International Journal of Research in Medical Sciences
Çeliker FB et al. Int J Res Med Sci. 2017 Nov;5(11):4708-4714
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012
DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20174920

Original Research Article

Comparison of ultrasound, mammography and histopathology findings of the cases with gynecomastia

Fatma Beyazal Çeliker[1]*, Ercan Inci[2], Nurten Sever[3], Ahmet Tan Cimilli[4], Arzu Turan[1]

[1]Department of Radiology, Faculty of Medicine, Recep Tayyip Erdoğan University, Rize, Turkey
[2]Department of Radiology, [3]Department of Pathology, Bakırköy Dr. Sadi Konuk Training and Research Hospital, İstanbul, Turkey
[4]Department of Radiology, Bağcılar Training and Research Hospital, İstanbul, Turkey

Received: 09 September 2017
Accepted: 06 October 2017

***Correspondence:**
Dr. Fatma Beyazal Çeliker,
E-mail: fabece@yahoo.com

ABSTRACT

Background: Gynecomastia is the development of a fibroepithelial structure in the male breast as a result of many benign and malignant effects. In this study, after the confirmation of gynecomastia diagnosis in the male cases with swelling, mass and tenderness in the breast using ultrasound and mammography examinations, its etiology was clarified by laboratory tests. In case of suspicion, the diagnosis was confirmed using Fine-Needle Aspiration Biopsy (FNAB). The adequacy of ultrasound and mammography was discussed with the obtained information and the information in the literature, and the etiological and radiological classification was done.
Methods: Ultrasound and mammography examinations were performed on 74 male patients with growth, palpable masses or pain in the breast. Biochemistry and hormone analysis were performed with imaging methods in the cases of possible gynecomastia. Biopsy was performed on the cases with the suspicion.
Results: Gynecomastia were divided into three types in ultrasonic and mammographic examination. The most frequent gynecomastia was observed as Type 3 (51.43%) in ultrasonic examination and as diffuse type (61.42%) in mammographic examination. Pain and tenderness accompanied with swelling at the breast were present in 37.84% of the cases. 31.42% had pubertal gynecomastia, 25.71% had gynecomastia secondary to drug use, and 15% had idiopathic gynecomastia.
Conclusions: Combined use of ultrasound and mammography in the diagnosis and classification of gynecomastia is highly sufficient and biopsy should be performed if malignancy is suspected.

Keywords: Gynecomastia, Mammography, Ultrasound

INTRODUCTION

Gynecomastia was first described by Basedow in 1848; and can be defined as the development of fibroepithelial structures in the male breast with the influence of various factors. Gynecomastia affects ductal structures and the stroma, and lobules are rarely found.[1] Gynecomastia is a symptom rather than a disease, and may develop as a result of physiological changes, diseases, tumors and some medications. However, the main mechanism is the increased estrogen stimulation. Male breast lesions other than gynecomastia, can be classified as breast cancer, lipoma, fat necrosis, lymph nodes, inclusion cyst, subcutaneous leiomyoma and sub areolar abscess.

While the diagnosis of these lesions is partly possible with the clinical examination, combined use of ultrasound and mammography in the differential diagnosis provides high diagnostic accuracy. In this study, we made the diagnosis and classification and also etiologic classification of gynecomastia.

METHODS

Seventy-four male patients aged between 10-94 years (40.9+/-22), who were clinically diagnosed with growth, mass and/or tenderness in breast, were included in the study. Ultrasound (US) and mammography examinations were performed in all cases. The mammograms were taken in the mediolateral oblique (MLO) position. Ultrasound and mammography were evaluated by two different radiologists.

According to their ultrasonic appearance, the gynecomastia was divided into three types as hypoechoic area in retro areolar region (Type 1), hypoechoic area surrounded by hyperechoic zone (Type 2), mixed echo pattern with hyperechoic-hypoechoic areas (Type 3) at different ratios. Mammographic appearances were classified as dendritic, nodular, and diffuse. Liver, kidney, thyroid function tests, estrogen, testosterone, prolactin, FSH, LH, TSH hormone analysis were performed for the etiology on the cases with the suspected gynecomastia. Drug use history, presence of congenital or chronic illness, exposure to major trauma and radiation, and eating habits were questioned.

