

Gynecomastia: a common indication for mammography in men of all age

Raffaella Capasso¹, A. Sica¹, M. D'Amora¹, Maurizio Mostardi², Ilenia Martella³, Marilina Totaro⁴, Giovanni Della Casa³, Manuela Vallara³, Antonella Pesce³, G. Gatta¹, S. Cappabianca¹

¹ Department of Internal and Experimental Medicine, Magrassi-Lanzara, Second University of Naples, Naples, Italy; ² ASL7 Siena, Italy; ³ Department of Surgical Sciences, Section of Radiological Sciences, University of Parma, Parma Hospital, Parma, Italy; ⁴ University of Ferrara - Morphology, Surgery and Experimental Medicine Dept. - Diagnostic Imaging Section, Ferrara, Italy

Summary. *Background and aim:* Gynecomastia (GM) is the most frequent cause of male breast-related signs and symptoms and represents also the most common indication for mammography (MX) in men. In this article, our 7-year long experience with MX in men suffering from GM is reviewed, and the mammographic features of GM are presented. *Methods:* MXs performed in male patients at our institution from January 2009 to January 2016 were retrospectively reviewed and patients with mammographic features of GM were selected. Informed consent was waived by the local institutional review board given the retrospective nature of the study. Mammograms were performed in both cranio-caudal (CC) and medio-lateral-oblique (MLO) views according to diagnostic needs. Clinical and pathologic data were obtained by review of patient charts. *Results:* 37 males (aged between 13-79 years, mean 59 years) referred for MX at our institution because of palpable lump (31/37; 83.8%), breast enlargement (33/37; 89.2%), tenderness or pain (25/37; 67.6%). Of the 37 patients evaluated, 32 (86.5%) had true GM while 5 (13.5%) had pseudoGM. *Conclusions:* The evaluation of GM can be complex but a stepwise approach that starts with careful history taking and physical examination may obviate the need for extensive work-up. In this context, MX has been shown to be an accurate diagnostic tool for detecting GM and should be the first imaging examination to be performed in all clinically suspicious lesions referred for imaging. (www.actabiomedica.it)

Key words: male mammography, male breast, gynecomastia, pseudogynecomastia

Introduction

Over the past decade, there has been a rise in the number of imaging studies performed in men, however, mammography (MX) is still an unusual examination in male patients (1, 2). Opposite to female diseases, male breast cancer is rare accounting for less than 1% of the total lesions, while the most common indication for MX in men is gynecomastia (GM) (2-4). GM represents also the most common cause of breast-related signs and symptoms in men, mainly represented by

palpable lump, breast enlargement, tenderness or pain (2, 3, 5).

In this article, our 7-year long experience with MX in men suffering from GM is reviewed, and the mammographic features of GM are presented.

Materials and methods

MXs performed in male patients at our institution from January 2009 to January 2016 were retro-

spectively reviewed and patients with mammographic features of GM were selected. Informed consent was waived by the local institutional review board given the retrospective nature of the study. Examinations were performed by using a dedicated digital MX system (Siemens Inspiration-Erlangen, Germany). Mammograms were performed in both cranio-caudal (CC) and medio-lateral-oblique (MLO) views according to diagnostic needs. Clinical and pathologic data were obtained by review of patient charts.

Results

37 males (aged between 13–79 years, mean 59 years) referred for MX at our institution because of palpable lump (31/37; 83.8%), breast enlargement (33/37; 89.2%), tenderness or pain (25/37; 67.6%). Of the 37 patients evaluated, 32 (86.5%) had true GM while 5 (13.5%) had pseudoGM (fatty breast disease without true GM). GM was bilateral and symmetrical in 8/32 cases, bilateral and asymmetrical with one breast more severely involved than the other in 13/32 cases (left predominant in 10 patients), and monolateral in 11/32 cases (right located in 8 patients). Symmetrical and bilateral GM was related to hormonal therapy for prostatic cancer in 1 patient, while it was associated to hepatic cirrhosis or dialysis in 5 and 2 cases respectively. Some (5/11) subjects affected by monolateral GM reported a story of digitalis preparations (3/11) or thiazides medications use (2/11).

In our study, pseudoGMs were all bilateral and were closely related with obesity clinical condition.

On MX examinations, GM appeared as an inhomogeneous and wide dense glandular proliferation extending from the nipple into the fatty tissue of the breast while pseudoGM showed the typical sign of the 'breast clear' for the prevalence of fatty component in the breast tissue without any mass or calcifications.

