Serum CA125 elevation is independently associated with serositis in SLE patients

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Abstract

Objective

Some studies have reported that serum CA125 level is elevated in SLE patients, and elevated CA125 level may be associated with kidney involvement and disease activity in SLE. However, none of the previous studies controlled confounding variables and the results remained controversial. The present study was aimed to investigate whether elevated serum CA125 level is independently associated with clinical and laboratory features of SLE by excluding various confounders in Chinese patients.

Methods

A total of 156 SLE patients, consisting of 139 women and 17 men, were included in the study. Some clinical and laboratory characteristics of the patients were obtained by medical record review. Serum CA125 levels were measured by electrochemiluminescence immunoassays.

Results

Compared with patients with normal CA125, those with elevated CA125 had significantly more serositis (37.5% vs. 1.9%, p<0.001) and lung involvement (37.5% vs. 12%, p=<0.001), higher SLEDAI scores (p<0.007). Furthermore, disease duration was significantly longer in those with elevated CA125. Univariate logistic regression analysis showed that elevated serum CA125 level was closely associated with disease duration (OR, 95%CI:1.005, 1.001–1.010; p=0.014), serositis (OR, 95%CI: 32.258, 6.993–142.857; p<0.001), renal involvement (OR, 95%CI: 2.283, 1.114–4.673; p=0.024), lung involvement (OR, 95%CI: 4.386, 1.927–10.000; p<0.001) and SLEDAI scores (OR, 95%CI: 1.098, 1.027-1.174; p=0.006). After controlling for various confounding variables, serositis and disease duration were the only two clinical variables significantly associated with elevation of serum CA125 level. The best cut-off value for CA125 using the ROC curve was 38 kU/L (sensitivity 85%, specificity 75%) and the area under the ROC curve was 0.777 with 95%CI of 0.685–0.868 (p<0.001). Furthermore, the serum CA125 levels can fall into the normal range again with the improvement of serositis.

Conclusion

Of various clinical and laboratory variables of SLE, only serositis is independently associated with serum CA125 elevation.

Key words

CA125, systemic lupus erythematosus, serositis

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Introduction

CA125 is a glycoprotein originally detected by a murine monoclonal antibody (OC125) that reacted with tumour cells from epithelial ovarian cancer (EOC) (1). Since then, CA125 has been widely used as a biomarker for evaluation of women with a pelvic mass and management of EOC. Actually, serum CA125 levels can be elevated by a number of common benign gynecologic and medical conditions, including endometriosis, leiomyomas, congestive heart failure, cirrhosis, benign pleuropulmonary diseases and some autoimmune diseases, *i.e.* systemic lupus erythematosus (SLE), rheumatoid arthritis, systemic sclerosis, etc. (2-8).

Systemic lupus erythematosus (SLE) is a complex autoimmune disease of unknown etiology, characterised by chronic immune activation and multiple immunologic phenotypes (8). SLE can involve various organ systems, including skin, musculoskeletal system, nervous system, haematologic elements, kidneys and serosal membranes. It has been previously reported that serum CA125 level is also elevated in SLE patients. Moreover, elevated CA125 level may be associated with kidney involvement and disease activity in SLE. Yet, the results remain controversial. For example, Szekanecz et al. reported a significant association of serum CA125 level with disease activity, but no association with kidney involvement of SLE, while it was opposite in another report by Miret *et al*. (9-10). The reasons may lie in two points. The first one is that the numbers of SLE patients included in these two reports are too small (40 in one report, 59 in the other). The other one is that a number of confounders such as serositis, lung or liver involvement and malignancies, can cause elevation of CA125. Therefore, the clinical significance of elevated CA125 level in SLE patients needs to be further evaluated. To determine whether elevated serum CA125 level is independently associated with clinical and laboratory features of SLE, we conducted the study of a relatively large number of Chinese patients by excluding various confounders.

