The importance of the VEGF-load in platelets in cancer patients

We read with interest the paper published by Colleoni and colleagues in which they measured pre- and post-treatment, serum and plasma levels of vascular endothelial growth factor (VEGF) and also platelets, in metastatic breast cancer patients [1]. Although they also analysed antitumor activity with methotrexate and cyclophosphamide in a larger number of patients \((n = 64)\), this letter will focus on the patient population with VEGF and platelet measurements \((n = 48)\).

Their finding that serum VEGF levels decrease after therapy is intriguing, especially when compared with the unaltered levels of plasma VEGF and platelets found after therapy for the whole patient population studied.

In a previous study, we measured serum and plasma VEGF levels and interleukin (IL)-6 in the vein draining colorectal tumours (vena mesenterica) [2]. We found that: 1) serum VEGF levels are \(~10\)-fold higher than plasma VEGF, in accordance with previous findings; 2) serum VEGF was not derived from the primary tumour in these patients; 3) IL-6 was consistently produced by the tumours, illustrated by the high IL-6 levels in the vein draining the tumour.

We and others have previously demonstrated that the VEGF-load in platelets accounts for the vast majority of the high serum VEGF levels encountered in patients with advanced cancer. We hypothesised that the higher platelet VEGF load found in cancer patients may be due to a tumour-derived cytokine (IL-6?)-mediated enhancement of VEGF-production in platelet precursors [3, 4]. The importance of a higher VEGF-load in platelets is illustrated by the association between high platelet VEGF-load and fast tumour growth kinetics and worse prognosis in patients with cancer [5, 6].

The findings of Colleoni and colleagues that serum VEGF levels decrease, but not plasma VEGF levels or platelet count, may be partly explained by a diminished platelet VEGF content in these patients. Furthermore, it is tempting to speculate that cyclophosphamide and methotrexate therapy in these patients affected the release of tumour-produced IL-6, here-with accounting for the lower platelet VEGF-load, and thus serum VEGF, without affecting tumour-production and release of plasma VEGF. Analysing and comparing the platelet VEGF load in their respective groups could help to explain the findings of Colleoni and colleagues.

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References


DOI: 10.1093/annonc/mdf320