Autoantibodies to p53 can Predate a Clinical Diagnosis of Ovarian Cancer - A Case Report

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Aim

There is currently no screening tool for ovarian cancer (OvCa). A high CA125 level is useful in predicting OvCa recurrence but is not a reliable biomarker for diagnosing the disease at an early stage, and can be found associated with benign conditions.

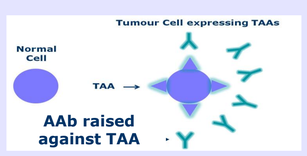
Autoantibodies (AAbs) to tumor-associated antigens (TAAs) have been described in a variety of cancers, and in some cases even detected prior to clinical presentation. Such AAbs have not however been described in individuals with pre-symptomatic OvCa.

The presence of AAbs to TAAs were investigated in an individual with myasthenia gravis (MG) who subsequently developed OvCa.

Background

Mutated, over-expressed, aberrantly expressed or post-translationally modified tumour associated antigens can often elicit a detectable autoimmune response.[1-3]

AAbs can provide an *in vivo* amplification of carcinogenesis, in some cases months to years before the tumour becomes otherwise clinically detectable.[3]



AAbs have been reported as being of diagnostic potential in a range of solid tumours.[1-5]

AAb testing is ideally suited to 'at-risk' groups in the population who are pre-disposed to developing cancer.

Patients and Methods

A 58 year old female with MG presented at the emergency room of her local hospital suffering from chest pain. Subsequent investigations identified OvCa.

CA125 levels were tested at the point of cancer diagnosis, at various time points up to 10 months post-cancer diagnosis as well as on a stored serum sample from a time when there were no symptoms of disease.

AAbs to a panel of 7 TAAs were measured, using the *Early*CDT®-Lung assay[4,5] , at 13 months pre-cancer diagnosis and 10 months post-cancer diagnosis. Optical densities (OD) were converted to calibrated reference units (RU)[4] and compared to commercial cut-offs.

Date of Sample	CA125 Levels
1. 01/02/2009	CA125 **17** U/ml **(CA125 and AAbs level measured in 2011)**
2. 09/03/2010	CA125 **982** U/ml Cancer Diagnosis
3. 16/03/2010	CA125 **792** U/ml
4. 14/04/2010	CA125 **838** U/ml (patient started chemo - 05/05/2010)
5. 14/06/2010	CA125 **102** U/ml
6. 29/06/2010	CA125 **56** U/ml
7. 21/07/2010	CA125 **38** U/ml
8. 10/08/2010	CA125 **25** U/ml (6 cycles chemo ended - 18/08/2010)
9. 06/12/2010	CA125 **29** U/ml
10. 06/01/2011	CA125 **564** U/ml
11. 17/01/2011	CA125 **926** U/ml **(AAbs measured)**

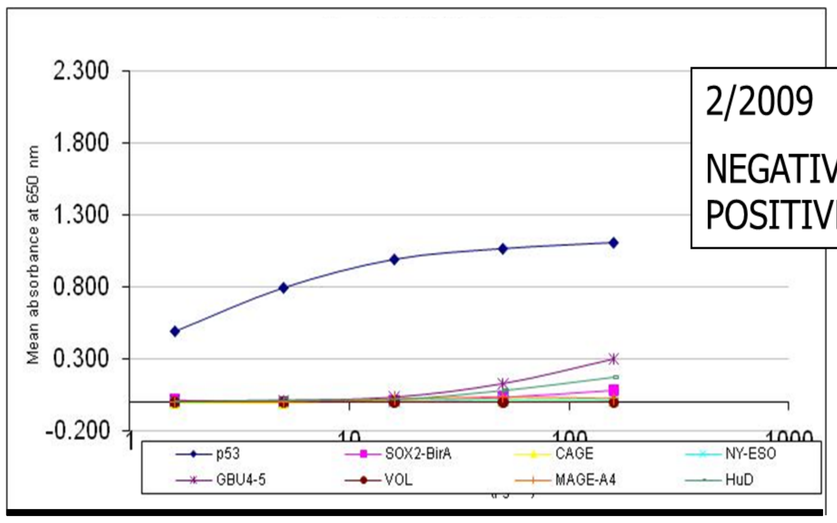
Results

CA125 levels were normal 13 months before the cancer presented clinically (17U/ml).