Patients and methods

Patient data

In this study, 156 SLE patients, consisting of 139 women and 17 men, were consecutively included from Changzheng Hospital, affiliated with the Second Military Medical University. The median age at onset of SLE and disease duration were 34 years (range: 11–77 years) and 12 months (range: 0.1–400 months), respectively. All patients were Chinese and met the 1997 revised American College of Rheumatology (ACR) SLE criteria (11). Some clinical and demographic characteristics and laboratory data of the patients were obtained by medical record review, including age, sex, medical history, other diseases, erythrocyte sedimentation rate (ESR), serum CA125, autoantibodies, hypersensitive C-reactive protein (hsCRP), immunoglobulins (Ig), etc. Of note, various clinical manifestations were assessed by physical examination, standard imaging techniques or laboratory tests. None of the patients ever had any malignancies. Moreover, all patients were further assessed by clinical sign analysis, chest x-ray or computer tomography (CT), abdominal ultrasound or CT, general laboratory analysis, as well as, if necessary, mammography or endoscopy in order to rule out underlying malignancies. Concurrent infections were also excluded by clinical analysis, laboratory analysis and if necessary, more detailed examinations and cultures. Lupus renal involvement was identified by the presence of at least one of the following four criteria (12): 1) persistently elevated urinary pH value (≥6.0); 2) persistently elevated serum creatinine level (>1.5 mg/dl or 132.5μmol/L) and/or impaired creatinine clearance (<50ml/min); 3) persistent proteinuria (≥500mg/day) for more than 3 months; 4) a pathologic urine sediment (consisting of >10 red blood cells per high-power field or red blood cell casts), which was confirmed by kidney biopsy according to the standard criteria. Serositis included pleurisy, pericaditis and peritonitis. Pleurisy was defined as pleuritic chest pain with pleural rub or effusion, or pleural thickening; pericaditis as pericardial pain with at least 1 of the following, rub, effusion, or

electrocardiogram or echocardiogram confirmation and peritonitis as either diffuse abdominal pain, with rebound or guarding, and/or ascites or bowel wall edema in the absence of other causes (13). Noteworthily, lung involvement, in this study, included lung infection, SLE-related lung involvement and interstitial pneumonia, but pleurisy was not considered as a lung involvement. The Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score (14) was determined for each patient at the time of the blood draw for laboratory tests. The study was approved by the research ethics committee of our institution and signed informed consents were obtained from all subjects.

Statistical analysis

All computations were performed using SPSS 10.0 statistical software. Since all the continuous variables were non-normally distributed by graphical and statistical examination for normality, data were presented as median and interquartile ranges (IQR). Categorical variables were reported as frequencies and percentages. The associations between clinical or laboratory characteristics and elevated serum CA125 level were analysed with chi-square test for categorical variables and Mann-Whitney U-test for continuous variables. In addition, all the variables were included in the univariate logistic regression analysis for the calculation of odds ratios (ORs) and 95% confidence intervals (CI). Significant variables with $p<0.05$ were included in the multivariate logistic regression analysis to exclude confounding variable interference. A receiver operating characteristic (ROC) curve was plotted and the area under the ROC curve (AUC) was calculated to assess the diagnostic strength of CA125 for serositis in SLE. A p-value of <0.05 was considered significant.

Table I. Association between elevated CA125 level and clinical and laboratory categorical variables in SLE patients.

Clinical and laboratory characteristics	Patients with elevated CA125 level (n=48)	Patients with normal CA125 level (n=108)	p-value
Female (%)	89.6	89.9	0.430
Age at onset(median, IQR, years)	34 (26-44)	36 (26-49)	0.795
Disease duration(median, IQR, years)	48 (5-102)	12 (2-50)	0.014
Fever (%)	22.9	19.4	0.779
cutaneous manifestations (%)	27.1	33.3	0.556
Oral ulcer (%)	6.3	16.7	0.132
Alopecia (%)	8.3	9.3	0.938
Arthritis (%)	29.2	39.8	0.274
Raynaud's phenomenon (%)	4.2	3.7	0.755
Secondary SS (%)	8.3	5.6	0.764
Neurologic disorder (%)	6.3	7.4	0.938
Leukopenia (%)	43.8	52.8	0.386
Anemia (%)	64.6	48.1	0.085
Thrombocytopenia (%)	50	32.4	0.056
Serositis (%)	37.5	1.9	<0.001
Renal involvement (%)	66.7	49.1	0.063
Liver involvement (%)	10.4	4.8	0.314
Lung involvement (%)	37.5	12.0	<0.001
Current prednisolone (%)	60.4	51.9	0.414
Current cyclophosphamide (%)	16.7	19.4	0.850
Anti-dsDNA antibody-positive (%)	43.8	45.4	0.989
Anti-SSA antibody-positive (%)	70.8	58.3	0.191
Anti-SSB antibody-positive (%)	25	22.2	0.862
Anti-U1RNP antibody-positive (%)	27.1	22.2	0.649
Anti-Smith antibody-positive (%)	22.9	24.1	0.962
C3 (median, IQR, g/L)	0.416 (0.299–0.762)	0.551 (0.338–0.808)	0.888
C4 (median, IQR, g/L)	0.090 (0.053–0.153)	0.091 (0.057–0.167)	0.269
IgG (median, IQR, g/L)	14.2 (9.26–17.8)	16.0 (9.38–23.4)	0.051
IgA (median, IQR, g/L)	2.19 (1.45–2.97)	2.6 (2.03–3.72)	0.07
IgM (median, IQR, g/L)	1.09 (0.75–1.36)	1.12 (0.64–1.62)	0.852
ESR (median, IQR, mm/h)	40 (25–78)	62 (28–86)	0.463
CRP (median, IQR, mg/L)	10.20 (3.08–22.30)	3.19 (2.98–11.70)	0.222
SLEDAI (median, IQR,)	14 (9–17)	12 (8–15)	0.007

