Severe drug-induced thrombocytopenia after treatment with trastuzumab but not with lapatinib

Drug-induced thrombocytopenia can be caused by many different medications [1]. We recently reported the case of a 54-year-old woman with metastatic breast cancer who developed severe thrombocytopenia within 4 days after the first trastuzumab infusion [2]. Platelet count recovered completely after treatment with high-dose steroids and intravenous immunoglobulins. Remarkably, the patient experienced a partial remission of the metastatic retroperitoneal lymphadenopathy after the single dose of trastuzumab. Moreover, the tumor markers carcinoembryonic antigen and CA 15-3 normalized. Subsequently, treatment consisted of antihormonal treatment with an aromatase inhibitor and stable disease was observed for 10 months. At this time point, the patient was found to have new liver lesions. In view of the uncommon clinical course, a biopsy of one of the lesions was carried out. Histology confirmed the presence of invasive ductal adenocarcinoma. Immunohistochemistry showed complete negativity for estrogen and progesterone receptors but HER2/neu was 3+ positive. In view of persistent overexpression of HER2/neu, we decided to treat the patient with lapatinib, a dual HER1 and HER2 oral tyrosine kinase inhibitor. The treatment with lapatinib (1250 mg daily) was well tolerated. Platelet count was monitored closely and the levels remained within normal range during the first 3 weeks of lapatinib monotherapy. Moreover, a significant decrease of the tumor markers was noticed. In view of the good tolerance, capecitabine (1000 mg/m² bd d1–14) was added from day 22 as planned and according to clinical trials [3]. The patient achieved a partial remission with a total of six cycles combination treatment and no unexpected toxicity occurred.

It has been reported that monoclonal antibodies that affect the immune response can cause thrombocytopenia similar to autoimmune thrombocytopenia. Although the exact mechanisms are unknown [1], this could be the reason for the trastuzumab-associated severe thrombocytopenia in our case. For tyrosine kinase inhibitors, no such observations have been described. Regarding lapatinib, integrated data from four monotherapy studies with lapatinib and two large randomized trials in metastatic breast cancer have reported only very low rates of thrombocytopenia (Table 1). The events were predominantly of grades 1 and 2 [3–5]. Therefore, we feel that lapatinib can be used safely in patients who have experienced severe thrombocytopenia with trastuzumab.
Table 1. Incidence of thrombocytopenia in clinical trials with lapatinib

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<th>Integrated lapatinib monotherapy (N = 452)</th>
<th>EGF30008 letrozole + lapatinib (N = 654)</th>
<th>EGF100151 lapatinib + capecitabine (N = 198)</th>
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<tbody>
<tr>
<td>Thrombocytopenia (all grades), %</td>
<td>≤1.0</td>
<td>1.0</td>
<td>2.0</td>
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references

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