesy of Dr. Stephen Simoneaux, Children's Healthcare of Atlanta at Egleston, Atlanta, GA)

and dilated ducts [3]. It is known as Swiss cheese disease because these distinctive features are evident at gross examination [1, 3]. It typically occurs in older adolescents, with a mean age of 19 years. These patients may have already had evaluation of prior benign breast masses [26]. Clinical findings are a firm, mobile mass in the periphery of the breast that may be confused for fibroadenoma, but imaging can help to differentiate the two [1, 3]. At US these lesions are ill-defined, with multiple peripheral anechoic cystic spaces complementing its gross and histological appearance [1, 3, 26]. Occasionally microcalcifications are present [3]. Using MR imaging, the characteristic cystic spaces are clearly discernible on T2-weighted sequences, and these lesions have a benign enhancement pattern after intravenous administration of gadolinium-based contrast agents [3].

Despite this lesion's benign histology, it has been associated with increased risk of both synchronous and metachronous breast cancer [1]. Approximately 5–15% of these cases have concurrent breast carcinoma [3]. Patients at highest risk of cancer have one of the following: positive family history, atypical histology, bilaterality, multifocality or recurrence [27]. Treatment is complete surgical excision, because incomplete resection inevitably leads to recurrence. The prognosis is not well-established given its rarity, and pending further scientific investigation, the current recommendation is annual clinical surveillance [27]. Juvenile papillomatosis is considered a marker for familial breast cancer, because 33–58% of these patients have a positive family history [1, 3]. Given this association, surveillance of family members is also advised [27].

Intramammary lymph node

Intramammary lymph nodes are classically located in the lateral breast, usually the upper outer quadrant [5]. They are hypoechoic, round or oval, and have a thin cortex of less than 2–3 mm [7, 18]. Most are less than 1-cm wide, and a characteristic echogenic fatty hilum is often visible (Fig. 14) [5]. Absence of a normal fatty nodal hilum implies infiltration by pathological cells, as seen in the settings of infection, inflammation and malignant spread of disease.

Skin mass

A skin mass is an intradermal lesion, most commonly in children representing either a pilomatricoma (benign neoplasm of hair matrix) or an epidermoid cyst (benign cyst lined by stratified squamous epithelium and containing keratin) [7, 18]. Pilomatricomas, although quite common in children, most often present on the head or neck and rarely present on the trunk or breasts. For any skin mass or cyst, US reveals a superficial round or oval well-circumscribed hypoechoic mass with low-level echoes and posterior acoustic enhancement (Fig. 15) [7, 18]. Pilomatricomas can contain calcifications, which are appreciable as hyperechoic foci with posterior shadowing [28]. When imaging any finding either within or

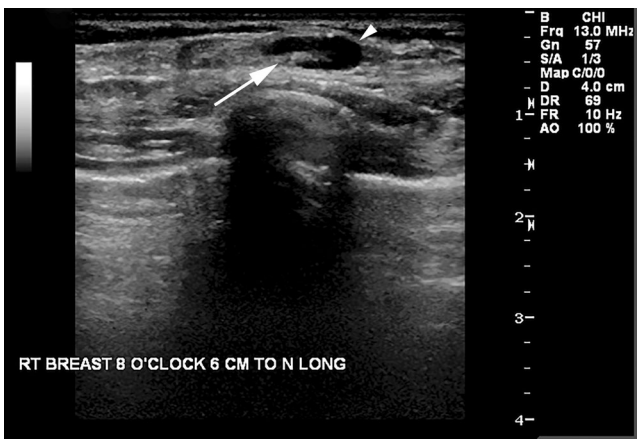

Fig. 14 Intramammary lymph node. Targeted breast US in an 18-year-old woman with palpable abnormality in the right breast shows a normal intramammary lymph node, characterized by hypoechoic cortex (*arrowhead*) and echogenic hilum (*arrow*)

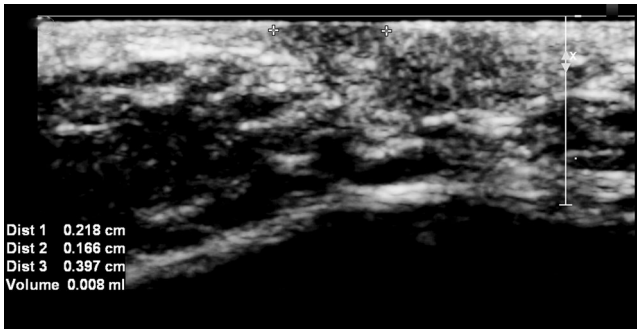

Fig. 15 Sebaceous cyst. Unilateral breast US in a 12-year-old boy with tender subcutaneous palpable nodule near the nipple shows a superficial, well-demarcated small hypoechoic structure at level of skin (marked by calipers), consistent with sebaceous cyst