Results

Comparison of clinical and laboratory characteristics between SLE patients with elevated and normal CA125 (Table I)

Increase of serum CA125 level (over normal upper limit 35 kU/L) was found in 48 (30.8%) patients. Compared with patients with normal CA125, those with elevated CA125 had significantly more serositis (37.5% *vs*. 1.9%, $p<0.001$) and lung involvement (37.5% *vs*. 12%, $p=<0.001$), higher SLEDAI scores ($p<0.007$). Furthermore, disease duration was significantly longer in those with elevated CA125 than with normal CA125. There were no significant differences in other clinical and laboratory variables including age, sex, cutaneous, joint, neuropsychiatric and other manifestations, serum autoantibodies, pharmacologic interventions, and so on.

Association of elevated CA125 with clinical and laboratory data in SLE patients

Univariate logistic regression analysis showed that elevated serum CA125 level was closely associated with disease duration (OR, 95%CI:1.005, 1.001–1.010; $p=0.014$), serositis (OR, 95%CI: 32.258, 6.993–142.857; $p<0.001$), renal involvement (OR, 95%CI: 2.283, 1.114–4.673; $p=0.024$), lung involvement (OR, 95%CI: 4.386, 1.927–10.000; $p<0.001$) and SLEDAI scores (OR, 95%CI: 1.098, 1.027–1.174; $p=0.006$), but not with other clinical and laboratory variables in SLE patients. (Table II)

In order to exclude confounder interference, multivariate logistical regression analysis was performed to include significant variables. As was shown in Table III, after controlling for various confounding variables, serositis and disease duration were the only two clinical variables significantly associated with elevation of serum CA125 level, while the association of elevated serum CA125 level with other variables (lung and renal involvement, and SLEDAI scores) was not significant any more (Table III).

The diagnostic value of serum CA125 concentration for serositis in SLE

A ROC curve was plotted and the area under the ROC curve was calculated to assess the diagnostic strength of CA125 for serositis in SLE. The best cut-off value for CA125 identified by the ROC curve was 38 kU/l (sensitivity 85%, specificity 75%) and AUC was 0.777 with 95%CI of 0.685-0.868 (p<0.001) (Fig. 1).

The change of CA125 concentration with serositis resolved in SLE

Retrospective follow up was performed by reviewing the medical records. Of 18 SLE patients with serositis, one patient was deceased because of respiratory failure, 2 patients did not come to this hospital any more. Fifteen other patients were reinvestigated for serum CA125 level after serositis resolved. Of those, 14 patients showed serum CA125 levels falling in the normal range, but one patient with renal involvement did not show any change for CA125 concentration (Fig. 2). In addition, another two patients with elevated serum CA125 levels but without serositis were also followed up. However, neither of them developed serositis by the end of data collection.

Table II. Unvariate logistic analysis with normal and elevated serum CA125 level as the dependent dichotomic variables (0/1: normal/elevated).

Clinical and laboratory characteristics	Serum CA125 level	
	OR (95% CI)	p-value
Female	1.075 (0.357–3.241)	0.898
Age at onset	0.996 (0.973–1.020)	0.768
Disease duration	1.005 (1.001–1.010)	0.014
Fever	0.841 (0.368–1.920)	0.681
cutaneous manifestations	1.425 (0.671–3.029)	0.357
Oral ulcer	0.333 (0.093–1.190)	0.091
Alopecia	0.770 (0.214–2.766)	0.689
Arthritis	1.684 (0.809–3.509)	0.164
Secondary SS	0.911 (0.161–5.152)	0.916
Neurologic disorder	0.647 (0.174–2.407)	0.516
Leukopenia	1.224 (0.310–4.833)	0.773
Anaemia	1.496 (0.753–2.971)	0.250
Thrombocytopenia	0.518 (0.256–1.048)	0.067
Serositis	32.258 (6.993–142.857)	<0.001
Renal involvement	2.283 (1.114–4.673)	0.024
Liver involvement	2.398 (0.659–8.696)	0.184
Lung involvement	4.386 (1.927–10.000)	<0.001
Current prednisolone	0.706 (0.354–1.408)	0.322
Current cyclophosphamide	1.207 (0.493–2.957)	0.681
Anti-dsDNA antibody-positive	1.068 (0.538–2.117)	0.851
Anti-SSA antibody-positive	0.576 (0.278–1.197)	0.139
Anti-SSB antibody-positive	0.843 (0.380–1.873)	0.676
Anti-U1RNP antibody-positive	1.185 (0.556–2.525)	0.661
Anti-Smith antibody-positive	1.067 (0.477–2.385)	0.875
C3	1.000 (0.999–1.001)	0.944
C4	0.999 (0.995–1.002)	0.463
IgG	0.999 (0.998–1.000)	0.195
IgA	0.998 (0.995–1.000)	0.071
IgM	0.999 (0.995–1.003)	0.684
ESR	0.997 (0.987–1.007)	0.546
CRP	0.999 (0.998–1.001)	0.381
SLEDAI	1.098 (1.027–1.174)	0.006