According to the results of the laboratory tests, further tests such as testis and abdomen ultrasound, thorax CT and cranial MR were added. Findings that could lead to gynecomastia were researched. Fine-Needle Aspiration Biopsy (FNAB) was made to the suspected cases. Gynecomastia was classified as radiological and etiologic under the light of the obtained data. The data were analyzed by SPSS (Statistical Package for Social Sciences), version 10.0 for Windows (IBM/SPSS Inc. Chicago/IL, USA). Ki-square and ANOVA were used for the comparison of the data and $p<0.05$ was accepted significance.

This study has been approved by the Ethics Committee of Dr. Sadi Konuk Training and Research Hospital and informed consents of the patients were obtained from their parents or legal representatives.

RESULTS

Symptoms were often in the form of breast tenderness, breast enlargement or mass. Pain or tenderness accompanied breast enlargement in 28 patients. On ultrasonic examination, 20 cases (28.57%) were evaluated as Type 1, 14 cases (20.00%) as Type 2, and 36 cases (51.43%) as Type 3. On mammographic examination, 8 cases (11.43%) were evaluated as dentritic, 16 cases (22.86%) as nodular and 43 cases (61.42%) as diffuse type (Figure 1-5). On mammographic examination of 3 cases (4.29%), suspicious density enhancement for gynecomastia in retro areolar area was observed and gynecomastia diagnosis was confirmed in these cases by with fine needle aspiration biopsy. Although clinically unilateral breast enlargement was present in 5 cases (7.14%), bilateral gynecomastia was detected on mammographic examination. Not to be able to clinically be detected was attributed to gynecomastia being asymmetric and fresh onset in the other breast.

Table 1a: LH, FSH, prolactin levels between age groups; there is no statistically significant difference. p>0.05.

Age group	<=25		26-50		51 and over			
	N	%	N	%	N	%	X^2	P
LH								
1	26	92.9	15	100.0	28	90.3		
2	1	3.6			3	9.7		
3	1	3.6					-	-
FSH								
1	28	100.0	15	100.0	28	90.3		
2					3	9.7	4.33	0.114
Prolactin								
1	28	100.0	15	100.0	31	100.0	-	-

In 10 (14.28%) cases, clinically bilateral asymmetric gynecomastia was present and there was pain and tenderness in the bigger breast. Although there were suspicious findings for gynecomastia in 1 case (1.35%) with painful breast enlargement and 3 cases with painless breast enlargement (4.05%) on ultrasonic examination, a homogenous radiolucent area compatible with adipomastia (increase in fibrous tissue-free fatty tissue) was observed on mammography. 18 patients (25.72%) were clinically and radiologically symmetric. Symmetric gynecomastia was classified as 9 (12.85%) diffuse, 4 (5.71%) nodular and 5 (7.14%) dendritic types. Fine-needle aspiration biopsy accompanied by ultrasound was performed on 15 patients suspected to be hypoechoic on sonographic examination and diffuse type on mammographic examination, and surgical resection was performed on 6 cases.

Table 1b: TSH, estradiol and testosterone levels between age groups; there is no statistically significant difference. p>0.05.

Age group	<=25		26-50		51 and over			
	N	%	N	%	N	%	X^2	P
TSH								
1	28	100.0	15	100.0	31	100.0	-	-
Estradiol								
1	25	89.3	13	86.7	27	87.1		
2	3	10.7	2	13.3	4	12.9	0.09	0.956
Testosterone								
1	26	92.9	15	100.0	30	96.8		
3	2	7.1			1	3.2	1.37	0.503

Table 1c: Diabetes between age groups; there is no statistically significant difference. p>0.05.

Age group	<=25		26-50		51 and over			
	N	%	N	%	N	%	X^2	P
Diabetes mellitus								
Type 2 diabetes					1	3.2		
Normal	28	100.0	15	100.0	30	96.8	1.40	0.495

Table 1d: Lung tumors between age groups; there is no statistically significant difference. p>0.05.