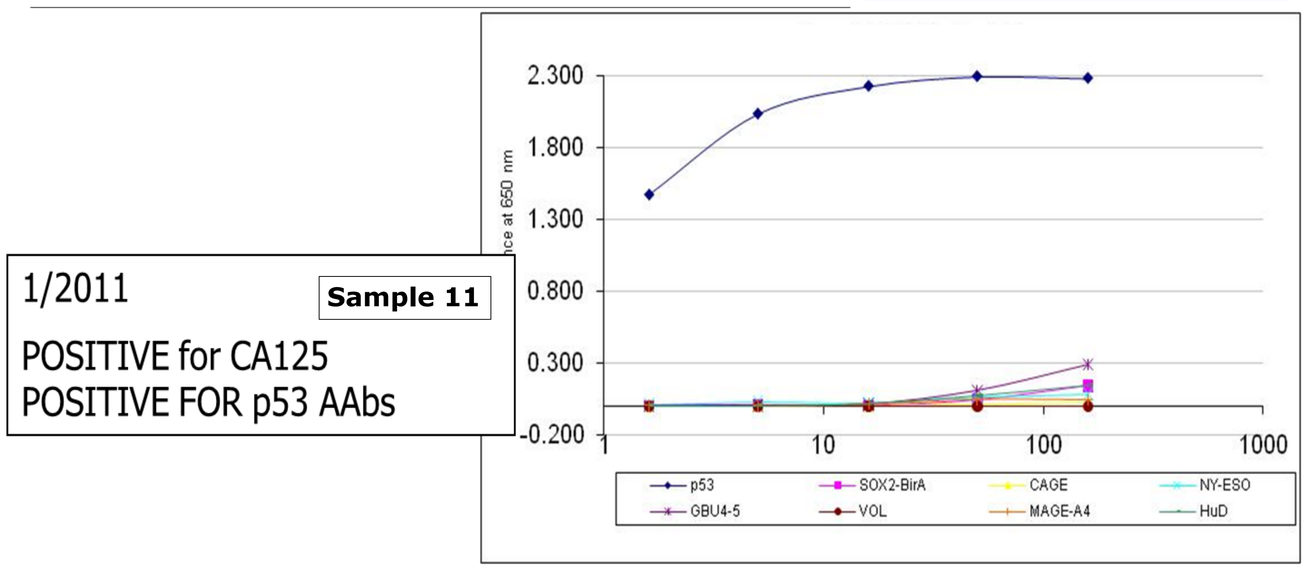
CA125 levels were raised at the point of diagnosis (982 U/ml) (when the patent presented with advanced disease), dropped during treatment but were again high (929 U/ml) 10 months post diagnosis.

AAbs to p53 were found to be elevated above cut-off (cut off RU =4.31) in both the pre-diagnostic (RU - 5.29) and post-diagnostic sample (RU - 8.11) (Figure 1).

Figure 1. Titration curves (at 2 time points: 01/02/2009 & 17/1/2011) showing AAbs in a patient with MG who subsequently developed OvCa



Curves demonstrate that levels of AAbs to p53 are beginning to rise (top curve – time point 1: 2/2009) before clinical presentation of the disease.



Discussion and Conclusion

AAbs to p53 have been described previously in a number of individuals with OvCa but due to the usual late presentation of this disease, pre-diagnostic samples are rarely available for analysis.

Here we describe raised levels of AAbs to p53 in the serum of an individual 13 months before she presented with clinical symptoms. Whilst it is unknown how early this was in the course of the disease, and is only a single patient case study, it clearly demonstrates that AAbs to p53 can also be found in pre-diagnostic samples in OvCa, as has been described in lung cancer.

Measurement of a panel of AAbs optimised for the detection of OvCa cancer may, in the future, provide an aid to the clinician for early diagnosis.

References

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Acknowledgments

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