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Breast masses in children and adolescents – expect infrequent but possible diagnosis

Туморске масе дојке код деце и адолесцената – страх од ретке али могуће дијагнозе

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Breast masses in children and adolescents – expect infrequent but possible diagnosis

Туморске масе дојке код деце и адолесцената – страх од ретке али могуће дијагнозе

SUMMARY

Introduction/Objective Breast masses are uncommon in children and adolescents. Fortunately, most of these breast entities are benign, self-limiting changes, although malignant diseases have also been described. The largest percentage of young patients have a diagnosis of fibroadenomas. However, biopsy and histopathological diagnosis are necessary in all suspected cases to exclude malignancy.

The study aims to indicate the importance of diagnosis and treatment of breast masses as well as to indicate the possibility of the development of malignant breast disease at this age, by presenting our case.

Methods We analyzed data from 27 patients who applied to our Clinic in the two-year interval. Breast ultrasound was performed on all applicants experiencing pain and oedema of their breasts. The breast masses were classified using the Adult Breast Imaging-Reporting and Data System (BI-RADS).

Results The median age of the 27 female patients was 15.44±1.39 years, with breast masses mostly located on the right side in 16 (59.26%) patients, and the prevalence of BI-RADS III in 18 (66.66%) patients. Only 2 patients (7.4%) were reported as BI-RADS IV and 7 (25.92%) as BI-RADS II. The most common mass lesions were fibroadenoma (20/27, 74.07%), benign phyllodes tumour (3/27, 11.11%), and hematoma, abscess, and juvenile papillomatosis (1/27, 3.70%), respectively. Breast cancer was diagnosed in one case (3.7%).

Conclusion Primary breast cancer is relatively uncommon in adolescents. However, clinicians should consider breast cancer in the differential diagnosis of a breast mass in adolescence.

Keywords: breast mass; carcinoma; puberty; adolescents

САЖЕТАК

Увод/Циљ Туморске промене у дојкама су изузетно ретке код деце и адолесцената. Срећном, већина ових промена су бенигне и самолимитирајуће, мада су описане и малигне промене. У највећем проценту дијагностује се фиброаденом, мада је у свим сумњивим случајевима неопходна биопсија и хистопатолошка дијагноза у циљу искључивања малигнитета.

Циљ студије је указати на значај дијагнозе и третмана туморских маса дојке као могућност развоја малигнитета у овој узрастној групи, као што је презентовано у нашем случају.

Методе Анализирани су подаци 27 болесница које су хоспитализоване на Клиници и лечени у периоду од 2 године. Ултразвук је рађен код свих болесница са болом и отоком у пределу дојке. Класификовање промена у ткиву дојке вршено је коришћењем система радиолошке класификације промена на дојци [*Breast Imaging-Reporting and Data Sistem* (*BI-RADS*)].

Резултати Средња старосна доб 27 болесница износила је 15.44 ± 1.39 година, при чему је десностране промена дијагностикована код 16(59.26%), а учесталост промена класификованих као *BI-RADS* III код 18 (66,66%) болесница. Код 2 болеснице (7,4%) промене су одговарале стадијуму *BI-RADS* IV а код 7 (25,92%) *BI-RADS* II стадијуму. Патохистолошким прегледом највећа је учесталост фиброаденома (20/27, 74.07%), следи бенигни филоидни тумор (3/27, 11.11%), а потом хематом, апсцес и јувенилна папиломатоза код по 1 болеснице (1/27, 3,7%). Карцином дојке описан у једном случају (3,7%).

Закључак Примарни карцином дојке је веома редак ентитет код деце и адолесцената. Ипак, увек се мора диференцијално дијагностички размишљати о његовом постојању код све деце и адолесцената са туморским масама дијагностикованим у ткиву дојке.

Кључне речи: туморске промене; карцином; пубертет; адолесценти

INTRODUCTION

With a prevalence of 3.2%, breast masses are uncommon in children and adolescents. Fortunately, most breast entities that arise during this age group are benign, self-limiting changes, although malignant diseases have also been described. Ninety-five per cent of surgically removed breast masses in children are benign fibroadenomas, and only 0.02% are malignancies

[1, 2, 3]. The differential diagnosis of breast masses includes fibroadenomas, phyllodes tumours, hemangioma, fibroadenoma, abscess, and primary breast cancer. Early clinical evaluation and careful follow-up are necessary to rule out malignancy. A detailed history, clinical examination, and meticulous breast palpation are crucial in the follow-up for girls with all breast masses.

