Autoantibodies in Ovarian Cancer

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Background

Most ovarian cancers are diagnosed at an advanced stage and the outlook for better prognosis depends on early diagnosis. Autoantibodies can be elicited in cancer patients and have been described in patient sera before cancer-associated antigens can be detected, and even before clinical symptoms present.

Aims

To assess the presence and diagnostic potential of a panel of tumour-associated autoantibody profiles in ovarian cancer.

Patients and Methods

Sera from epithelial ovarian cancer patients (n=104), age-matched normal controls (n=104), patients with borderline ovarian malignancy (n=12) and patients with benign ovarian masses (n=65) were investigated for the presence of autoantibodies to seven bacterially produced tumour-associated antigens (NY-ESO-1, CA125, HOXA7, SPAG9, lamin A, TRAG3 and Cathepsin D) by enzyme-linked immunosorbent assay.

Results

- At a specificity for the detection of ovarian cancer of 95%, compared to normal age-matched controls, 22% of individuals with ovarian cancer had raised levels of autoantibodies to at least one of the panel of tumour-associated antigens whereas only 6% of individuals with benign conditions, and 1% of those with borderline malignancies had raised autoantibodies (Table 1 & figure 1).
- Staging was available on 97 samples and the panel detected 38% stage 1 (5/13), 21% stage 2 (11/52), 23% stage 3 (7/30) and 0% (0/2) stage 4 cancers (Table 2).
- The highest level of autoantibody positivity was to NY-ESO-1 (13%) and CA125 (8%) in ovarian cancer sera.

Figure 1. Scatter dot plots showing levels of autoantibodies to CA125, NYESO-1, HOX7,SPAG9, lamin A, TRAG3 and Cathepsin D.

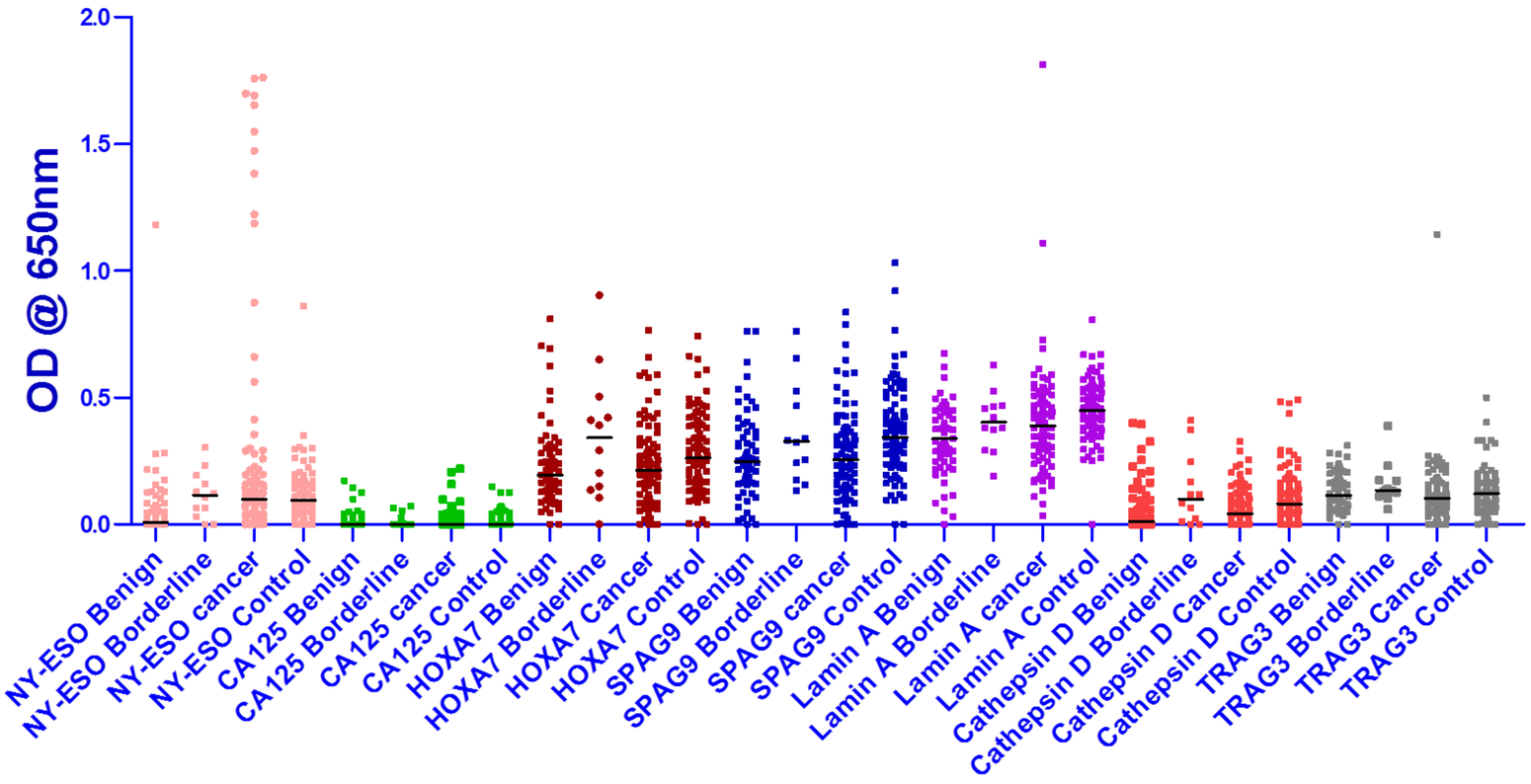

Table 1. Autoantibody assay sensitivity and specificity (per patient group) using a cut-off for positivity as a value greater than the mean+4SD of the matched control group.

Antigen	Sensitivity [Number/(%)]			Specificity
	Malignant (n=104)	Borderline (n=12)	Benign (n=65)	Normal (n=104)
NY-ESO-1	14 (13%)	0	1 (1.5%)	99%
CA125	8 (8%)	0	3 (4.6%)	98%
HOXA7	1 (1%)	1 (1.5%)	0	100%
SPAG9	0	0	0	99%
Lamin A		0	0	99%
Cathepsin D		0	0	99%
TRAG3		0	0	99%
Panel (1 of 7)		1 (1.5%)	4 (6%)	95%

Table 2. Autoantibody assay sensitivity and specificity in ovarian cancer by tumour stage. Positivity calculated as detailed in Table 1.

AAB responses [(positive / number tested (%)] cut-off=mean+4SD							
Stage	**NY-ESO-1**	**CA125**	**HOXA7**	**SPAG9**	**Lamin A**	**Cathepsin D**	**TRAG3**	**Panel (1 of 7)**
Stage I	3/13 (23)	1/13 (7.6)	0/13 (0)	0/13 (0)	1/13 (8)	0/13 (0)	2/13 (15)	5/13 (38.4)
Stage II	7/52 (13.3)	3/52 (5.7)	0/52 (0)	0/52 (0)	1/52 (2)	1/52 (2)	0/52 (0)	11/52 (21)
Stage III	4/30 (13.3)	4/30 (13.3)	1/30 (3.3)	0/30 (0)	0/30 (0)	0/30 (0)	0/30 (0)	7/30 (23.3)
Stage IV	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)	0/2 (0)

Conclusions

Autoantibodies to tumour associated antigens could be detected in individuals with ovarian cancer and, as in the case of lung cancer, appear to be elevated at early as well as late stages of disease and therefore provide an opportunity for early detection. Detection of autoantibodies to an optimised panel of antigens may aid the clinician in identifying early stage disease.

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