closely associated with the skin, a standoff pad can be helpful to better define location and connection to skin surface [7]. An uncomplicated cyst is avascular, but if it is inflamed there might be considerable associated hyperemia [18]. The majority of skin findings are evident on clinical exam, but in equivocal cases, imaging can often definitively localize the mass within the skin. In general, biopsy should be avoided due to risk of severe inflammatory response if the cyst ruptures [18], with short-interval imaging follow-up favored for cases of likely but not definitive skin masses.

Malignant breast masses

Breast cancer is the leading cause of cancer in women and the leading cause of death in women age 35–50, but it is rare in girls and even more so in males [29]. Pediatric breast cancer accounts for less than 0.1% of breast cancers and less than 1% of childhood cancers [29, 30]. Disseminated hematological disease is the most common etiology for a malignant breast mass in a child. The malignant histological subtype of cystosarcoma phyllodes is the most common primary breast malignancy in children [3].

Metastatic disease

The most common cause of a malignant pediatric breast mass is hematological malignancy or metastasis, usually lymphoma/leukemia, rhabdomyosarcoma or neuroblastoma [1, 3]. Rhabdomyosarcoma, usually of the alveolar subtype, is the most common malignancy to metastasize to the breast, occurring in 6% of cases, but it rarely arises primarily in the breast [30, 31]. The female breast is more commonly involved by disseminated disease, but metastases also occur in the male breast [3].

The finding of multiple or bilateral masses might evoke suspicion for metastases; however, benign lesions such as fibroadenomas also present as multiple or bilateral [3]. US findings are variable, although metastases tend to be irregular and heterogeneously hypoechoic. Posterior acoustic shadowing or associated axillary adenopathy may be observed, suggesting a more ominous diagnosis [3]. Lymphadenopathy or chest wall invasion is sometimes present, especially in the case of lymphoma [3, 32].

It should be emphasized that although certain features suggest malignancy, any breast lesion in the presence of a known cancer should be deemed suspicious (Fig. 16). Regardless of whether the mass demonstrates a benign appearance, further evaluation with biopsy should be considered, because presence of breast metastases usually portends disseminated disease and a poor prognosis [2].

Cystosarcoma phyllodes

Cystosarcoma phyllodes, or simply phyllodes tumor, is a very rare type of fibroepithelial neoplasm and is the main differential consideration for fibroadenoma [3]. This mass can be categorized as benign, intermediate or malignant based on histology [33]. The malignant variety is rare and displays features of a low-grade spindle cell sarcoma (Fig. 16) [6, 20]. These masses are typically found in women in their fourth decade and account for less than 1% of pediatric breast masses [3]. Nonetheless, they are the most common cause of primary malignant breast mass in adolescents and have a 3% mortality rate [6, 30]. Although 85% of pediatric cases are benign, they rarely show invasion, metastasis and recurrence, and fatal cases have been reported [3, 34].

On US, phyllodes tumor is often indistinguishable from fibroadenoma. Typically phyllodes tumors are well-defined, oval masses that may have a lobulated border [6]. They commonly demonstrate heterogeneous or homogeneously hypoechoic echotexture with posterior acoustic enhancement [20]. Phyllodes tumors more commonly exhibit fluid-filled peripheral cysts or clefts than fibroadenomas; however, this feature is not pathognomonic [3, 6, 20]. Features that suggest phyllodes tumor and that should prompt core needle biopsy include rapid growth (Fig. 17) and the presence of intralesional cysts [1, 3, 20, 30, 33–35]. Solid masses larger than 6 cm are also suspicious and should undergo surgical excision [1, 3]. Because differentiating phyllodes tumor from fibroadenoma is so challenging because of the significant overlap in imaging appearances [3, 31, 35], this distinction can only be made with tissue sampling for histological evaluation [3, 33, 34]. Fine-needle aspiration might not be sufficient because the cytological features suggestive of phyllodes, such as hypercellular stromal fragments and multinucleated giant cells, are not specific enough to make a firm diagnosis [35, 36]. Instead, US-guided core needle biopsy should be used [1, 36]. Although there is the chance that core needle biopsy might only yield a pathological interpretation (e.g., fibroepithelial tumor, phyllodes tumor cannot be ruled out), practitioners at our institution prefer core needle biopsy over