The best screening tool for characterising the breast entity and detecting the presence of solid and cystic masses in adolescent girls and teenagers without exposing them to radiation is ultrasound (US). A fixed solid mass with secretion and nipple retraction raises an intense fear of cancer. Mammography is rarely used in adolescents due to the dense nature of breasts, which significantly reduces the sensitivity of this examination. Fine needle aspiration can provide a pathological diagnosis. Magnetic resonance is the most reliable method in suspected malignancy or disseminated disease cases [4].

There have been 39 published cases of primary breast cancer in pediatric patients [2, 5]. Primary breast cancer is sporadic in children and adolescents, with a frequency of one in 1,000,000 [6]. Younger people are more likely to have a large mass at the time of breast cancer diagnosis, characterised as a firm, fixed, poorly limited lump. Breast retraction and axillary metastases are uncommon.

In patients with breast malignancy, an individual therapeutic concept is required. This principle is based on considering hereditary factors, future fertility, tumour type, and the presence of axillary and distant metastases. Surgical excision of a breast mass is recommended in the case of fast-growing masses with altered architecture of the breast parenchyma, as well as in tumours larger than 5 cm, even if they have fibroadenoma characteristics on ultrasound [6].

Aim

The study aimed to indicate the importance of timely diagnosis of breast mass in puberty and adolescence, as well as to indicate the frequency of development of malignant breast disease at this age. Consequently, the goal is to define the sequence of diagnostic procedures and therapeutic options.

METHODS

The 41 patents were identified by searching electronic records in the local medical information system using the terms "breast", "mass" and “female” within a two-year interval (January 2021-

December 2023), according to the requested terms, and all of them had at least 12 months of follow-up. Of these, 14 individuals were excluded from the study: 10 were diagnosed through clinical examination and the US, but there was no increase in breast mass over the 12-month follow-up period; therefore, the biopsy and histopathology (HP) examination were not performed, and 4 patients rejected the biopsy. Finally, 27 participants were enrolled in the study and analyzed.

An expert ultrasonographer performed all of the US exams. The patient was in the supine position, using high-resolution linear probes (16MHz) (ACUSON NX3 Siemens, Healthineers, Mountain View, CA). The radiologist examined the breast in four quadrants, the nipple and the axilla. In the case of detecting suspicious changes, several images were taken in different planes, and the exact location and size of the lesions were defined. After the completion of both bilateral examinations, the images were archived on the hard drive. The breast masses were classified using the Adult Breast Imaging-Reporting and Data System (BI-RADS) criteria established by the American College of Radiology (BI-RADS 0- incomplete, BI-RADS 1-negative, BI-RADS 2- benign, BI-RADS- probably benign, BI-RADS 4- 4-suspicious for malignancy, BI-RADS 5: highly suggestive of malignancy, BI-RADS 6: known biopsy-proven malignancy)

Statistical analysis

A database was generated in MS Office Excel (Microsoft, St.Redmond, WA, USA) and processed using IBM's SSPS software. Continuous variables are shown as means ± standard deviation (SD). Categorical variables were reported as simple numbers and percentages (n, %), with p-values ≤0.05 indicating statistical significance.

Ethics: The study received approval by the Institutional Review Board, of the Clinical/Hospital Centre Ethics Committee of Kosovska Mitrovica, Serbia on February 22, 2024, by (No. 1361).

RESULTS

The median age of 27 female patients was 15.44±1.39 years. The breast masses were mostly on the right side in 16(59.26%), with statistical significance (p ≤0.05), and prevalence of BI-RADS III in 18 (66.66%) (p ≤0.05). Additionally, only 2 patients (7.40%) were reported as BI-RADS IV and 7 (25.92%) as BI-RADS II (Table 1).

A total of 27 patients underwent breast mass excision, and excised tissue samples were sent for pathohistological (Ph) examination. Table 2. summarises the breast mass distribution based on age, size, side, Ph examination, and tumour type (benign or malignant).

