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BRCA1 AND MICRORNAS 7, 10B, 205AB, 218A EXPRESSION AS PROGNOSTIC MARKERS IN PRIMARY BREAST CANCERS – A RETROSPECTIVE COHORT STUDY

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Micro-RNAs (miRs) are post-transcriptional regulators of gene expression involved in several important biological processes. BRCA1 is a tumor suppressor gene and BRCA1-silent breast cancers (BC) tend to be more aggressive. Since BRCA1 may be regulated at post-transcriptional level by miRNAs, the purpose of this study was to evaluate the prognostic value of human miR-7, miR-10b, miR-205ab and miR-218b and BRCA1 expression levels in BC. A set of 36 triple-negative (TN) and 56 nontriple-negative (NTN) breast tumors was analyzed. Total miRNA was extracted from formalin-fixed paraffin-embedded (FFPE) BCs collected from the Pathology Department of Araújo Jorge Hospital-ACCG (Goiânia, Goiás, Brazil). MiRs expression was quantified by Quantitative Real-Time PCR (qRT-PCR) and BRCA1 expression was evaluated by immunohistochemistry (IHC). The present study was approved by the institutional Ethics Committee of Araújo Jorge Hospital (Report n° 948.930, 2015). The relative expression levels of miRs and clinic pathological features of breast cancers were compared. Overall survival in 60 months was 72.8%, and it was influenced by TNBC phenotype (p=0.044), tumor size (p=0.007), lymph node involvement (p=0.038), distant metastasis (p=0.0008), BRCA1 negative expression (0.039), miR-7 (p=0.026) and miR-10b (p=0.011) overexpression. MicroRNA hsa-miR-7 overexpression was associated with larger tumors (>2 cm) (p=0.041), higher histological grade (p=0.028), TN phenotype (p=0.012), BRCA1-negative expression (p=0.047) and worse survival (p=0.026). Overexpression of hsa-miR-10b was associated with larger tumors (p=0.047), lymph node (p=0.032) and distant metastases (0.019), higher histological grade (p=0.009), TN phenotype (p=0.027), BRCA1-negative expression. (p=0.006) and worse survival (p=0.011). Meanwhile, underexpression of hsa-miR-205ab was associated with larger tumors (p=0.027), lymph node (p=0.046) and distant metastases (p=0.014), BRCA1-negative expression (p=0.027), TN phenotype (p=0.038) and worse survival (p=0.024). While, hsa-miR-218a underexpression was associated with a larger tumor size (p=0.032), lymph node (p=0.011) and distant metastases (p=0.022), TN phenotype (p=0.019), negative expression of BRCA1 (p=0.039) and worse survival (p=0.003). Our results show that BRCA1 protein expression assessment, miR-7 and miR-10b overexpression and miR-205ab and miR-218b underexpression could be useful in evaluating BCs prognosis, especially for patients with triple negative tumors.