Age group	<=25		26-50		51 and over			
	N	%	N	%	N	%	X^2	P
Lung tumor								
With lung tumor					4	12,9		
No lung tumor	28	100,0	15	100,0	27	87,1	5,86	0,053

Table 2a: Right and left side ultrasonography findings between age groups; there is no statistically significant difference. p>0.05.

	<=25		26-50		51 And Over		
Ultrasonography	**Average**	**SS**	**Average**	**SS**	**Average**	**SS**	**P**
Right	29.21	10.20	28.33	14.86	28.45	10.65	0.958
Left	29.50	12.06	31.33	16.24	28.77	10.13	0.803

Table 2b: Right and left side mammography findings between age groups; there is no statistically significant differences. p>0.05.

Mammography	<=25		26-50		51 and over		
	Average	**SS**	**Average**	**SS**	**Average**	**SS**	**P**
Right	26.36	8.38	26.33	9.90	24.55	8.77	0.691
Left	25.54	9.09	28.67	12.34	27.16	8.51	0.581

Table 3: Mammography density findings between age groups; there is no statistically significant difference. p>0.05.

	<=25		26-50		51 And Over		
Mammography density	**Average**	**SS**	**Average**	**SS**	**Average**	**SS**	**P**
Right	29.93	11.00	35.00	12.98	32.29	12.31	0.412
Left	31.29	11.84	32.00	14.14	31.61	9.79	0.981

Table 4: Clinical findings between age groups; there is no statistically significant difference. p>0.05.

Age group	<=25		26-50		51 and over			
	N	%	N	%	N	%	X^2	P
Clinically								
No pain	23	82.1	6	40.0	9	29.0		
Pain and tenderness	5	17.9	9	60.0	22	71.0	17.58	0.000

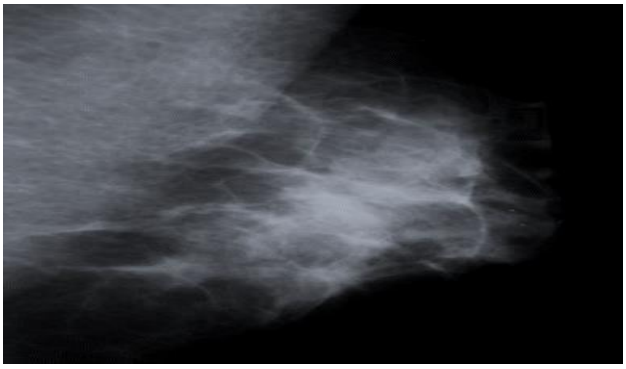

Figure 1: 17-year-old male patient with unilateral diffuse gynecomastia. Tenderness and asymmetrical growth on the left breast.

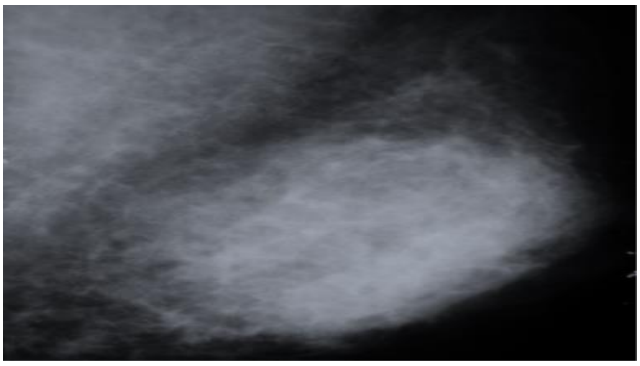

Figure 2: 55-year-old male patient. Painful growth on the left breast. Unilateral nodular gynecomastia.

Figure 3: 34-year-old male patient. Painful growth on the right breast. Unilateral dendritic type gynecomastia.