Fibroadenomas (FA) were found in 20 (74.07%) patients, benign phyllodes tumour in 3 (11.11%), and hematoma, abscess, and juvenile papillomatosis in 1 patient (3.70%), respectively, which is of statistical significance ($p \leq 0.05$) (Table 3). Breast cancer was diagnosed in only one case (3.70%), in a 16-year-old girl.

A 16-year-old girl was admitted to the Department of Pediatric Surgery due to a palpable mass, swelling, and redness in the enlarged right breast. A huge breast mass was observed in the upper outer quadrant, with a venous drawing and lobulated surface, without secretion from the nipple (Figure 1). The girl was diagnosed with schizoaffective disorder, according to the International Classification of Diseases (ICD) M25.9, and had a very poor interaction with her guardians in the foster family. Because of this, she did not report a mass in her breast for months until it became visible to the people around her.

The skin above the tumour and lymph nodes in the anterior part of the right axilla was fixed. There was no family history of breast or ovarian cancer, nor had there been any previous radiation exposure. Secondary sexual features were normally developed. The findings in the left breast and axilla were normal. The ultrasound assessment of the abdomen, chest, endocranium, and spine revealed no changes.

Ultrasound examination revealed a hypoechogenic tumorous formation 81x98 mm, with irregular morphology, shape, unclear margins, increased rim vascularisation, and no calcifications. (BI-RADS IV). Ipsilateral axillary lymph nodes were enlarged up to 25 mm (Figure 2).

US examination of the contralateral breast as well as the entire abdomen was normal. Due to the high suspicion of malignancy by clinical and US examination, a needle biopsy was done. The specimen was sent for HP examination. The result of the pathohistological finding was ductal adenocarcinoma.

Immunohistochemistry was used to evaluate the expression of estrogen (ER) and progesterone receptors (PR). The tumour was ER and PR negative. Considering the type of tumour, age, and negative family history, a segmental mastectomy with axillary dissection was performed. The resection margins were clean, without malignant cells.

Histopathological examination confirmed ductal carcinoma with metastases in all 22 excised lymph nodes (Figure 3). On the seventh postoperative day, the patient was discharged home

and referred to the Breast Cancer Oncology Council, and chemotherapy was started. The patient was in good condition three months after the operation, but she had only one follow-up with the Pediatric Surgery Department, with no evidence of recurrence. When she was an adult (just 15 months after the surgery), she was admitted to General Surgery in a very poor condition with recurrence of the breast tumour. She died after a few days.

DISCUSSION

Breast changes are uncommon in young children and pubertal girls, but up to 3% of adolescents may develop a breast lesion before adulthood. When they occur, they are associated with tremendous stress for patients and family members.

Fibroadenoma (FA) is a benign lump formed by the proliferation of connective tissue stroma in the breast lobules. It accounts for 91% of all solid breast masses in girls under 19 [3, 4, 6], which completely correlates with the results of our study. Usually, these estrogen-sensitive tumours are not detected before puberty. FA can be simple or complex. Complex FA include cysts, sclerosing adenosis, and epithelial calcifications in the papillary regions. They are more common among older teenagers and adolescents with a slightly higher chance of developing breast cancer [7]. Usually, FA is clinically „silent" and manifested by accidental palpation of the tumour mass that is most often first noticed by the patient. If a clinical diagnosis of FA cannot be made, a US examination is required for additional study. It is a precise, non-invasive tool that does not require ionising radiation exposure. FA is a fast-developing tumour that distorts the surrounding skin. The presence of the breast mass can be extremely frustrating for children and parents, and the most common reason to insist on its surgical removal. Children's breast lesions are treated differently depending on the type of lesion, its size, location, features, and whether it is benign or malignant. If FA and other benign breast lesions in children are small, asymptomatic, and not expanding, ultrasound follow-up is sufficient [8]. When benign breast lesions are growing, causing pain or discomfort, or creating cosmetic issues, surgery is necessary, favouring excisional biopsy as a minimally invasive surgical approach that can be used to remove the lesion while protecting breast tissue [9]. According to recently released American Pediatric Surgical Association guidelines, low-risk breast lesions <5 cm that show ultrasound evidence of FA should be monitored only 6-12 months, since no chance of recurrence. and post-operative surveillance does not raise the risk of developing breast cancer again after complete excision [8].

