April, 2020

PharmacologyOnLine

Special issue • 2020 • vol.1 • 39-45

IS THERE A HIGH-RISK MAMMOGRAPHIC PATTERN IN B3 LESIONS?

Crivelli P.[1], Ledda R.E.[2], Piga G.[3], Lampus M.L.[3], Sotgiu M.A.[4], Soro D.[1], Conti M.[3]

[1]AOU Sassari, Institute of Diagnostic Imaging 2, Italy

[2]Section of Radiology, Unit of Surgical Sciences, Department of Medicine and Surgery (DiMeC), University of Parma, Parma, Italy

[3]Department of Clinical and Experimental Medicine, Institute of Diagnostic Imaging 2, University of Sassari, Italy

[4]Department of Biomedical Sciences, Medical School, University of Sassari, Sassari, Italy.

Email: paocri2000@gmail.com

Abstract

Introduction: Breast lesions of uncertain malignant potential (B3) include different histopathological subtypes. Vacuum assisted biopsy (VAB) excision and surveillance have been more recently proposed as a valid alternative to the more traditional surgical approach. A significant association between radiological findings and malignancy in excision biopsy has not been proved as yet.

Aim of this paper is to find a prevalent mammographic pattern for each histological B3 subtype in order to identify a "high-risk mammographic pattern".

Methods and materials: We retrospectively included all B3 patients referred from spontaneous screening to the Breast Radiology Service at the University Hospital of Sassari, Italy, from January 2012 to June 2018. All patients underwent a mammography and a histological characterization. Six different mammographic patterns and six histological subtypes were identified.

Results: 69 patients were enrolled. Median (IQR) age was 50 (44-57) years; the majority of lesions was localized in the left breast (37, 53.6%). Clustered microcalcifications was the most prevalent mammographic pattern in our series, whereas ADH was the most common histological subtype. A prevalent mammographic pattern was found within each pathological subtype (p-value=0,02).

Discussion: B3 subtypes, whose cellular atypia is the characteristic feature, showed clustered microcalcifications as their prevalent mammographic pattern ("high-risk mammographic pattern"). In this context, the VAB biopsy is likely to change the management of B3 lesions, assuming a therapeutic role too and, thus, reducing both biological and economic costs.

Larger and multicentric studies are necessary to find a generalizable mammographic pattern for the lesser common B3 histological subtypes.

Keywords: *B3 lesions, atypia, biopsy, therapeutic approach*

.

Introduction

Breast cancer is the most common female tumour, it manifests at different ages with different histotypes 1-3], and several factors are involved in the carcinogenesis, even environmental [4, 5]. Early diagnosis, performed by conventional and innovative imaging techniques, is mandatory to prevent metastasis, improving clinical outcome [6-8]. Breast lesions of uncertain malignant potential (B3) encompass different histological entities [9-12]. The number of B3 diagnoses, often incidental, has been increasing over the last decades due to the implementation and scaling up of mammographic screening programs [13] and to a larger availability of minimally invasive biopsy techniques (core-needle biopsy, CNB, and vacuum assisted biopsy, VAB) [14-16]. Although surgical excision remains the preferred therapeutic option, VAB excision and surveillance have been more recently proposed as alternative approaches in some selected cases [11]. A significant association between radiological findings and malignancy in excision biopsy has never been proved, assigning the histology the exclusive role to orientate the management of these heterogeneous lesions [15, 18, 19].

This paper aims to find a prevalent mammographic pattern for each histological B3 subtype.

Methods

It was carried out a retrospective study including all patients diagnosed with B3 lesions who referred from spontaneous screening to the Breast Radiology Service at the University Hospital of Sassari, Italy, from January 2012 to June 2018. All patients underwent a bilateral digital mammography in standard projections (cranio-caudal and oblique) using Selenia® Dimensions® Mammography System (Hologic). Where required, radiological exam was completed with an ultrasound (US) breast scan using a linear probe of a MyLab™ClassC (Esaote). Images were reviewed by two expert breast radiologists who classified B3 lesions in patterns, considering single mammographic findings as described in previous literature, and their possible combination [11, 15]. Six different mammographic patterns were identified as following: clustered microcalcifications, mass and parenchymal distortion, mass with microcalcifications, mass with parenchymal distortion and parenchymal distortion with microcalcifications. Histological samples were obtained by a 14-16G spring-loaded CNB under ultrasound or by VAB, using a 9-11G device under stereotactic mammography guidance. All specimens were evaluated by two expert breast pathologists and results classified into 6 subtypes as per the European guidelines [9] (atypical ductal hyperplasia, ADH, flat epithelial atypia, FEA, lobular intraepithelial neoplasia, LIN 1/2, papillary lesion, PL, benign phyllodes tumours, PT, and radial scar, RS). Following a multidisciplinary (MDT) discussion, involving breast surgeons, radiologists, radiotherapists and pathologists, all patients underwent surgery.