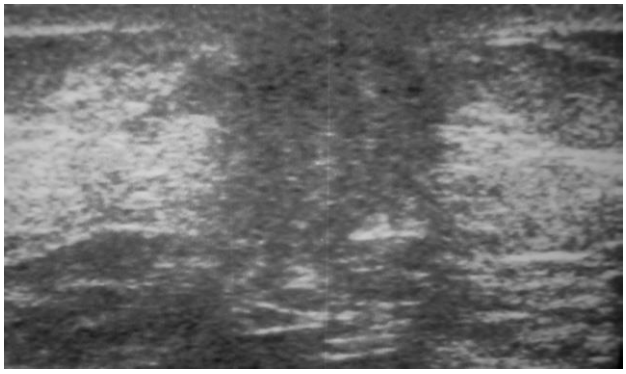

Figure 4: 55-year-old male patient breast sonography; appearance of hypoechoic surrounded by hyperechoic area (mixed type gynecomastia).

These cases were diagnosed cytologically and histologically as gynecomastia. Gynecomastia cases were compared with literature according to etiologic factors. There was no statistically significant difference according to age, mammographic appearance and etiologic factors.

DISCUSSION

Normal male breast consists of several rudiment secretory ducts, connective tissue and oil. On mammography, normal male breast is observed as a few linear densities of connective tissue, cooper ligament and ductal elements extending from the breast to the periphery in the radiolucent areas of fatty tissue.[2]

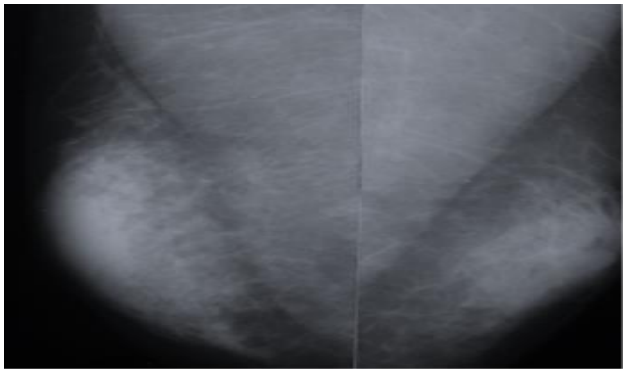

Figure 5a: 22-year-old male patient. Painful growth on bilateral breast. Bilateral symmetrical and diffuse type gynecomastia.

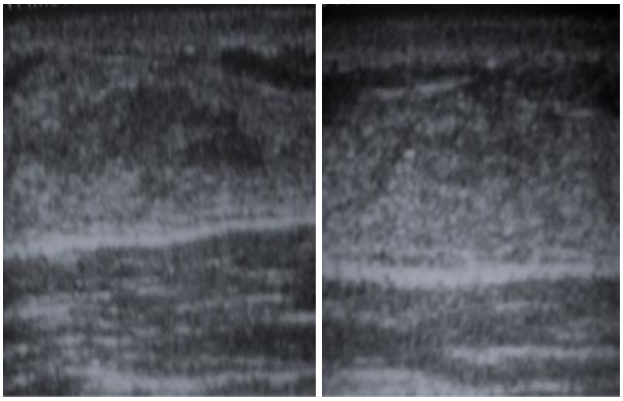

Figure 5b: Bilateral mixt type gynecomastia on the breast sonography of the same patient.

In gynecomastia, there is proliferation of stromal structures and hyperplasia of ductal structures with hypervascularity. The proliferation of stromal and ductal structures is characterized by diffuse localized intraductal epithelial hyperplasia at the early stage. In the late period, cellular stroma increase and hyalinization are seen. Many physiological and pathological conditions can cause gynecomastia. Physiological gynecomastia is seen in neonatal, pubertal and old age. Pubertal gynecomastia is the most common form of physiological gynecomastia. Mahoney explained pubertal gynecomastia with the increase in the conversion of adrenal androgens to estrogens in peripheral tissues while the production of testosterone is still low.[2] In our study, there were 23 (31.42%) pubertal gynecomastia. Many diseases that alter the ratio of estrogen/androgen in favor of estrogen may cause gynecomastia. If estrogen is at a high level, estrogen-producing malignancy should be considered first. Testicular neoplasms are the most common tumors that produce estrogen. Serum beta-HCG is frequently elevated in these tumors. Gynecomastia development is explained by increased estrogen/androgen ratio due to chorionic gonadotropin stimulation.[3] In our study, we studied 3 testicular neoplasms radiologically. Apart from this, we detected testicular microlithiasis in 5 (7.14%) cases (Figure 6).

