LETTER TO THE EDITOR

Surgery-Induced Immunomodulation and the Importance of the Perioperative Period

Recently, we have reported our finding in this Journal that breast cancer surgery produces substantial immunomodulation as indicated by decreased HLA-DR expression, decreased NKCA, and a pro-inflammatory response [1]. Chen et al. [2] agreed with our overall-conclusion in their comment, but brought forward some questions. It is the purpose of our reaction to underline once more the importance of surgery-induced immunomodulation and to advance some remarks on how to subdue this response and why the focus is mainly on innate immunity.

In 1999, we have demonstrated that conventional fundoplication results in an activation of the systemic immune response and in immunosuppression [3], which was weaker in a laparoscopic approach. We have later shown that in colorectal carcinoma surgical trauma is directly related to peritoneal cancer recurrence [4]. Moreover, we have demonstrated in a pilot study that low doses of perioperative immunomodulation could partly counteract this immunosuppression [5]. Recently, we have put forward the thesis that the perioperative period is an underutilized window of therapeutic opportunity in patients with colorectal cancer [6]. We also showed that we could prevent surgery-induced liver metastasis through antibody therapy, which was mediated by the innate immune network [7]. This result is in agreement with the findings of other researchers working in this field [8].

According to the opinion of Chen et al. a measurement of Th1 and Th2 cytokines in serum would be more convincing, whereas we measured the capacity of PMBCs to produce cytokines. From our earlier data (see above) we have concluded that surgery-related immunomodulation is mainly mediated by the innate immune network and that cytokines produced in vitro better represent the immunomodulation response than measurements in vivo, which were suggested by Chen et al. These authors also question whether IL-12 is a typical Th1 cytokine and whether IL-6 is a typical Th2 cytokine, as we suggested. However, even when these two cytokines are left out of consideration, our conclusion about the cytokine shift still holds. Finally, we and others have recently described that macrophages and—among the macrophages—the balance between M1 and M2 macrophages [9] play a major role in tumor development [10], which can partly be related to IL-12 (being a M1 cytokine).

Chen et al. are also interested in the relationship between breast cancer staging and the peri-surgical cytokine/cortisol alteration. However, patients with distant metastases were excluded in our study, and the number of patients with stage II was only 11%. We can also exclude peri-operational infection as a confounder, since we did not encounter this complication in our study population.

In conclusion, we [1,2] agree on the overall-conclusion that breast cancer surgery also produces immunomodulation and that future studies should be directed to prevent or utilize this effect, which is presently a hot topic [1,2,7,8].

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