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ORIGINAL ARTICLE / ОРИГИНАЛНИ РАД

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

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SUMMARY

Introduction/Objective Breast masses are uncommon in children and adolescents. Fortunately, most of these breast lesions are benign, self-limiting changes, although malignant diseases have also been described. The largest proportion of young patients are diagnosed with fibroadenoma. However, biopsy and histopathological examination are necessary in all suspected cases to exclude malignancy.
This study aims to highlight the importance of the diagnosis and treatment of breast masses, as well as the possibility of developing malignant breast disease at this age, by presenting our case.

Methods We analyzed data from 27 patients who presented to our clinic in the two-year period. Breast ultrasound was performed on all patients presenting with pain and breast oedema. The breast masses were classified using the 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 two patients (7.4%) were reported as BI-RADS IV and seven (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, 3.7%), 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

INTRODUCTION

With a prevalence of 3.2%, breast masses are uncommon in children and adolescents. Fortunately, most breast lesions that arise in 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 fibroadenoma, phyllodes tumor, hemangioma, 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 breast masses.

The best screening tool for characterizing the breast lesion 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 nipple discharge and nipple retraction raises significant concern for 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 (FNA) can provide a cytopathological diagnosis. Magnetic resonance imaging (MRI) is the most reliable method for 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 patients are more likely to have a large mass at the time of breast cancer diagnosis, characterized as a firm, fixed, poorly defined lump. Breast retraction and axillary metastases are uncommon.

In patients with breast malignancy, an individualized therapeutic plan is required. This principle is based on considering hereditary factors, future fertility, tumor 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 tumors larger than 5 cm, even if they have fibroadenoma characteristics on US [6].

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Aim

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

METHODS

The 41 patients 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 US, but there was no increase in breast mass over the 12-month follow-up period; therefore, biopsy and histopathological (HP) examinations were not performed, and four patients rejected the biopsy. Finally, 27 participants were enrolled in the study and analyzed.

An expert ultrasonographer performed all US examinations. Patients were in the supine position, using high-resolution linear probes (16 MHz) (ACUSON NX3, Siemens, Healthineers, Mountain View, CA, USA). The radiologist examined the breast in four quadrants, the nipple, and the axilla. When suspicious changes were detected, several images were taken in different planes, and the exact location and size of the lesions were defined. After the completion of bilateral examinations, the images were archived on the hard drive. The breast masses were classified using the 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 3: probably benign; BI-RADS 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, Redmond, WA, USA) and processed using IBM SPSS Statistics software (IBM Corp., Armonk, NY, USA). 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 from the Review Board of the Kosovska Mitrovica Clinical-Hospital Centre Ethics Committee, Kosovska Mitrovica, Serbia, on February 22, 2024 (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 a prevalence of BI-RADS III in 18 (66.66%) (p ≤ 0.05). Additionally, only two patients (7.4%) were reported as BI-RADS IV and seven (25.92%) as BI-RADS II (Table 1).

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)
Σ 27,100			**11 (40.74)**	**16 (59.26)***	**7 (25.92)**	**18 (66.66)***	**2 (7.4)**
X ± SD 15.44 ± 1.39			p-values ≤ 0.05*		p-values ≤ 0.05*		

BI-RADS – Breast Imaging Reporting and Data System

A total of 27 patients underwent breast mass excision, and excised tissue samples were sent for HP examination. Table 2 summarizes the breast mass distribution based on age, size, side, HP examination, and tumor type (benign or malignant). Fibroadenomas (FA) were found in 20 (74.07%) patients, benign phyllodes tumor in 3 (11.11%), and hematoma, abscess, and juvenile papillomatosis in one patient (3.7%), respectively, which was statistically significant (p ≤ 0.05) (Table 3). Breast cancer was diagnosed in only one case (3.7%), 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 prominent venous pattern and lobulated surface, without nipple discharge from the nipple (Figure 1). The girl was diagnosed with schizoaffective disorder, according to the International Classification of Diseases (ICD) ICD-10 F25.9, 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 tumor and lymph nodes in the anterior part of the right axilla were 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, cranium, and spine revealed no abnormalities.

Ultrasound examination revealed a hypoechogenic tumorous formation 81 × 98 mm, with irregular morphology and shape, unclear margins, increased rim vascularization, and no calcifications (BI-RADS IV). Ipsilateral axillary lymph nodes were enlarged up to 25 mm (Figure 2).