Primary breast cancer under the age of eighteen is extremely uncommon in girls, with only cases found in boys reported in the literature [4].

Until the year 2000, Murphy described 38 cases of primary breast cancer in girls aged up to 19 years, while in the period 2000-2015, a total of 18 patients were recorded, of which the most common type was ductal breast cancer [11]. The literature has proven the existence of several risk factors that influence the development of breast cancer: a strong family predisposition (diagnosed breast cancer in a close female relative, mother, daughter, or sister), genetic mutations (BRCA1/BRCA2), or earlier radiation [12, 13]. Patients who receive radiation therapy for pediatric chest cancers are more likely to get breast cancer in the future. Breast tissue is most severely damaged by radiation therapy between the ages of 10 and 16, when it is developing to its fullest. After 20 years, about 40% of girls who received radiation therapy for Hodgkin's lymphoma and thyroid cancer may develop breast cancer. It has been proven that all types of ionising radiation, regardless of origin (both as part of radiation treatment for primary carcinoma and during wartime activities), can cause the development of secondary tumours [1, 14, 15, 16, 17].

The most prevalent primary breast cancer in children, secretory adenocarcinoma, was found in 31 out of 39 cases (84%) [18]. Secretory adenocarcinoma is presented as a well-defined cystic formation with a thickened capsule during ultrasound examination. The clinical characteristics of this tumour are significantly different in children compared to the adult population. Namely, the tumour shows benign clinical characteristics and prolonged growth, which, combined with the ultrasound findings, can mislead the clinician into believing it is benign [12].

Medullary and inflammatory carcinomas are far less common malignancies in children, but they are much more aggressive and have a higher mortality rate. Children with breast cancer rarely develop axillary metastases, as was the case with our patient. If axillary metastases are found, they seldom involve more than three lymph nodes in the axilla [19, 20].

Similar to adult breast modifications, benign cysts, phyllodes tumours, sarcoma, lymphangioma, hemangioma, intraductal papilloma, fibroadenoma, abscesses, metastatic malignancy, or galactocelae in young boys are all included in the differential diagnosis for pediatric breast alterations [21, 22]. In our study, two patients had breast masses unrelated to breast epithelium and fibrous tissue. One girl had a hematoma with a US presentation like BI-RADS III, while a 13-year-old girl with a breast mass on the left side presented in the US as BI-RADS II.

The diagnosis of breast cancer in children is usually delayed due to the non-specific clinical picture and the low degree of suspicion of malignancy. Therefore, medical history and clinical

evaluation are essential. As the first diagnostic tool, the US provides the best image for pediatric patients. According to the Expert Consensus Recommendations of the APSA Cancer Committee, fine needle biopsy (FNB) is essential for pathological diagnosis, for masses larger than 3 cm in diameter, and in all suspected cases [8], although most parents insist on removing tumour alterations even HP diagnosis is benign [23], as was in our case series. Mammography is not a sufficiently specific nor reliable method in children, due to the different composition of the breast parenchyma compared to the adult population [24]. Magnetic resonance imaging (MRI) excludes radiation in children, but the effectiveness and accuracy of breast MRI assessment in children are still not validated [25].

Wide local excision should be the initial treatment for all breast masses in prepubescent girls, and mastectomy should only be used if and when the cancer is diagnosed or has progressed. A modified radical mastectomy, followed by radiation and chemotherapy, is required in patients with advanced cancer and axillary metastases. Additionally, a sentinel lymph node sample must be performed [2, 26, 27, 28]. Postoperative radiation therapy reduces the risk of local recurrences. Consideration should be given to the advantages and disadvantages of radiation and chemotherapy in the context of the tumour type and the stage of the disease [14].

A lack of required screening, more severe disease, and a delayed diagnosis may all contribute to a poor prognosis in children and adolescents. A multidisciplinary team approach is recommended in order to optimize patient care for the rare malignant lesions [9].

CONCLUSION

Breast cancer should always be considered when making a differential diagnosis of breast nodules in prepubertal girls, teenagers, and adolescents. The most common imaging modality to determine the features of breast swelling is the US. Excisional biopsy and HP evaluation are mandatory to rule out atypical but possibly malignant lesions. The primary goal of surgical treatment is the complete excision of the tumour mass with the preservation of normal breast tissue if possible. The management of breast masses and breast cancer is still controversial, based on the limited data available in the literature, and larger series are required to standardise the treatment protocol in children. A multidisciplinary team approach is recommended in order to optimize patient care for the rare malignant lesions.