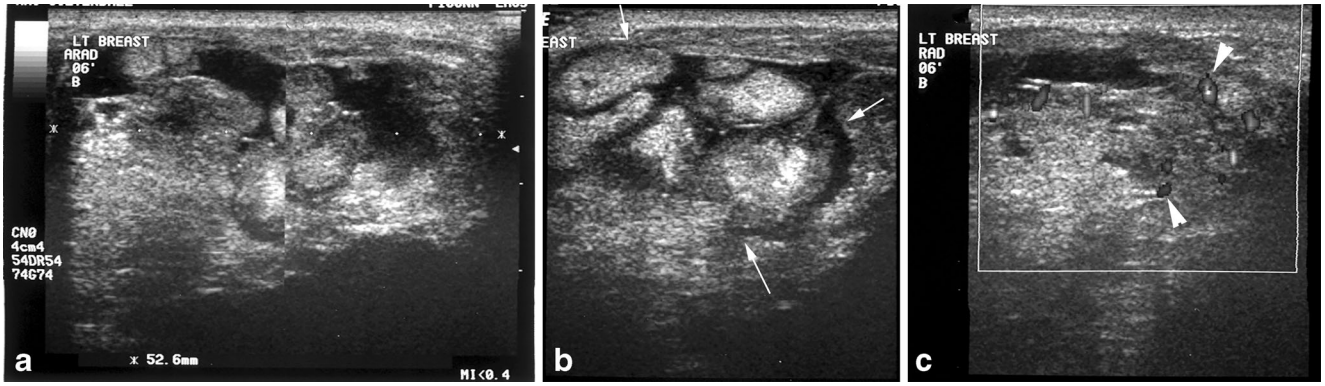

Fig. 16 Malignant sarcoma of the breast. Longitudinal (**a**) and transverse (**b**) unilateral breast US in a 13-year-old girl (same 13-year-old as Fig. 12) with palpable left breast mass and clinical history of Li–Fraumeni syndrome and strong family history of multiple tumor types shows a large (>5 cm, calipers in **a**), partly well-circumscribed (*arrows* in **b**), heterogeneous solid mass within the breast. **c** Color Doppler shows internal vascularity (*arrowheads*). Because of the large size of the mass and strong family history of cancer, mastectomy was performed. Pathology indicated malignant spindle cell sarcoma, thought to be an aggressive malignant phyllodes tumor

fine-needle aspiration and alert the interpreting pathologist to the diagnostic query so that specific features can be searched more effectively. Core needle biopsy in advance of planned surgical excision of a large, ovoid, well-demarcated breast mass may influence the surgical approach: if pathology yields a diagnosis of fibroadenoma, the surgeon might not attempt to obtain wide margins; however if the pathology indicates findings suspicious for phyllodes tumor, then the surgeon will plan for excision with wide margins.

Although long-term prognosis is favorable, local control of these tumors can be challenging — up to 20% of benign phyllodes tumors recur following complete excision [2]. Surgery is the mainstay of treatment, with the goal to excise with wide margins of at least 1–2 cm [34]. Metastasis is unusual but when it occurs hematogenous spread is usually to the lungs [3].

Primary breast carcinoma

Primary breast carcinoma is remarkably rare in the pediatric population, with an incidence of 0.03 cases per 100,000 people younger than 20 years [3]. There is a marked increase in prevalence after the age of 25 years [3]. A major risk factor is a history of cancer, particularly in people treated with chest wall radiation. Such cases are most frequently seen in girls who underwent mantle field radiation for Hodgkin disease. Such patients have a 75-fold higher risk for breast cancer than the general population, especially if treated between the ages of 10 and 16 years [1]. In such patients, the American College of Radiology recommends screening mammography 8–10 years after therapy completion (but not before the age of 25), and adjunct breast MRI screening [1, 37]. Familial cancer syndromes such as *BRCA1* and *BRCA2* may also elevate the risk [3].

Historically the literature has focused on secretory carcinoma as the main pediatric subtype of breast carcinoma. Originally this carcinoma was called "juvenile carcinoma" by McDivitt and Stewart [38] in 1966, described as an unusual subtype of breast cancer observed in seven children ranging 3–15 years old. It is now recognized that secretory carcinomas can occur in both children and adults [29]. Clinically these secretory carcinomas exhibit an indolent growth pattern and carry a favorable prognosis [29]. On histopathology tumor cells exhibit eosinophilic vacuolated cytoplasm and abundant mucinous secretion. Interestingly, a large study notes that secretory carcinoma accounts for only 10% of pediatric breast carcinoma, with infiltrating ductal carcinoma accounting for the majority of cases and carrying a worse prognosis [30].