Data were retrieved from medical files using an ad-hoc electronic form, including demographic, clinical, epidemiological, radiological and histological variables. Quantitative covariates were summarized with means and standard deviations (SD) or medians and interquartile ranges (IQR) in case of a parametric or non-parametric distribution, respectively, whereas qualitative variables were described using absolute frequencies and percentages. Statistical computations were performed with the statistical software Stata13.0 (StataCorp, College Station, TX, USA).

Results

Sixty-nine female patients were retrospectively enrolled. Median (IQR) age was 50 (44-57) years; the majority of lesions was localized in the left breast (37, 53.6%). Mammographic patterns were as following: 54 (78.3%) clustered calcifications, 8 (11.6%) mass, 4 (5.8%) mass with microcalcifications, 1 (1.5%) parenchymal distortion, 1 (1.5%) parenchymal distortion with calcifications, and 1 (1.5%) mass with parenchymal distortion. Histology showed 44 (63.8%) cases of ADH, 10 (14.5%) of PL, 7 (10.1%) of FEA, 4 (5.8%) of RS, 3 (4.4%) of LIN 1/2, and 1 (1.5%) of PT (Table 1). A prevalent mammographic pattern was found within each pathological subtype (p-value=0,02). All ADHs presented with calcifications, either in isolated clusters (86.4%) or associated with mass or parenchymal distortion (4.6%) (Table 2)

Discussion

Six different mammographic patterns (Figure 1) were identified and their prevalence within the six histological subtypes investigated (Figure 2). Clustered microcalcifications represented the most prevalent mammographic pattern in our series, whereas ADH was the most common histological subtype.

As previously demonstrated, ADH, LIN 1/2 and FEA are associated with an increased risk for malignancy presenting cellular atypia as their characteristic feature, whereas other B3 subtypes may or may not contain cellular of altered morphology [12,17-19]. Our series showed that these three "high-risk subtypes" presented clustered microcalcifications as their prevalent mammographic pattern, which could be considered a mammographic expression of an underlying atypia, configuring a "high-risk mammographic pattern". Following the detection of this "high-risk mammographic pattern", it is mandatory for the interventional breast radiologist to perform a radical VAB excision, offering a valid alternative to surgery. In this context, the VAB biopsy has changed the management of these borderline lesions, obtaining a therapeutic purpose too, as clearly expressed in the B3 First International Consensus Conference recommendations [11,20]. Despite the small number of patients enrolled, our results reinforce the concept of a radical VAB biopsy, which could reduce both biological and economic costs.

This study has several limitations: the retrospective nature, the small patients sample size and the inclusion of patients from a single center make harder to generalize results.

In conclusion, larger and multicentric studies will be needed to validate our preliminary results and to find a generalizable mammographic pattern for the lesser common B3 histological subtypes.

References

1. Amadu AM, Soro D, Marras V, Satta G, Crivelli P, Conti M, Meloni GB. Primary breast chondrosarcoma: Imaging and pathological findings. Eur J Radiol Open. 2017 Nov 5; 4:138-140.

2. Vestito A, Mangieri FF, Gatta G, Moschetta M, Turi B, Ancona A Breast carcinoma in elderly women. Our experience. G Chir 2011 Oct; 32 (10):411-6.

3. Amadu AM, Marras V, Crivelli P, Soro D, Conti M, Meloni GB. Isolated breast metastasis 4 years after nephrectomy. Breast J. 2018 Jan; 24 (1):85-87.

4. Oggiano R, Solinas G, Forte G, Bocca B, Farace C, Pisano A, Sotgiu MA, Clemente S, Malaguarnera M, Fois AG, Pirina P, Montella A, Madeddu R. Trace elements in ALS patients and their relationships with clinical severity Chemosphere. 2018 Apr; 197:457-466.

5. Forte G, Bocca B, Oggiano R, Clemente S, Asara Y, Sotgiu MA, Farace C, Montella A, Fois AG, Malaguarnera M, Pirina P, Madeddu R. Essential trace elements in amyotrophic lateral sclerosis (ALS): Results in a population of a risk area of Italy. Neurol Sci. 2017 Sep; 38(9):1609-1615.

6. Di Grezia G, Somma F, Serra N, Reginelli A, Cappabianca S, Grassi R, Gatta G. Reducing Costs of Breast Examination: Ultrasound Performance and Inter-Observer Variability of Expert Radiologists Versus Residents. Cancer Invest. 2016 Jul 20: 1-6.

7. Crivelli P, Ledda RE, Parascandolo N, Fara A, Soro D, Conti M. A New Challenge for Radiologists: Radiomics in Breast Cancer. Biomed Res Int. 2018 Oct 8; 2018:6120703.