Discussion

Normal male breast

Similar to the female breast, the male breast extends from the second through the sixth anterior ribs

having the sternum as the medial border and the midaxillary line demarcating the lateral extent (1). The breast tissues of both sexes, identical at birth, are influenced by hormonal changes which take place at puberty (3). Until puberty, breasts are composed of fibrofatty tissue and ducts (5, 6). During the peripubertal period, estrogen level increase stimulates breast tissue in opposition to androgen level rise which causes involution and atrophy of the ducts (3, 5). Therefore, in boys there is a transient proliferation of the ducts and stroma followed by involution and atrophy of the ducts while lobular development, which requires both estrogen and progesterone, is usually not observed in men (3). As a result, normal male breast is characterized predominantly by subcutaneous fatty tissue and stroma, a small nipple-areolar complex, and few poorly developed subareolar ducts; this structure is distinctly different from women's breast composition where ducts, stroma, and glandular tissue predominate. Cooper ligaments, found in female breasts, are absent in male breasts (1, 3, 5).

Mammographically male breast appears widely homogeneously lucent, having a few lean connective components without architectural disposition, with a prominent pectoralis muscle seen posteriorly (Figure 1) (2, 5).

MX technique in male patients

In contrast to imaging the female breast, there are no standardized protocols for imaging the male breast and there is a wide variability among individual practices in the availability and utilization of MX in men (1,3). Given its high sensitivity, MX is generally the initial imaging examination to evaluate suspicious or indeterminate clinical findings (1). Despite the relatively small size of the male breast, our experience also suggests that MX is generally technically possible and can be a useful supplement to clinical examination. At our institution, the standard mammographic views, CC and MLO views of each breast are routinely obtained. Magnification and spot compression views may also be used. In men with well-developed pectoral muscles obscuring the breast tissue, pectoralis-displaced views can be obtained. Although we do not acquire these views routinely, these additional images



Figure 1. Normal male breast; A) left medio-lateral oblique and B) cranio-caudal mammograms show the presence of sub-cutaneous fat and the predominant pectoralis muscle posteriorly (asterisk)

allow a better assessment of the full extent of the breast tissue in these patients (1).

Gynecomastia

GM is the most common cause of palpable mass and the most frequent indication for MX in men (2, 5). The term “gynecomastia”, derived from the Greek “gynaik-” meaning “female” and “mastos” meaning “breast” (1). Histologically, GM results from non-neoplastic hyperplasia of the galatophorous ducts, which

lengthen and ramify while epithelium becomes thickened and multilayered, beyonds evidence of acinar structure. The predominant element is represented by connective tissue that results hyperplastic and very thick. Surrounding stroma presents increased vascularization and cellularity and can be found inflammatory cells (2, 4). GM has two typical peak periods of presentation: in adolescence and again with advancing (>50 years) age (2, 5, 7).

GM can be distinguished in physiological, idiopathic and pathologic types. Physiological GM is described as symptomless GM occurring in three periods of life associated with an increased estradiol-to-testosterone serum ratio: infancy, adolescence and senescence (8). In our study physiological GM was detected in 13/32 (40.6%) cases (2 adolescents and 11 men older than 50 years), and this is in agreement with the consideration that about 30-85% of cases of this type of GM is showed in men aged 50 to 80 (8).

Idiopathic, of unknown origin GM competes with physiological one as the most commonly diagnosed type of GM, and constitutes 25% of all cases (8). In our study, idiopathic GM was observed in 6/32 (18.7%) patients.

Pathologic GM has been associated with hormonal imbalance, and it can be related to several clinic conditions, like neurologic syndromes, hormonal disorders, systemic diseases as chronic kidney failure or liver cirrhosis, neoplasms, and obesity (4). Drug-induced GM is reported to constitute 10-25% of all cases and, according to this, we observed drug-related GM in 6 (18.7%) patients. It often represents a consequence of chronic application of hormonal drugs, antibiotics, preparations for the treatment of cardiovascular diseases, ulcers, chemotherapeutics, retroviral therapy and some antipsychotic medications (1, 2, 4, 7, 8). Prognosis depends on cause. Generally, in adolescence it recedes spontaneously (2).

GM can be bilateral or monolateral, mild, moderate, or severe in degree (1). Men usually present with a palpable abnormality on physical examination, a growth in the volume of the breast made up mostly of fat and then soft at palpation, or a subareolar solid mass, discoid, well defined or diffuse, with focal tenderness, or a burning sensation. Tenderness and pain are usually caused by the rapid growth of glandular tissue

(1, 6, 8). In our study sample, breast enlargement and the presence of a palpable mass were the main cause of presentation. The enlargement of the breasts is usually bilateral and symmetrical; however, GM may also be asymmetrical, with major enlargement of the left breast as observed in our study, or it may occur unilaterally (8). On MX, benign enlargement of male breast is related both to one of the three distinct patterns of GM (nodular, dendritic and diffuse) and to the presence of fat without any visible parenchyma (4, 5).

