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Technology Assessment

FLOW CYTOMETRIC ANALYSIS OF CYTOTOXIC T-CELL SUBPOPULATIONS CHANGES INDUCED BY ANTHRACYCLINE-BASED CHEMOTHERAPY IN ADVANCED BREAST CANCER PATIENTS

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INTRODUZIONE

Anthracycline-based chemotherapy (CT) is a conventional treatment for breast cancer and it has been thought to be immunosuppressive by negatively affecting the pt immune system. However, increasing evidences suggest the concept of "immunogenic" CT, indicating that some cytotoxic drugs can also induce a tumor-specific immune response in different tumors. Experimental evidences and clinical studies in breast cancer (BC) suggest that some anti-tumor therapies generate a stimulation of the immune system that accounts for tumor clinical responses. The concept of immunomodulation via CT (with or without the association with target therapies) opens possible clinical applications in BC but the variability in immune responses induced by CT requires a careful pt selection. Also, monitoring functional competence of immune cell populations in clinical routine represents a major technical challenge so that changes in sub-populations of cytotoxic (CD8+) T-cells, which have been reported in aging and in conditions of chronic immune stimulation, are not well documented in patients with advanced cancer undergoing CT.

METODI

Using a high-resolution multiparametric flow cytometry whole-blood assay CD8+ T-cell subsets were analyzed in 29 pts (median age 52, range 34 - 72 yrs) with advanced BC undergoing anthracycline-based CT and in an older control group of 12 healty women during a 6-month longitudinal study, to explore variations in CD8+ T-cells and the effects of CT on different T-cell sub-populations.

RISULTATI

As expected, in all BC pts there was a consistent decrease in absolute numbers of leukocytes, lymphocytes, T-cells and CD8+ T-cells, starting from the first course and persisting during all the CT program. Among the T-cells, there was a lower CD8-/CD8+ ratio, persisting over 6 months, in pts compared to controls. The proportion of CD28-CD57+ cells also remained higher among pts with cancer throughout the sampling duration. The number of CD28+CD57- and CD28-CD5- cells decreased faster during CT than CD28+CD57+ and CD28-CD57+ cells, while only CD28-CD57- cells showed a significant reconstitutive capacity after 6 months

CONCLUSIONI

Recently, it has been reported that anti-tumor therapy in BC pts can produce clinical benefits by restoring the responsiveness of T cells and by increasing the frequency and activation in peripheral blood of tumor specific T cells present in the tumor before therapy. We have confirmed that Anthracycline-based CT is able to elicit several changes in some immune-related parameters in these pts, including the composition and phenotype of immune cells. The immune system is weakened by age-related changes in immune responses and in our study these changes appeared to be more pronounced in BC pts, with senescent CD8+ T-cells playing an important role. Notably, the normal condition was not restored after 6 months of CT. Our results reinforce the importance of monitoring, using multi-parameter flow cytometry based assays, patient's immune parameters during cancer CT.