Conflicts of interest: None declared.

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Table 1. Distribution of breast masses by age, side, and BI-RADS classification

Age			Side		BI-RADS classification N (%)		
Years	N	%	Left N (%)	Right N (%)	II	III	IV
13	3	11.1	1 (3.7)	2 (7.4)	2 (7.4)	1 (3.7)	0
14	5	18.51	2 (7.4)	3 (11.11)	2 (7.4)	3 (11.11)	0
15	5	18.51	2 (7.4)	3 (11.11)	1 (3.7)	4 (14.81)	0
16	5	18.51	3 (11.11)	2 (7.4)	2 (7.4)	2 (7.4)	1 (3.7)
17	9	33.33	3 (11.11)	6 (29.62)	0	8 (29.62)	1 (3.7)
∑ 27,100			**11 (40.74)**	**16 (59.26)***	**7 (25.92)**	**18 (66.66)***	**2 (7.40)**
X ± SD 15.44 ± 1.39			p-values ≤ 0.05*		p-values ≤ 0.05*		

Table 2. The age, side, size, classification, HP diagnosis, and type of malignancy of all breast lesions in 27 female patients

No.	Age (years)	Side L/R	BI-RADS classification	Size (mm)	HP diagnosis	Tumor type
1	16	L	III	27 × 36	Fibroadenoma complex mammae	Benign
2	17	R	III	33 × 35	Fibroadenoma juvenile mammae	Benign
3	14	L	II	42 × 28	Fibroadenoma mammae	Benign
4	15	R	III	29 × 31	Fibroadenoma complex mammae	Benign
5	14	L	III	44 × 52	Haemathoma mammae	Benign
6	17	R	III	59 × 48	Tu phyllodes mammae benignum	Benign
7	17	R	III	53 × 32	Tu phyllodes mammae benignum	Benign
8	17	R	III	44 × 41	Fibroadenoma complex mammae	Benign
9	17	R	III	35 × 39	Fibroadenoma mammae	Benign
10	13	R	II	29 × 40	Fibroadenoma juvenile mammae	Benign
11	16	R	IV	81 × 98	**Carcinoma ductale mammae**	**Malignant**
12	15	R	III	21 × 23	Fibroadenoma juvenile mammae	Benign
13	14	R	III	19 × 22	Fibroadenoma juvenile mammae	Benign
14	16	L	II	18 × 23	Fibroadenoma juvenile mammae	Benign
15	14	R	II	21 × 22	Fibroadenoma mammae	Benign
16	13	R	III	30 × 32	Fibroadenoma mammae	Benign
17	15	L	III	18 × 22	Fibroadenoma mammae	Benign
18	17	L	III	34 × 24	Fibroadenoma mammae	Benign
19	17	L	IV	55 × 48	Juvenile papillomatosis	Benign
20	16	L	III	44 × 39	Fibroadenoma complex mammae	Benign
21	15	R	II	40 × 35	Fibroadenoma juvenile mammae	Benign
22	14	R	III	19 × 23	Fibroadenoma juvenile mammae	Benign
23	13	L	II	22 × 36	Abscessus mamme	Benign
24	15	L	III	32 × 26	Tu phyllodes mammae benignum	Benign
25	17	D	III	44 × 39	Fibroadenoma mammae	Benign
26	16	D	II	43 × 40	Fibroadenoma mammae	Benign
27	17	L	III	34 × 32	Fibroadenoma mammae	Benign

L – left; R – right; BI-RADS – Breast Imaging-Reporting and Data System; HP – histopathological diagnosis

Table 3. Distribution of the surgical patients according to tumor type

Tumor type	N	%
Fibroadenoma	20	74.07*
Phyllodes tumor	3	11.11
Hematoma	1	3.7
Abscess	1	3.7
Juvenile papillomatosis	1	3.7
Breast cancer	1	3.7
Σ	27	100