Physical exam in children with primary breast cancer might reveal a painless, firm, poorly circumscribed mass [3, 37]. Characteristic US features include a heterogeneously hypoechoic, poorly circumscribed mass with irregular or microlobulated margins. Posterior acoustic shadowing and antiparallel orientation (in other words, taller than wide) are highly suspicious (Fig. 18) [3]. No sonographic features are known to reliably differentiate primary breast cancer subtypes.

Given the overall rarity of pediatric breast carcinoma, there is no treatment consensus, but most cases involve surgical excision, preferably breast-conserving surgery when feasible [39]. There are axillary metastases in 20–30% of cases, so some advocate for sampling of a sentinel lymph node for more accurate staging [29, 39, 40].

Imaging management

The overwhelming majority of lesions are benign, and thus breast masses are typically managed conservatively (Table 2). The imaging appearance in combination with key clinical features such as rate of growth, associated pain and other symptoms, and cancer history guide the course of action [1]. Careful US evaluation often allows one to categorize a lesion as benign and allows for US follow-up.

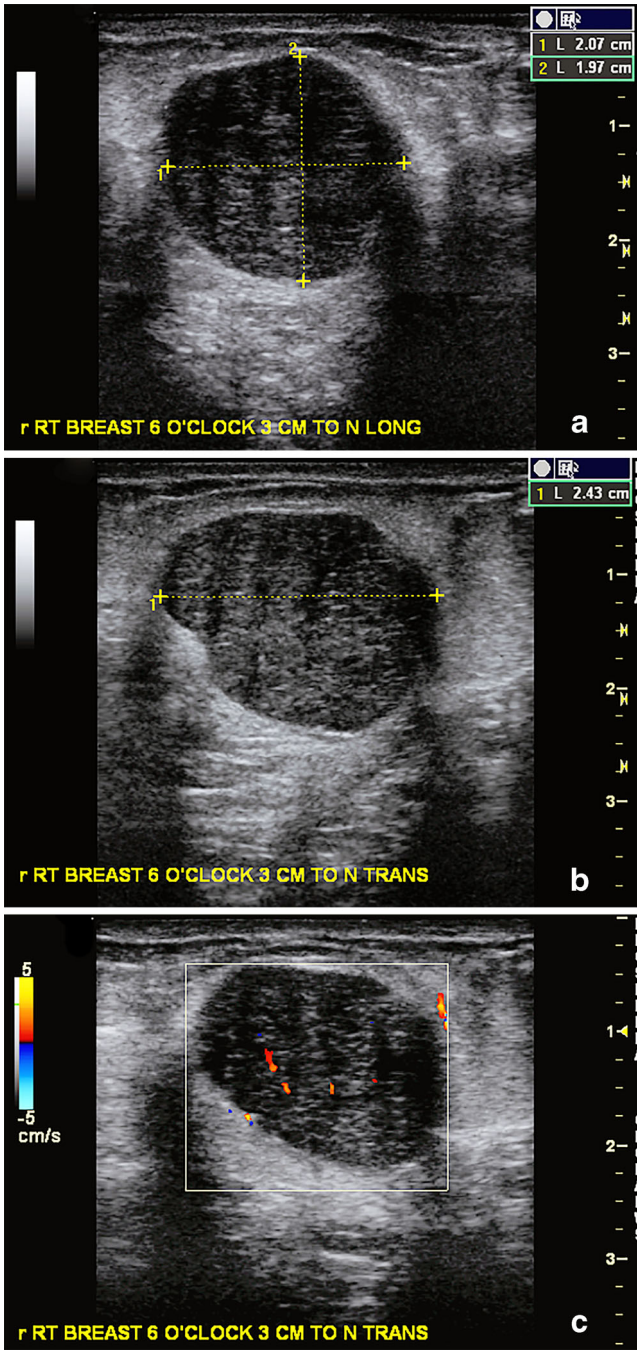

Fig. 17 Phyllodes tumor. US in a 17-year-old girl who presented with a palpable mass in the right breast; she said the mass had grown noticeably within the last month. **a** Gray-scale longitudinal and (**b**) transverse targeted US images demonstrate a well-demarcated, round hypoechoic solid mass measuring approximately 2×2×2.4 cm (*calipers*). **c** Color Doppler shows some internal vascularity. Because of the reported rapid growth the mass was sampled by core needle biopsy, which confirmed benign phyllodes tumor

