

SHORT COMMUNICATION

**DIFFERENCES IN GATA3 EXPRESSION AMONG HISTOLOGICAL/
MOLECULAR SUBTYPES AND GRADES IN INFILTRATING BREAST
CARCINOMA (IBC) ARE IMPORTANT IN THE DIAGNOSIS OF
METASTATIC BREAST CARCINOMA**SIMONA STOLNICU¹, CSILLIP TUNDE¹, ANA CADAR¹, MONICA BOROS²¹Department of Pathology, University of Medicine, Pharmacy, Sciences and Technology (UMFTS) of Târgu Mureș, Romania²Department of Pathology, Faculty of Medicine and Pharmacy, University of Oradea, Romania

GATA-binding protein 3 (GATA3) is a sensitive and relatively specific marker in invasive breast carcinomas (IBC). The aim of the present study was to determine GATA3 expression among different histological and surrogate molecular breast carcinoma subtypes.

Immunohistochemical staining of ER, PR, Ki67, HER2 and GATA3 was performed in a cohort of 84 consecutive cases of primary IBCs. The association of GATA3 expression with different histological subtypes, grades and surrogate intrinsic molecular subtypes was assessed.

The overall positivity of GATA3 across various histological subtypes was 71.43% with no correlation with histological type ($p = 0.849$). Our study also confirmed that GATA3 exhibits a relatively high sensitivity for IBC (78.57%). GATA3 expression was positively correlated with low histological grades (G1/G2) vs. G3: $p = 0.001$ with most of G3 (57.89%) cases being negative and with luminal A (72.22%) and B (84.62%) subtypes ($p = 0.00001$) while most of the triple negative (87.5%) and HER2-overexpressed (66.67%) being negative.

Caution must be paid however when dealing with an IBC metastasis of HER2-overexpressed or triple negative molecular subtypes or G3, since in these categories according to the present study, GATA3 is more frequently negative than previously reported and may be useless for diagnosis of tumor origin.

Key words: infiltrating breast carcinoma, GATA3, histologic, molecular subtypes.

GATA-binding protein 3 (GATA3) is a well-studied transcription factor found to be essential in the development of luminal breast epithelium. Moreover, GATA3 was proposed as a sensitive and relatively specific marker in primary IBC as well as for primary genital extramammary paget disease [1]. Its diagnostic and prognostic utility in primary IBC has been confirmed although by limited studies revealing that high expression of GATA3 is associated with posi-

tive estrogen (ER) and progesterone (PR) receptors tumors, smaller tumor size and lower nuclear grade, and as a consequence with a better survival while loss of GATA3 expression was found to be associated with unfavorable outcome [2]. This finding is not universally accepted as published data on GATA3 as a prognostic markers are conflicting [3]. We read with interest the paper by Shaoxian *et al.* on characterization of GATA 3 expression in IBC [4]. In that

particular study, on a larger cohort of patients with primary IBC, the authors demonstrated that GATA3 exhibits a relatively high sensitivity for IBCs, being more sensitive than GCDFP15 and mammaglobin in luminal-like and HER2 overexpression subtypes, and being more likely associated with IBC of luminal subtype and low histologic grade. Similar results were found by Ni *et al.* on histologic specimens as well as by Hafez *et al.* and El Hag *et al.* on cytological cell block materials [5, 6, 7]. Of interest, the negative rate for GATA3 was recorded as being of 28% in grade 3 tumors by the recent study of Lu *et al.* with more GATA3 negative tumors occurring in grade 3 of no special type, metaplastic and apocrine IBCs [3]. Consequently, in the routine practice, especially when dealing with a metastatic IBC, the role of GATA3 may be limited. We aimed to further investigate the role of GATA3 expression among different histological subtypes, surrogate molecular IBC subtypes and

histological grades in a prospective study. Immunohistochemical staining of ER, PR, ki67, HER2 and GATA3 was performed in a cohort of 84 consecutive cases of primary IBCs. The association of GATA3 expression with different histological subtypes, grades and surrogate intrinsic molecular subtypes was assessed [8, 9].