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; Ph – pathophysiological

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

*$p \leq 0.05$

US examination of the contralateral breast, as well as the entire abdomen, was normal. Due to the high suspicion of malignancy on clinical and US examination, a core-needle biopsy was performed. 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 tumor was ER- and PR-negative. Considering the type of tumor, 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. Fifteen months after the surgery, by which time she had reached adulthood, the patient was admitted to General Surgery in a very poor condition with recurrence of the breast tumor. 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.

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 tumors 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 tumor 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 ionizing radiation exposure. FA is a fast-developing tumor 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, favoring 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 there is no chance of recurrence. Postoperative surveillance does not raise the risk of developing breast cancer again after complete excision [8].

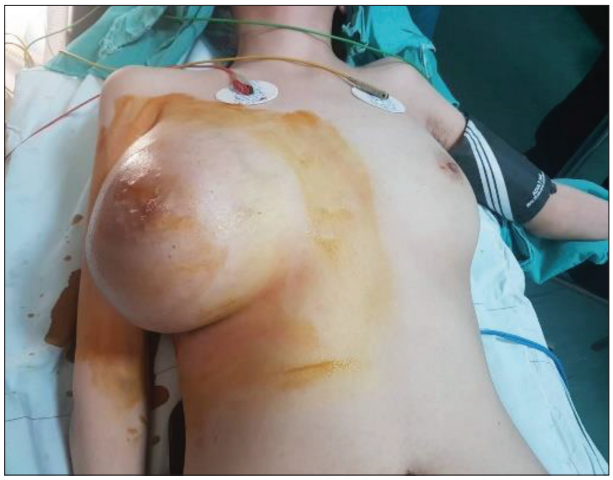

Figure 1. Clinical presentation of the breast mass in the right breast in a 16-year-old girl

