Relationship between genetic polymorphisms of methylenetetrahydrofolate reductase and breast cancer chemotherapy response

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ABSTRACT. Activity of methylenetetrahydrofolate reductase (MTHFR), an enzyme involved in folate metabolism, is influenced by mutations in the corresponding gene, contributing to a decrease in 5,10-MTHF. Due to such polymorphisms, individuals differ in MTHFR enzyme activity and plasma folate levels. We investigated the relationship between two common *MTHFR* polymorphisms (C677T and A1298C) and breast cancer (BC) chemotherapy response. From February 2013 to January 2016, 148 advanced BC patients at the Center Hospital of Cangzhou were enrolled and treated with six different chemotherapy regimens. Subjects were genotyped using polymerase chain reaction-restriction fragment length polymorphism. Forty-one (27.7%), 70 (47.3%), and 37 (25.0%) patients carried the C/C, C/T, and

T/T C677T genotypes, respectively; 101 (68.2%), 42 (28.4%), and 5 (3.4%) had the A/A, A/C, and C/C genotypes of A1298C, respectively. Total chemotherapy efficacy was 66.9% (99/148), with 7 (4.7%), 92 (62.2%), 36 (24.3%), and 13 (8.8%) cases showing complete response, partial response, no change, and progressive disease, respectively. Chemotherapy regimens did not differ in effectiveness ($P > 0.05$). Efficacy rates associated with C677T C/C, C/T, and T/T genotypes were 58.5, 58.6, and 91.9%, respectively, with T/T carriers exhibiting significantly better responses than the C/C ($P < 0.05$) and C/T groups ($P < 0.05$). Effectiveness among A1298C A/A, A/C, and C/C carriers was 70.6, 64.3, and 0.0%, respectively, but no difference was established between these genotypes in this regard ($P > 0.05$). The *MTHFR* C677T genotype may be associated with BC chemotherapy response, and could be of great value in guiding individualized treatment for this disease.

Key words: Genetic polymorphisms; Chemotherapy sensitivity; Methylenetetrahydrofolate reductase; Breast cancer