The age ranged from 35 to 83 years with median age of 61.9 years (no statistically significant differences between with median age in GATA3 positive and negative cases and between pre or postmenopausal IBC patients) ($p = 0.832$). The overall positivity of GATA3 across various histological subtypes was 71.43% with no correlation with histological type ($p = 0.849$). GATA3 expression was positively correlated with low histological grades (G1/G2 vs. G3: $p = 0.001$) with most of G3 (57.89%) cases being negative and with luminal A (72.22%) and B (84.62%) subtypes ($p = 0.00001$) while most of

Table I. Correlation between GATA3 expression and age, histological type and grade and molecular profile

PARAMETER	GATA						OR, CI, P
	N	%	POSITIVE	%	NEGATIVE	%	
Total	84		60	71.4	24	28.57	
Age median	61.9		63.08		58.95		
Range	35-83		39-83		35-76		
Age < 50 years	13	15.48	9	69.23	4	30.77	Age < 50 years vs. age \geq 50 years OR = 0.832, 95% CI: 0.248-3.070 $p = 0.832$
Age \geq 50 years	71	84.52	51	71.83	20	28.17	
Histologic type							
NST	71	84.52	51	71.83	20	28.17	Histologic type NST vs. others OR = 1.133 95% CI: 0.313-4.102 $p = 0.849$
Lobular	8	9.52	6	70.00	2	25.00	
Apocrine	1	1.19	0	75.00	1	100.00	
Micropapillary	1	1.19	1	0.00	0	0.00	
Papillary	1	1.19	1	100.00	0	0.00	
Mucinous	1	1.19	1	100.00	0	0.00	
Mixed	1	1.19	0	100.00	1	100.00	
Histologic grade							
G1	13	15.48	12	92.31	1	7.69	Histological grade 1.2 vs. 3 OR = 5.747 95% CI: 1.869-17.543 $p = 0.001$
G2	44	52.38	34	77.27	10	22.73	
G3	19	22.62	8	42.11	11	57.89	
N/A	8	9.52	6	75.00	2	25.00	
Luminal A	18	21.43	13	72.22	5	27.78	Molecular Type Luminal A,B vs. HER2+,TRN OR = 17.544 95% CI: 4.202-71.429 $p = 0.00001$
Luminal B	52	61.90	44	84.62	8	15.38	
HER2 overexpressed	6	7.14	2	33.33	4	66.67	
Triple negative	8	9.52	1	12.50	7	87.50	

OE – odds ratio; CI – confidence interval; NST – no special type invasive breast carcinoma; TRN – triple negative; HER2+ – HER2 overexpressed

