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Falsely Low Results in CA 125 Determination Due to Anti-Idiotypic Antibodies Induced by Infusion of [^{131}I]F(ab′)$_2$ Fragments of the OC125 Antibody

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Summary: We investigated a one-step immunometric CA 125 assay, which employs new anti-CA 125 antibodies as capture antibodies and OC125 antibodies for detection, for interference due to antibodies induced by repeated administration of F(ab′)$_2$ fragments of the anti-CA 125 antibody OC125. Testing 33 samples, obtained from 13 patients treated with OC125 fragments, we found falsely high CA 125 concentrations only in samples with exceptionally high concentrations of both anti-idiotypic antibodies and non-specific human anti-mouse antibodies. In contrast, the recovery of added CA 125 was already diminished in the presence of low anti-idiotypic antibody concentrations. Both interferences disappeared after removal of serum IgG. It was possible to eliminate the falsely high results, but not the reduction in recovery rate, by adding non-specific murine IgG. When the binding of the detector antibodies was performed in a separate incubation step, no reduction in recovery rate was observed. Our results suggest that non-specific human anti-mouse antibodies are responsible for falsely high results. The reduction in the recovery rate is obviously due to an inhibition of the binding of OC125 detector antibodies by anti-idiotypic antibodies. In patients receiving OC125 antibodies CA 125 can be measured using OC125 detector antibodies if a two-step assay is performed. An increase in CA 125 following OC125 infusion should be confirmed after the addition of non-specific murine IgG.

Introduction

For the last couple of years the murine monoclonal antibody OC125, initially developed by *Bast* et al. (1, 2) to measure immunometrically the concentration of CA 125 in the serum of ovarian cancer patients, has also been used in vivo for radioimmunodetection of CA 125 (3, 4). Recently we demonstrated that in vivo application of F(ab′)$_2$ fragments of the OC125 antibody is useful for therapy of ovarian cancer as well, leading to a significant prolongation of the survival rate of patients (5–7).

One effect of in vivo application of OC125 F(ab′)$_2$ fragments is the induction of antibody formation (8). In a previous investigation we demonstrated that among the antibodies directed against epitopes common to all murine antibodies, anti-idiotypic antibodies directed against the hypervariable region of the applied F(ab′)$_2$ fragments are formed as well (9). These anti-idiotypic antibodies interfere with the determination of CA 125 when a homologous immunometric assay with OC125 antibodies as both the immobilized and the labelled antibody is used. In an assay of this kind, anti-idiotypic antibodies can cross-link both antibodies, resulting in falsely high values for CA 125 (9, 10). Obviously, the occurrence of falsely high values can be eliminated using other anti-CA 125 antibodies on the solid phase (9, 11, 12). However, in two test kits involving various anti-CA 125 capture antibodies we observed falsely low results in samples with elevated concentrations of anti-idiotypic antibodies (11, 12). Our results suggested that depending on the test protocol, anti-idiotypic antibodies can reduce the assay response resulting in falsely low values for CA 125, especially when OC125 antibodies are used for detection.