ABSTRACT #102: REAL-WORLD EVIDENCE OF IMMUNOHISTOCHEMICAL DISCORDANCE IN BREAST CANCER BRAIN METASTASES

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BACKGROUND

This study assessed immunohistochemical (IHC) discordance between primary breast cancer (BC) and brain metastases (BCBM) in a Brazilian population. While 20-40% of BC patients develop BCBM, particularly those with HER2-positive or triple-negative subtypes, phenotypic changes may occur during disease progression, driven by tumor heterogeneity and alterations in the tumor microenvironment (TME). Due to the limited availability of BCBM samples, data on IHC discordance remain scarce. This study aimed to determine the frequency of IHC discordance between primary BC and paired BCBM in a Brazilian cohort, and to explore its associations with clinicopathological and sociodemographic characteristics, as well as its potential impact on survival outcomes.

METHODS

This retrospective cohort study included women who underwent neurosurgical resection for BCBM between January 2015 and December 2022 at the Brazilian National Cancer Institute (INCA). Clinical and pathological data were extracted from medical records. IHC markers — estrogen receptor (ER), progesterone receptor (PR), HER2, and Ki67 — were assessed in BCBM samples and compared with the corresponding archival primary breast cancer specimens. An alluvial diagram was used to visually represent patterns of IHC discordance.

CONCLUSION

A notably high frequency of IHC discordance between primary breast tumors and brain metastases was observed in this real-world Brazilian study, exceeding rates previously reported in the literature. To our knowledge, this is the first Brazilian study to investigate IHC changes in this context, conducted in a population with a high proportion of Black and mixed-race individuals. These results underscore the biological heterogeneity of breast cancer in underrepresented populations and emphasize the need for more precise, individualized management strategies for patients with BCBM.

RESULTS

Among the 105 eligible patients, 67 patients (64%) were Black or mixed-race, mean age was 49 years (SD ±10), and 61 (58%) were premenopausal, as presented in **table 1**. De novo metastatic disease was identified in 15 (14%) patients. Regarding the BC biopsy, most patients (87%) had invasive ductal carcinoma, while 47 (45%) were grade 2 and 48 (46%) were grade 3. HER2-positive subtype was the most frequent: 51 (48%) patients, as shown in **table 2**. Pathological characteristics regarding BCBM are presented in **table 3**.

IHC discordance between primary BC and BCBM was found in 46 (44%) patients, as illustrated in **figure 1**, but this was not associated with differences in survival outcomes, including overall survival (OS) (p = 0.96), recurrence-free survival after BCBM diagnosis (post-BCBM RFS) (p = 0.81), or OS after BCBM diagnosis (post-BCBM OS) (p = 0.53) (**Figure 2**). The most common phenotypic changes were loss of ER/PR expression (35 patients, 76%) and enrichment of HER2 expression (7 patients, 15%). Loss of ER/PR expression was not associated with post-BCBM risk of death (p = 0.52). **Figure 3** shows a tissue microarray (TMA) example from a representative discordant case.

Table 1. Sociodemographic and clinical characteristics of study population

Characteristics	Concordants N (%) 59 (56%)	Discordants N (%) 46 (44%)	Total N (%) 105 (100%)	p-value
Age – Mean (SD)	48 (±11)	50 (±8)	49 (±10)	0.222
Race				0.243
White	18 (30)	20 (43)	38 (36)	
Black/Brown	41 (70)	26 (57)	67 (64)	
Menopausal status				0.492
Pre-menopausal	36 (61)	25 (54)	61 (58)	
Post-menopausal	20 (34)	20 (44)	40 (38)	
Not reported	3 (5)	1 (2)	4 (4)	
Clinical staging				0.204
I	0 (0)	1 (2)	1 (1)	
II	7 (12)	10 (23)	17 (16)	
III	33 (56)	26 (56)	59 (56)	
IV	11 (19)	4 (9)	15 (14)	
Not reported	8 (13)	5 (10)	13 (13)	

Abbreviations: SD: Standard deviation. BMI: Body mass index. ECOG-PS: Performance Status - Eastern Cooperative Oncology Group. HBOC: hereditary breast and ovarian cancer syndrome