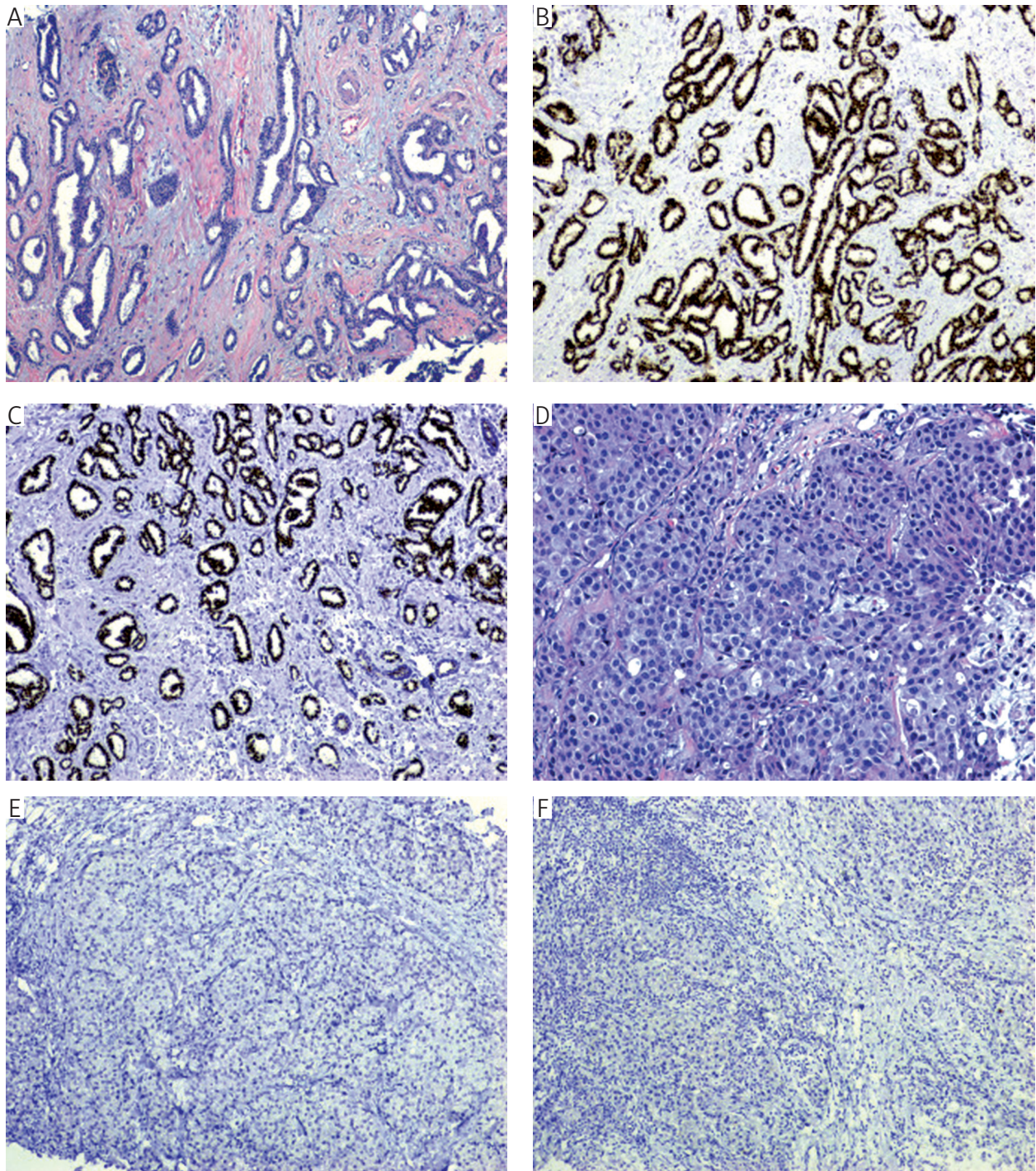


Fig. 1. Infiltrating breast carcinoma of no special type, histologic grade 1 (haematoxylin-eosin) (A), positive for ER (B) and GATA3 (C); Infiltrating breast carcinoma of no special type, histologic grade 3 (haematoxylin-eosin) (D), negative for ER (E) and GATA3 (F)

the triple negative (87.5%) and HER2-overexpressed (66.67%) being negative for GATA3 (Table I; Fig. 1). Our study confirmed that GATA3 exhibits a relatively high sensitivity for IBC (78.57%). GATA3 expression is associated with IBC most frequently encountered histological subtypes with luminal A/B molecular subtype and low G1/G2 histological grade. Caution must be paid however when dealing with

an IBC metastasis of HER2-overexpressed or triple negative molecular subtypes or G3, since in these categories according to the present study, GATA3 is more frequently negative than previously reported and may be useless for diagnosis of tumor origin.

The authors declare no conflict of interest.

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Address for correspondence

Simona Stolnicu
Department of Pathology
University of Medicine, Pharmacy,
Sciences and Technology (UMFTS) of Târgu Mureş
Gheorghe Marinescu Street Nr 38
540139 Targu Mures, Romania
e-mail: stolnicu@gmx.net