8. Di Grezia G, Prisco V, Iannaccone T, Grassi R, Serra N, Gatta G Personality disorder and temperamental traits in patients with breast disease: preliminary results Minerva Psichiatrica 2016 Sept; 57(3):85-92

9. Perry N, Broeders M, de Wolf C, Tornberg S, Holland R, von Karsa L. European guidelines for quality assurance in breast cancer screening and diagnosis. Fourth edition–summary document. Ann Oncol. 2008; 19:614–622.

10. Purushothaman HN, Lekanidi K, Shousha S, Wilson R. Lesions of uncertain malignant potential in the breast (B3): what do we know? Clin Radiol. 2016 Feb; 71(2):134-40. d

11. Rageth CJ, O'Flynn EA, Comstock C, Kurtz C, Kubik R, Madjar H, Lepori D, Kampmann G, Mundinger A, Baege A, Decker T, Hosch S, Tausch C, Delaloye JF, Morris E, Varga Z. First International

Consensus Conference on lesions of uncertain malignant potential in the breast (B3 lesions). Breast Cancer Res Treat. 2016 Sep; 159(2):203-13.

12. Friederichs Sinn H. Lesions of uncertain malignant potential (B3). 2016. AGO eV, Comisson Mamma.

13. Fancellu A, Sanna V, Sedda ML, Delrio D, Cottu P, Spanu A, Giuliani G, Conti M, Piras R, Crivelli P, Porcu A. Benefits of Organized Mammographic Screening Programs in Women Aged 50 to 69 years: A Surgical Perspective. Clin Breast Cancer. 2019 Oct; 19(5):e637-e642.

14. Pinder SE, Shaaban A, Deb R, Desai A, Gandhi A, Lee AH, Pain S, Wilkinson L, Sharma N. NHS Breast Screening multidisciplinary working group guidelines for the diagnosis and management of breast lesions of uncertain malignant potential on core biopsy (B3 lesions). Clin Radiol. 2018 Aug;73(8):682-692. doi: 10.1016/j.crad.2018.04.004.

15. Taffurelli M, Pellegrini A, Ghignone F, Santini D, Zanotti S, Serra M. Positive predictive value of breast lesions of uncertain malignant potential (B3): Can we identify high risk patients? The value of a multidisciplinary team and implications in the surgical treatment. Surg Oncol. 2016 Jun; 25(2):119-22.

16. Gatta G, Di Grezia G, Ancona A, Capodieci M, Coppolino F, Rossi C, Feragalli B, Iacomino A, Cappabianca S, Grassi R "Underestimation of atypical lobular hyperplasia and lobular carcinoma in situ at stereotaxic 11-gauge vacuum-assisted breast biopsy" European Journal of Inflammation 2013; 11(3): 825-835Taffurelli M, Pellegrini A, Ghignone F, Santini D, Zanotti S, Serra M. Positive predictive value of breast lesions of uncertain malignant potential (B3): Can we identify high risk patients? The value of a multidisciplinary team and implications in the surgical treatment. Surg Oncol. 2016 Jun; 25(2):119-22.

17. Mayer S, Kayser G, Rücker G, Bögner D, Hirschfeld M, Hug C, Stickeler E, Gitsch G, Erbes T. Absence of epithelial atypia in B3-lesions of the breast is associated with decreased risk for malignancy. Breast. 2017 Feb; 31:144-149.

18. de Beça FF, Rasteiro C, Correia A, Costa S, Amendoeira I. Improved malignancy prediction by B3 breast lesions subclassification. Ann Diagn Pathol. 2013 Oct; 17(5):434-6.

19. Hoffmann O, Stamatis GA, Bittner AK, Arnold G, Schnabel R, Krüger K, Kimmig R, Heubner M. B3-lesions of the breast and cancer risk - an analysis of mammography screening patients. Mol Clin Oncol. 2016 May; 4(5):705-708.

20. Pieri A, Hemming D, Westgarth J, Lunt L. Vacuum-assisted biopsy is a viable alternative to surgical biopsy in the investigation of breast lesions of uncertain malignant potential. Surgeon. 2017 Apr; 15(2):59-64.

Table 1. Demographic data, histological subtypes and mammographic patterns of B3 patients.

Variables		
Mediana age (IQR), years		50 (44-57)
Left side, n (%)		37 (53.6)
Diagnosis, n (%)	*ADH*	44 (63.8)
	PL	10 (14.5)
	FEA	7 (10.1)
	RS	4 (5.8)
	LIN 1/2	3 (4.4)
	PT	1 (1.5)
Mammographic pattern, n (%)	*Clustered microcalcifications*	54 (78.3)
	Mass	8 (11.6)
	Mass with microcalcifications	4 (5.8)
	Parenchymal distortion	1 (1.5)
	Parenchymal distortion with microcalcifications	1 (1.5)
	Mass with parenchymal distortion	1 (1.5)

Table 2. Mammographic patterns and histological subtypes (p-value: 0.02).