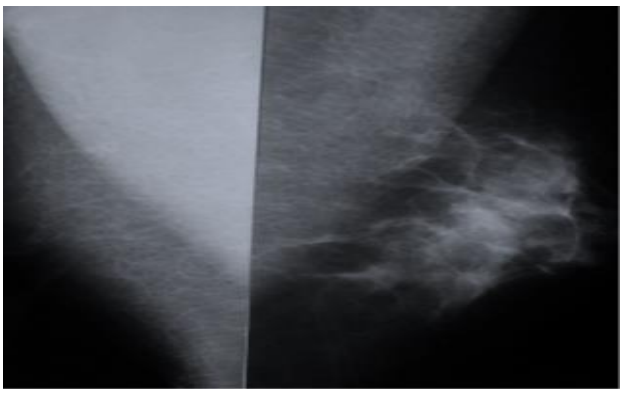

Figure 6a: 27-year-old male patient. Pain on bilateral breast, growth on the left breast. Left breast normal, diffuse type gynecomastia on the left breast.

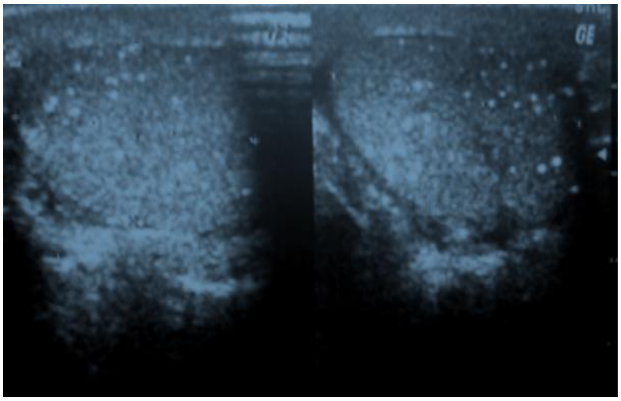

Figure 6b: Testicular microlithiazis in scrotal sonography of the same patient.

These cases were young age groups. Hormone analysis was found normal in these cases. The cases were followed up with sonographic follow-up for possible testicular cancer. No progression was detected after two-year testis sonography follow-up. We did not find any association between testicular microlithiasis and gynecomastia in the literature. Surrenal-derived tumors secrete high amounts of steroid precursors and become the source of estrogen conversion. In one study, 52 patients with adrenal tumors were reported to have gynecomastia at the rate of 98%.[4] Adrenal pathology was not detected in our study.

In lung cancer, gynecomastia may develop due to beta-HCG production of the tumor. A 62-year-old patient (1.4%) in our study had gynecomastia with small-cell carcinoma in the lung. In our three cases, we detected central squamous cell lung cancer. However, in these cases, the laboratory findings were within normal limits and were taken into simultaneous idiopathic gynecomastia classification.

Galactorrhea and gynecomastia may develop in the presence of hyperprolactinemia. The prolactin level was high in 2 (2.85%) of our patients with nodular type gynecomastia. After 3 months of medical treatment, prolactin level returned to normal and gynecomastia was markedly regressed in these cases where no pathology was detected in the MR examination for hypophysis. This response to treatment was found to be consistent with early phase gynecomastia.[5]

Many drugs can cause gynecomastia.[6] In our study, chemotherapy was used in 1 case, digital glycosides in 15 cases, antidepressant in 1 case, drug use in 1 case of psoriasis. In some of the cases during follow-up, gynecomastia was observed to have declined decline in size after the drug was released. The number of gynecomastia developed due to drug use was found 18 (25.71%).

Gynecomastia may develop in liver and kidney failure. In our study, liver function was insufficient in 8 (11.47%)

cases. Renal failure was detected in four (5.71%) cases. Rarely, prisoners can get gynecomastia after bad diet. We found that gynecomastia developed in one (1.42%) of our patients after returning to normal weight after an excessive weight loss after a hunger strike. There was no significant change between age groups in laboratory findings of the patients with gynecomastia (Table 1a-d).

