Bevacizumab is active in malignant effusion

VEGF is supposed to play a major role in the pathogenesis of malignant and non-malignant effusions [1]. We recently reported on a patient with cardiac amyloidosis suffering from refractory pleural effusion [2]. He was successfully treated with a single dose (5 mg/kg) of the anti-VEGF antibody bevacizumab [3]. In contrast, no significant reduction of malignant effusions was seen in two cancer patients after treatment with bevacizumab using an identical dose. It is well known from the literature that malignant effusion is associated with high levels of VEGF in serum/plasma as well as in malignant effusions [4]. This and our observations led to the assumption that ‘conventional’ dosages of bevacizumab might be too low to treat malignant effusions successfully. This was based on our finding that one of the two patients in whom bevacizumab was not effective still had high VEGF plasma levels after administration of 10 mg bevacizumab per kg. The other patient (heavily pretreated for NSCLC) experienced a slight reduction of her pleural effusion after having received a second dose of bevacizumab which was associated with a decrease of the VEGF plasma level from 89 pg/ml (after the first dose of bevacizumab) to 23 pg/ml.

Therefore, a higher bevacizumab dose (15 mg/kg) was applied in two patients (one with pretreated metastatic colon cancer, the other with pretreated adenocarcinoma of unknown origin) with malignant ascites requiring centesis every 1 to 2 weeks. One patient had centesis prior to bevacizumab treatment, the other patient refused centesis. Pretreatment VEGF plasma levels were 347 and 178 pg/ml, respectively. Treatment with bevacizumab was successful in both patients. In the patient who needed weekly centesis prior to bevacizumab, ascites did not reappear during a follow-up of 6 weeks. In the second patient, a significant reduction of ascites was observed within two days. Of interest, both patients had a marked decrease of their VEGF plasma level after bevacizumab treatment (30 and 27 pg/ml from 347 and 178 pg/ml, respectively). In order to measure the total VEGF load including VEGF stored in platelets, we also determined VEGF serum levels and found that pretreatment VEGF levels in serum were considerably higher than pretreatment VEGF levels in plasma (1.957 versus 347 pg/ml; 3.148 versus 178 pg/ml). However, after therapy with bevacizumab, there was no difference between serum and plasma (25.9 versus 30; 33 versus 27). These data suggest that the total VEGF load was almost completely neutralized by bevacizumab.

We conclude from our preliminary experience that treatment of malignant effusion with bevacizumab might require higher dosages than treatment of the underlying cancer. Responding patients had higher bevacizumab dosages and lower VEGF levels as compared to non-responders.

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References


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