	ADH	***PL***	***RS***	***PT***	***LIN 1/2***	***FEA***
Mass	3 (6.8)	3 (30.0)	2 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)
Mass with microcalcifications	1 (2.3)	1 (10.0)	1 (25.0)	1 (100.0)	0 (0.0)	0 (0.0)
Mass with parenchymal distortion	1 (2.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Parenchymal distortion with microcalcifications	1 (2.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Clustered microcalcifications	38 (86.4)	5 (50.0)	1 (25.0)	0 (0.0)	3 (100.0)	7 (100.0)
Parenchymal distortion	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Figure 1. Six mammographic pattern

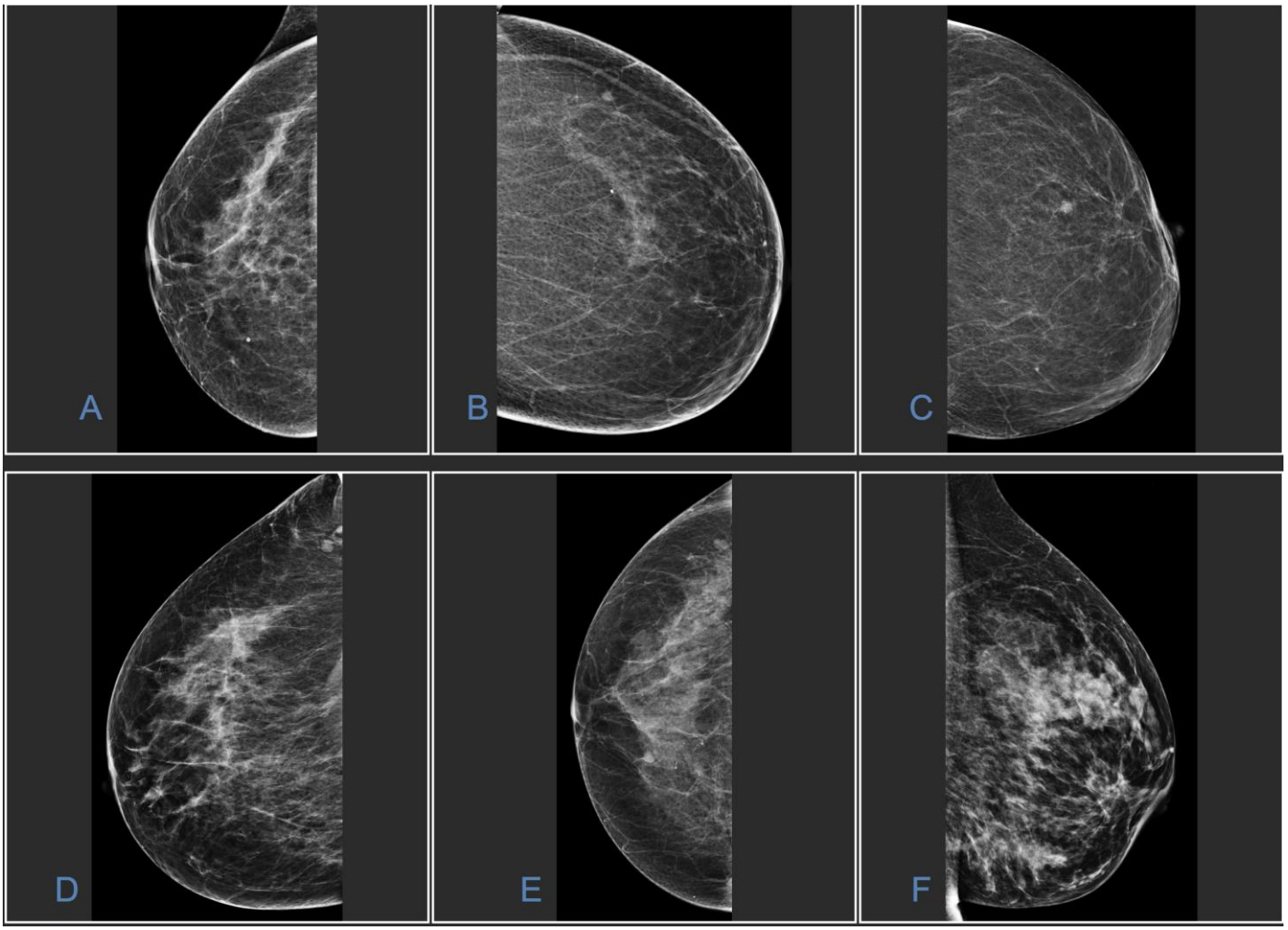

Figure 2. Six histological pattern