Clinically, gynecomastia is palpated as soft, mobile mass or diffuse breast growth in the retro areolar area. It is usually bilateral. However, in our study, there were 28 (40.00%) bilateral and 42 (60.00%) unilateral gynecomastia. In contrast to the literature, gynecomastia was frequently unilateral in our study and no statistically significant difference was observed when it was correlated with the age groups in terms of right and left side localization (Table 2a-b).

Early mammographic finding of gynecomastia is the appearance of ductal structures in the sub areolar area. As the disease progresses, it is an increased density in the sub areolar area or most of the breast.[7] In our study, no significant difference was observed when density differences in the mammograms were correlated with age groups (Table 3). The appearance can be homogeneous and nonhomogeneous. According to their mammographic appearance, gynecomastia is divided into three types, recognition of these typing facilitating differential diagnosis, but gynecomastia may mask cancer in the presence of diffuse increased density.[8] In our study, gynecomastia was diagnosed in 67 (95.72%) cases using mammographic classification. Gynecomastia may be painful and tender.[6] Pain and tenderness were expressed by 36 (48.64%) of the cases (Table 4).

Ultrasound is a complementary method to mammography in male breast. Hypoechoic fatty tissue can be seen between the pectoral muscle and the skin in the normal male breast.[9] According to the type of gynecomastia, three characteristic sonographic patterns (retro areolar hypoechoic, hypoechoic center surrounded with hyperechoic area and mixed echo), formed by varying processes from glandular hyperplasia to diffuse fibrotic proliferation, have been described.[10,11] Rarely, early stage carcinoma, gynecomastia, and pseudogynechoastin are difficult to distinguish in ultrasound. All three are hypoechoic. In our study, gynecomastia was observed in 20 of 25 cases who were followed hypoechoic in the ultrasound in mammographic correlation and pseudogenesomastia in 4 cases and were pathologically confirmed.

Male breast cancer is clinically palpable in the form of a rigid, fixed mass. Bloody or serous nipple discharge, nipple retraction, deep thickening and pathological axes may be accompanied by lymphadenopathies. However, these findings are not specific for cancer.[12] In a study conducted by Evans et al., nipple retraction was reported in 58% of cancer cases.[5] There was nipple retraction in 1 case with gynecomastia. Excisional biopsy was performed in this case for possible malignancy. There was no malignancy associated with gynecomastia in the pathology. In one case, serous nipple discharge was present. Cytologically, it was evaluated as intraductal papilloma together with gynecomastia. In one case, the painless mobile mass in the upper external quadrant of the breast was assessed as lipoma after fine needle aspiration biopsy. In the mammogram of this case, the lipoma was observed as a radiolucent area with a well-defined fine capsule. In the ultrasonic examination, mobile, well-defined, hypoechoic area was observed in this localization. It is reported in the literature that 0-20% of gynecomastia cases may have breast cancer.[13] In another study, gynecomastia was reported in 50% of breast cancer cases.[6] However, none of our cases were detected to have associated breast cancer.