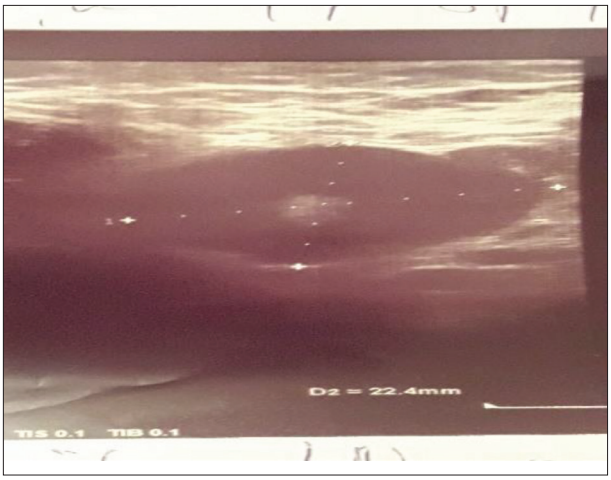

Figure 2. Ultrasound findings of the axilla – enlarged axillary lymph node

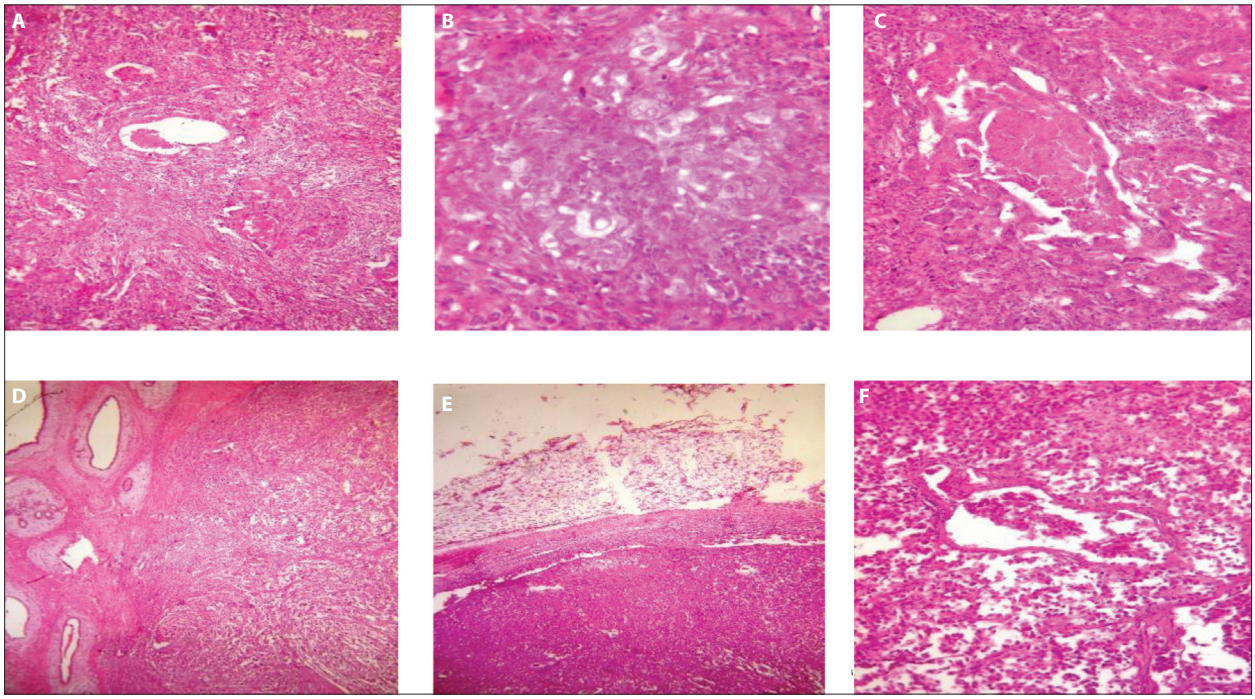

Figure 3. Histopathological findings; **A**: clusters of tumor cells in the stroma showing retraction, surrounding edema, and moderate mixed inflammatory infiltrate (H&E, 100 ×); **B**: marked pleomorphism of cells, irregular distribution of chromatin with prominent nucleoli (H&E, 200 ×); **C**: extensive 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 ×)

Primary breast cancer under the age of 18 is extremely uncommon in girls, with only cases in boys also reported in the literature [4].

Until the year 2000, Murphy et al. [11] 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. 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 ionizing radiation, regardless of origin (both as part of radiation treatment for primary carcinoma and during wartime activities), can cause the development of secondary tumors [1, 14–17].

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 tumor are significantly different in children compared to the adult population. Namely, the tumor 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 pathologies, benign cysts, phyllodes tumors, sarcoma, lymphangioma, hemangioma, intraductal papilloma, fibroadenoma, abscesses, metastatic malignancy, or galactoceles 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 consistent with 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, FNA 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 tumor alterations even if the HP diagnosis is benign [23], as was in our case series. Mammography is not a sufficiently specific or reliable method in children, due to the different composition of the breast parenchyma compared to the adult population [24]. MRI avoids ionizing radiation in children, but the effectiveness and accuracy of breast MRI assessment in children have not yet been 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 biopsy must be performed. 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 tumor 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 tumor 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 standardize 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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Туморске масе дојке код деце и адолесцената – страх од ретке али могуће дијагнозе

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САЖЕТАК

Увод/Циљ Туморске промене у дојкама су изузетно ретке код деце и адолесцената. Срећом, већина ових промена су бенигне и самолимитирајуће, иако су у литератури описани и случајеви малигних промена. У највећем проценту дијагностикује се фиброаденом, али је у свим сумњивим случајевима неопходна биопсија и хистопатолошка анализа ради искључивања малигнитета.

Циљ студије је указати на значај дијагностике и третмана туморских маса у дојкама, имајући у виду могућност развоја малигнитета у овој узрастној групи, као што је приказано у нашем случају.

Методе Анализирани су подаци 27 болесница које су хоспитализоване на Клиници и лечене у периоду од две године. Код свих болесница са болом и отоком у пределу дојке урађен је ултразвучни преглед. 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. Десностране промене дијагностиковане су код 16 (59,26%) болесница, а промене класификоване као *BI-RADS* III код 18 (66,66%) болесница. Код две болеснице (7,4%) промене су одговарале стадијуму *BI-RADS* IV, а код седам (25,92%) стадијуму *BI-RADS* II. Патохистолошком анализом утврђено је да је највећа учесталост фиброаденома (20/27, 74,07%), следи бенигни филоидни тумор (3/27, 11,11%), а потом хематом, апсцес и јувенилна папиломатоза код по једне болеснице (1/27, 3,7%). Карцином дојке описан је у једном случају (3,7%).

Закључак Примарни карцином дојке је веома редак код деце и адолесцената. Ипак, увек се мора размишљати о његовом постојању у оквиру диференцијалне дијагнозе туморских маса у ткиву дојке код болесница овог узраста.

Кључне речи: туморске промене; карцином; пубертет; адолесценти