*$p \leq 0.05$

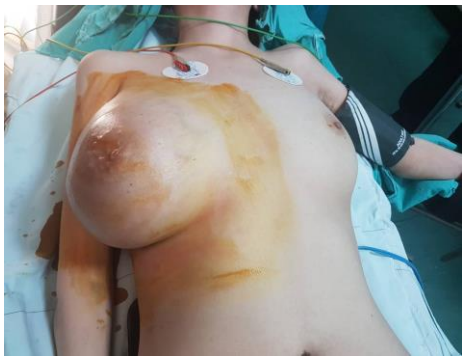

Figure 1. Clinical presentation of the breast mass in the right breast in a 16-year-old girl

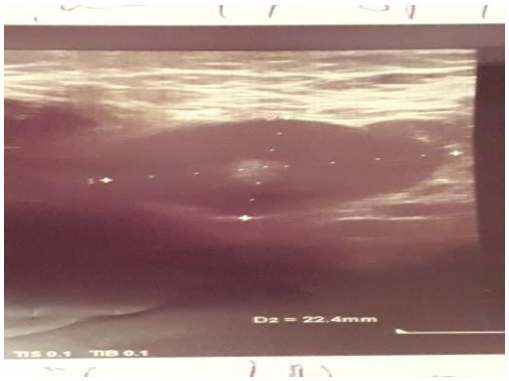

Figure 2. Ultrasound findings of the axilla – enlarged axillary lymph node.

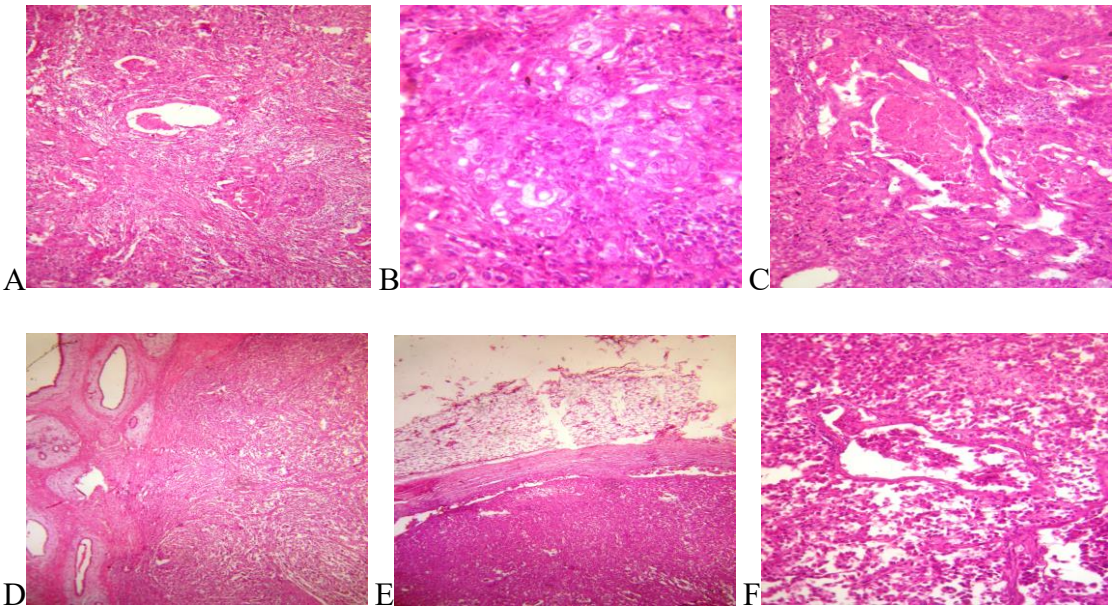

Figure 3. Histopathological findings; A: clusters of tumor cells in the stroma showing retraction, surrounding edema, and moderate mixed inflammatory infiltrate (H&E, 100 ×); **B**: marked pleomorphism of cells, irregular distribution of chromatin with prominent nucleoli (H&E, 200 ×); **C**: extensive zone of necrosis in the tumor parenchyma (H&E, 400 ×); **D**: border between preserved breast tissue and tumor-altered tissue (H&E, 400 ×); **E**: lymph node parenchyma almost completely replaced by metastatic tumor tissue with spread into the node capsule, without perinodal tissue invasion (H&E, 200 ×); **F**: lymphovascular invasion (H&E, 200 ×)