Nodular GM occurs during the florid phase of the disease (<1 year), which is thought to be the early phase of GM. On MX, it appears as a nodular or fan-shaped density radiating from the nipple; it may be symmetric or more prominent in the superior-outer quadrant. The density usually blends gradually in the

surrounding fat, but it may be more spherical (Figure 2 A, B) (4, 5). Dendritic GM occurs with long-standing disease (>1 year) representing its quiescent phase. On MX it presents as a flame-shaped subareolar density with finger-like extensions radiating from the nipple in the deeper adipose tissue (Figure 2 C, D) (4, 5). Diffuse GM is usually observed in the setting of hormonal therapy, and on MX it appears as heterogeneous density with components of both nodular and dendritic type resembling female breast (Figure 2 E) (4, 5). PseudoGM is characterized by increased sebaceous fat without enlargement of the glandular component thus MX reveals increased lucent subareolar fat (Figure 3) (4, 5).

The differential diagnosis of a palpable breast mass in male patients includes GM and pseudo GM,



Figure 2. Medio-lateteral oblique mammograms of 5 different patients with gynecomastia; A-B) nodular pattern, C-D) dendritic pattern and E) diffuse gynecomastia

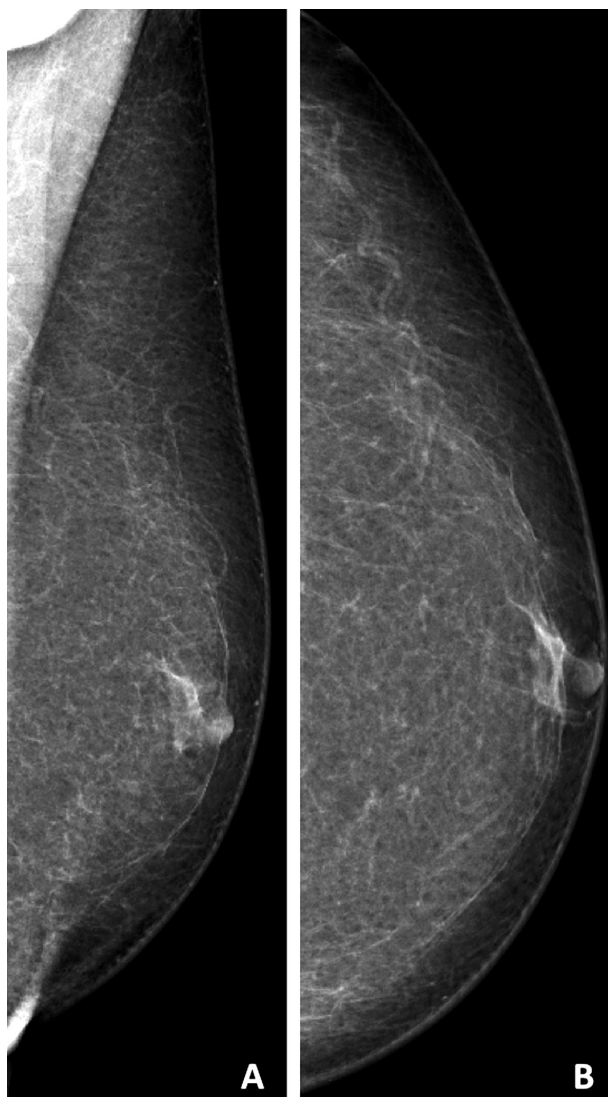


Figure 3. Pseudogynecomastia A) left medio-lateral oblique and B) cranio-caudal mammograms show the presence of increased subcutaneous fat without an increase in the glandular component of the breast

breast cancer and several benign conditions (lipoma, hematoma, epidermal cyst etc.) (9).

MX is the preferred imaging modality in the diagnosis of GM: when classic mammographic findings of GM are observed, no further imaging work-up is needed. Sonography can be employed as an adjunctive second line modality if there is concern for an underlying mass or questionable findings at MX as well as lesions that are difficult to image with MX (Figure 4); in our study sample 19 men underwent ultrasound exam-