Table 2. Pathological characteristics of breast cancer biopsy

Characteristics	Concordants N (%) 59 (56%)	Discordants N (%) 46 (44%)	Total N (%) 105 (100%)	p-value
Histology				0.247
Ductal	49 (83)	43 (94)	92 (87)	
Lobular	1 (2)	1 (2)	2 (2)	
Histopathological grade				
1	0 (0)	1 (2)	1 (1)	0.334
2	29 (49)	18 (39)	47 (45)	
3	25 (42)	23 (50)	48 (46)	
ER status				0.047
Negative	30 (51)	14 (30)	44 (42)	
Positive	28 (47)	32 (70)	60 (57)	
ER expression (%) - Median (IQR)	90 (55 to 100)	60 (31 to 95)	70 (40 to 100)	0.148
HER2 status				0.542
IHC 0	19 (32)	13 (28)	32 (31)	
IHC 1+	5 (9)	4 (9)	9 (9)	
IHC 2+ with negative FISH	2 (3)	3 (6)	5 (4)	
IHC 2+ with positive FISH	1 (2)	4 (9)	5 (4)	
IHC 3+	25 (42)	21 (46)	46 (44)	
Not reported	7 (12)	1 (2)	8 (8)	
KI67 (%) - Median (IQR)	50 (30 to 75)	45 (30 to 75)	50 (30 to 75)	0.986
IHC profile				<0.001
HR+/HER2-	12 (20)	21 (46)	33 (32)	
HR+/HER2+	15 (26)	20 (43)	35 (33)	
HR-/HER2+	11 (19)	5 (11)	16 (15)	
HR-/HER2-	19 (32)	0 (0)	19 (18)	
Not reported	2 (3)	0 (0)	2 (2)	

Abbreviations: IHC: Immunohistochemistry. IQR: Interquartile range. FISH: Fluorescent in situ hybridization. ER: Estrogen receptor. HR: Hormone receptor. PR: Progesterone receptor.

Table 3. Pathological characteristics of breast cancer brain metastases

Characteristics	Concordants N (%) 59 (56%)	Discordants N (%) 46 (44%)	Total N (%) 105 (100%)	p-value
ER status				
Negative	31 (52)	39 (85)	70 (67)	0.001
Positive	28 (48)	7 (15)	35 (33)	
ER expression (%) – Median (IQR)	50 (5 to 82)	50 (27 to 90)	50 (5 to 85)	0.831
HER2 status				
IHC 0	32 (54)	18 (39)	50 (48)	0.186
IHC 1+	0 (0)	1 (2)	1 (1)	
IHC 2+	0 (0)	0 (0)	0 (0)	
IHC 3+	27 (46)	27 (59)	54 (51)	
Ki67 expression (%) – Median (IQR)	15 (5 to 57)	10 (5 to 37)	10 (5 to 40)	0.426
IHC profile				
HR+/HER2-	12 (20)	2 (4)	14 (13)	0.007
HR+/HER2+	16 (27)	7 (15)	23 (22)	
HR-/HER2+	11 (19)	20 (44)	31 (30)	
HR-/HER2-	20 (34)	17 (37)	37 (35)	

Abbreviations: IHC: Immunohistochemistry. IQR: interquartile range. ER: Estrogen receptor. HR: Hormone receptor. PR: Progesterone receptor.

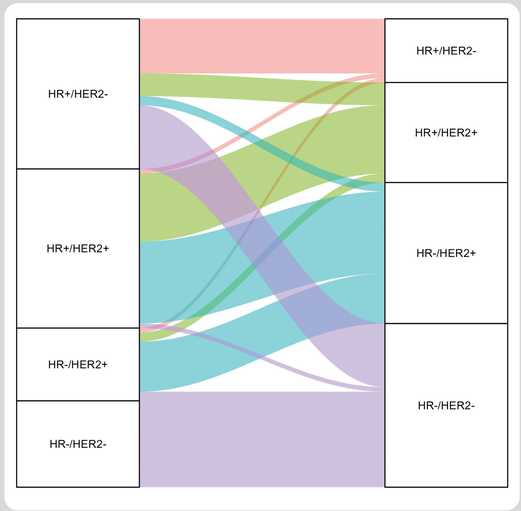


Figure 1. Alluvial diagram illustrating the pattern of IHC discordance between primary BC (left) and paired BCBM (right)

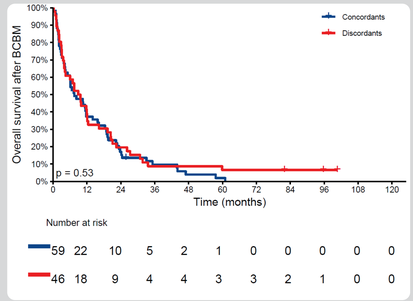


Figure 2. Kaplan–Meier curve of post-BCBM OS stratified by IHC discordance status

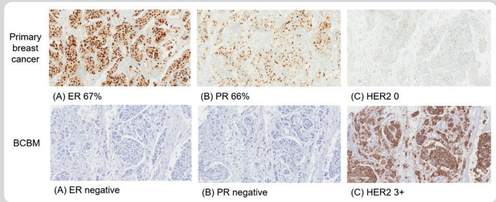


Figure 3. TMA image (20× magnification) showing the intensity grading of IHC staining for ER (A), PR (B), and HER2 (C) of a representative patient with IHC discordance

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