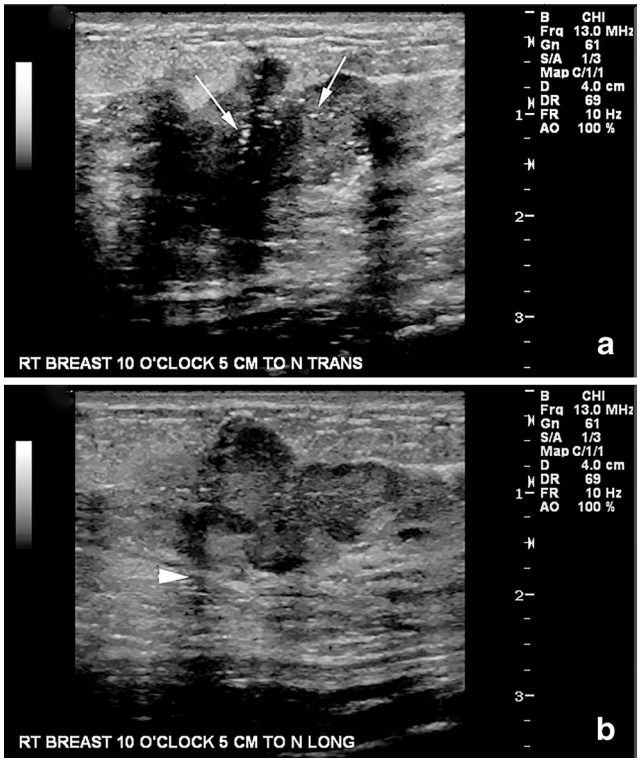

Fig. 18 Invasive breast carcinoma. US in a 22-year-old woman who presented with a palpable mass in the right breast. **a** Transverse and (**b**) sagittal targeted US images demonstrate an irregular-shape mass with angular and indistinct margins, calcifications (*arrows*) and posterior acoustic shadowing (*arrowhead*). A mammogram (not shown) demonstrated extensive microcalcifications within the right breast. Biopsy yielded invasive ductal carcinoma

Because of the considerable differences in breast diseases between children and adults, the American College of Radiology (ACR) BI-RADS® reporting system [41] is not routinely applied to pediatric cases. Imaging findings and impressions are conventionally descriptive and follow routine diagnostic imaging report formats. When the clinical exam and US findings are benign, reassurance should be offered [5]. Mass lesions presumed to be benign, however, do fulfill criteria for the BI-RADS® US category 3 (probably benign finding, with malignancy being highly unlikely) [41]. For this category, likelihood of malignancy is <2%, and the recommendation is short-term follow-up with US [25]. At our institution monitoring is performed over a 2-year period, with two 6-month US examinations the first year, followed by a 12-month interval US exam.

Although malignancy is rare, it does occur in children. Thus, when there are atypical features such as non-circumscribed margins, complex solid and cystic components, posterior acoustic shadowing, or a history of growth, prior chest radiation, known concurrent non-breast cancer or familial breast cancer, biopsy should be considered; core needle biopsy is favored to minimize the risk of affecting normal breast development [1, 25]. It is important to acknowledge that surgical management of solid breast masses in girls should be based on clinical findings, medical history and the patient and family's preferences; applying imaging criteria alone could result in unnecessary biopsies and surgical

excisions. However, any breast lesion in the presence of a known cancer history should be deemed suspect. Regardless of whether the mass demonstrates a benign appearance, further evaluation with biopsy should be considered in that clinical scenario.

Options for image-guided sampling of a mass include fine-needle aspiration and core needle biopsy, two techniques used with variable preference at different centers. Centers with expert cytologists who can be present at the time of a procedure and verify the sample is diagnostic might prefer to use fine-needle aspiration over core needle biopsy, arguing that needle aspiration is the less-invasive option. However core needle biopsy might have an advantage over fine-needle aspiration in the context of differentiating phyllodes tumor from fibroadenoma [36].

Conclusion

The approach to the pediatric breast mass differs from that in adults in differential diagnosis, imaging evaluation and management. It must be underscored that in children most lesions are benign and management is conservative. Knowledge of the normal breast anatomy, common pitfalls and common benign entities will allow the radiologist to comfortably characterize a lesion as benign. US is the backbone of the imaging evaluation, and although many benign masses appear similar on US, a specific tissue diagnosis is not usually necessary; short-interval US follow-up is commonly all that is required. The role of the radiologist is to provide reassurance to patients and clinicians in cases of masses that are caused by normal anatomy or physiology or are almost certainly benign, while also being able to recognize lesions with atypical findings that require further histopathological evaluation.

Conflicts of interest None

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