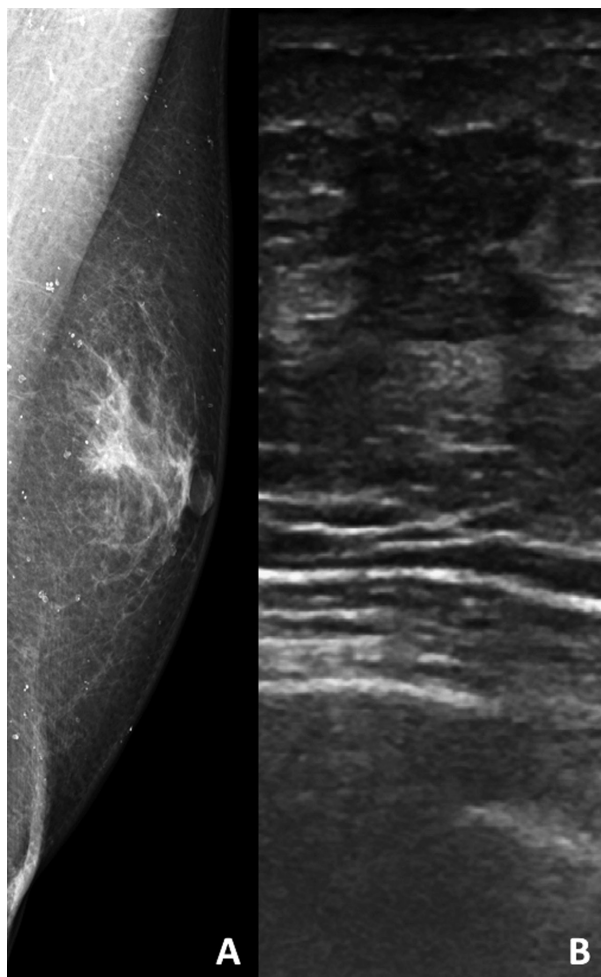


Figure 4. A) medio-lateral oblique mammogram shows the presence of true gynecomastia and a possible underlying mass; ultrasound evaluation B) reveals a subareolar hypoechoic nodule surrounded by echogenic fat

ination (3-5, 10). Although mammographic features of GM and breast cancer do not overlap, not always GM could be easily distinguished from carcinoma (2, 4); a certain amount of eccentricity can be present in GM although it is more pronounced in carcinoma and even nipple retraction can be associated to GM. In such cases biopsy could be necessary to rule out diagnosis of malignancy (2, 4, 5).

Conclusions

The majority (99%) of male breast lesions are benign; among these ones, GM represents the most

common benign condition requiring diagnostic imaging assessment. The evaluation of GM can be complex but a stepwise approach that starts with careful history taking and physical examination may obviate the need for extensive work-up. In this context, MX has been shown to be an accurate diagnostic tool for detecting GM and should be the first imaging examination to be performed in all clinically suspicious lesions referred for imaging. Subsequent selective sonographic evaluation, laboratory testing or biopsy allow to exclude possible neoplasms, detect underlying disorders and guide therapy (3, 5, 7, 9, 10).

References

1. Iuanow E, Kettler M, Slanetz PJ. Spectrum of disease in the male breast. *AJR Am J Roentgenol* 2011; 196(3): W247-59.
2. Dershaw DD. Male mammography. *AJR Am J Roentgenol* [Internet]. 1986 Jan [cited 2016 May 22]; 146(1): 127-31.
3. Chen L, Chantra PK, Larsen LH, Barton P, Rohitopakarn M, Zhu EQ, et al. Imaging characteristics of malignant lesions of the male breast. *Radiographics* 2006; 26(4): 993-1006.
4. Appelbaum a H, Evans GF, Levy KR, Amirkhan RH, Schumpert TD. Mammographic appearances of male breast disease. *Radiographics* 1999; 19: 559-68.
5. Chau A, Jafarian N, Rosa M. Male Breast: Clinical and Imaging Evaluations of Benign and Malignant Entities with Histologic Correlation. *Am J Med*. 2016 Feb 1.
6. Ferraro GA, Romano T, De Francesco F, Grandone A, D'Andrea F, del Giudice EM, et al. Management of prepubertal gynecomastia in two monozygotic twins with Peutz-Jeghers syndrome: from aromatase inhibitors to subcutaneous mastectomy. *Aesthetic Plast Surg* 2013; 37(5): 1012-22.
7. Carlson HE. Approach to the patient with gynecomastia. *J Clin Endocrinol Metab* 2011; 96(1): 15-21.
8. Derkacz M, Nowakowski A. Gynecomastia - a difficult diagnostic problem Ginekomastia - trudny problem diagnostyczny 2011; 62(2): 190-202.
9. Johnson RE, Murad MH. Gynecomastia: pathophysiology, evaluation, and management. *Mayo Clin Proc* [Internet]. 2009; 84(11): 1010-5.
10. Di Grezia G, Romano T, De Francesco F, Somma F, Rea G, Grassi R, et al. Breast ultrasound in the management of gynecomastia in Peutz-Jeghers syndrome in monozygotic twins: two case reports. *J Med Case Rep* 2014; 8: 440.

Correspondence:

Raffaella Capasso: Department of Internal and Experimental Medicine, Magrassi-Lanzara, Second University of Naples, 80138 Naples (Italy)
E-mail: dott.ssacapasso@gmail.com