Male breast cancer is clinically palpable in the form of a rigid, fixed mass. Bloody or serous nipple discharge, nipple retraction, deep thickening and pathological axes may be accompanied by lymphadenopathies. However, these findings are not specific for cancer.[12] In a study conducted by Evans et al., They reported that nipple retraction was seen in 58% of cancer cases.[5] In the gynecomastia 1 case, there was retraction at the nipple. Excisional biopsy was performed in this case in terms of possible malignancy. There was no gynecomastia associated malignancy in the pathology. In one case serous nipple discharge was present. Cytologically, it was evaluated as intraductal papilloma together with gynecomastia. In one case, the painless mobile mass in the upper external breast of the breast was assessed as the final lipoma of fine needle aspiration biopsy. In the mammogram of this case, the lipoma was seen as a radiolucent area with a well-defined fine capsule. Ultrasonic examination; In this localization, mobile, smoothly confined, hypoechoic area was observed. It has been reported in the literature that 0-20% of gynecomastia cases may have breast cancer.[13] In another study, gynecomastia was reported in 50% of breast cancer cases.[6] However, none of our cases have associated breast cancer. In this study, 74 male cases were evaluated in different age groups who were diagnosed as painless, painful or sensitive breast growth by clinical examination. 70 cases with gynecomastia were classified according to their ultrasonic and mammographic appearance. Cases with suspicious mammograms were diagnosed with early stage gynecomastia by biopsy. Diffuse type gynecomastia was common with mammographic typing and mixed type gynecomastia was common with sonographic typing. Diseases causing or accompanied by gynecomastia were investigated. Pubertal gynecomastia reported in 25% of cases in the literature was high of our study with the rate of 31.42%. Idiopathic gynecomastia reported as the second most common in the literature was found 15% in our study. Gynecomastia secondary to drug use was the second most common (25.71%) in our study. This rate is reported as 10-20% in the literature.[14] In addition, primer hypogonadism, which is reported to be the cause in 8% of

gynecomastia cases in literature, was not observed in our study.

CONCLUSION

As a result, gynecomastia is a symptom rather than a disease. It may be idiopathic as well as many physiological and pathological reasons. In gynecomastia, US, mammography or combined use should be highly enough and in case of suspicion fine needle aspiration biopsy should be performed.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Ethics Committee of Dr. Sadi Konuk Training and Research Hospital and informed consents of the patients were obtained from their parents or legal representatives

REFERENCES

1. Donegan WL. Common benign contitions of the breast. Gynecomastia. Cancer of the Breast. London: WB Saunders. 1995:100-3.
2. Gabrilove JL, Sharma DC, Wotiz HH, Dorfman RI. Feminizing adrenocortical tumors in the male: a review of 52 cases including a case report. Medicine. 1965;44(1):37-79.
3. Wigley KD, Thomas JL, Bernardino ME, and Rosenbaum JL. Sonography of gynecomastia. Am J Roentgen. 1981;136(5):927-930.
4. Hodson GR, Urdaneta LF, Al-Jurf AS, and Jochimsen PR. Male breast carcinoma. The Am Surg. 1985;51(1):47-49.
5. Norris HJ, Taylor HB. Relationship of histologic features to behavior of cystosarcoma phyllodes. Analysis of ninety-four cases. Cancer. 1967;20(12):2090-9.
6. Chantra PK, So GJ, Wollman JS, and Bassett LW. Mammography of the male breast. AJR. 1995;164(4):853-858.
7. Michels LG, Gold RH, and Arndt RD. Radiography of Gynecomastia and Other Disorders of the Male Breast 1. Radiology. 1977;122(1):117-122.
8. Harper P. The male breast. Imaging characteristics. Ultrasound mammography, Baltimore P. Harper. University Park Press. 1985;7:11.
9. Cole-Beuglet C, Schwartz GF, Kurtz AB, Patchefsky AS, and Goldberg BB. Ultrasound mammography for male breast enlargement. J Ultras Medic. 1982;1(8):301-305.
10. Wigley KD, Thomas JL, Bernardino ME, and Rosenbaum JL. Sonography of gynecomastia. Am J Roentgen. 1981;136(5):927-930.
11. Thomas DB. Breast cancer in men. Epidemiologic reviews. 1992;15(1):220-231.
12. Appelbaum AH, Evans GF, Levy KR, Amirkhan RH, and Schumpert TD. Mammographic appearances of male breast disease 1. Radiographic. 1999;19(3):559-568.
13. Evans GF, Anthony T, Appelbaum AH, Schumpert TD, Levy KR, Amirkhan RH, and Turnage RH. The diagnostic accuracy of mammography in the evaluation of male breast disease. Am J Surg. 2001;181(2):96-100.
14. Braunstein GD. Gynecomastia. New Eng J Medic. 1993;328(7):490-495.

Cite this article as: Çeliker FB, Inci E, Sever N, Cimilli AT, Turan AT. Comparison of ultrasound, mammography and histopathology findings of the cases with gynecomastia. Int J Res Med Sci 2017;5:4708-14.