Table III. Multivariate logistic analysis with normal and elevated serum CA125 level as the dependent dichotomic variables (0/1: normal/elevated).

Clinical and laboratory characteristics	Serum CA125 level	
	OR (95% CI)	p-value
Disease duration	1.005 (1.000-1.010)	0.045
Serositis	24.390 (5.102-125.000)	0.008
Renal involvement	1.445 (0.537-3.876)	0.466
Lung involvement	2.475 (0.112-6.757)	0.076
SLEDAI	1.055 (0.863-1.167)	0.127

Discussion

It has been reported that serum CA125 level may be increased in SLE patients with pleural effusion, ascites or pericardial effusion all of which may reflect the presence of serositis (15-18). However, the phenomenon was found only in a few case reports, and by far, there has been no study exploring whether or not the elevation of serum CA125 level is independently associated with serositis in SLE. Therefore, this is, to our knowledge, a novel observation that serositis can be the only clinical variable significantly associated with the elevation of serum CA125 level, independent of other clinical and laboratory variables in SLE patients. Based on the good association and AUC, increased serum CA125 level may have diagnostic value for the presence of serositis in SLE.

Although elevated serum CA125 level has been found in SLE, rheumatoid arthritis and other systemic rheumatic diseases, by several evidences (19-21), only a few studies explored the association of elevated serum CA125 level with clinical and laboratory characteristics of SLE and some results remained controversial. In the present study, the results of the univariate logistical regression analysis indicated that several clinical and laboratory variables including serositis, disease duration, lung involvement, and disease activity (SLEDAI) seemed to be associated with elevated serum CA125 level. However, when we performed multivariate logistical regression analysis to rule out confounding variable interference, which was not done in any previous related study, only serositis remained significantly associated with elevated serum CA125 level. Furthermore, the association is very strong, since the presence of serositis can lead to 24.39-fold increase in the risk of serum CA125 elevation. These results suggested that if the confounding variables can not be controlled, the inferential statistics may lead confusing results, such as the association between elevated serum CA125 level and

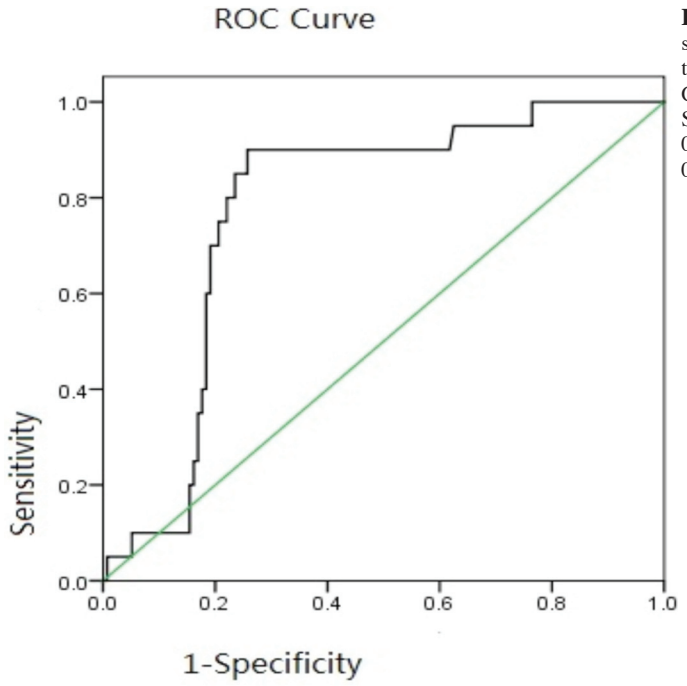

Fig. 1. ROC curves showing the diagnostic strength of serum CA125 for serositis of SLE. The AUC was 0.777 with 95%CI of 0.685-0.868 (P<0.001).

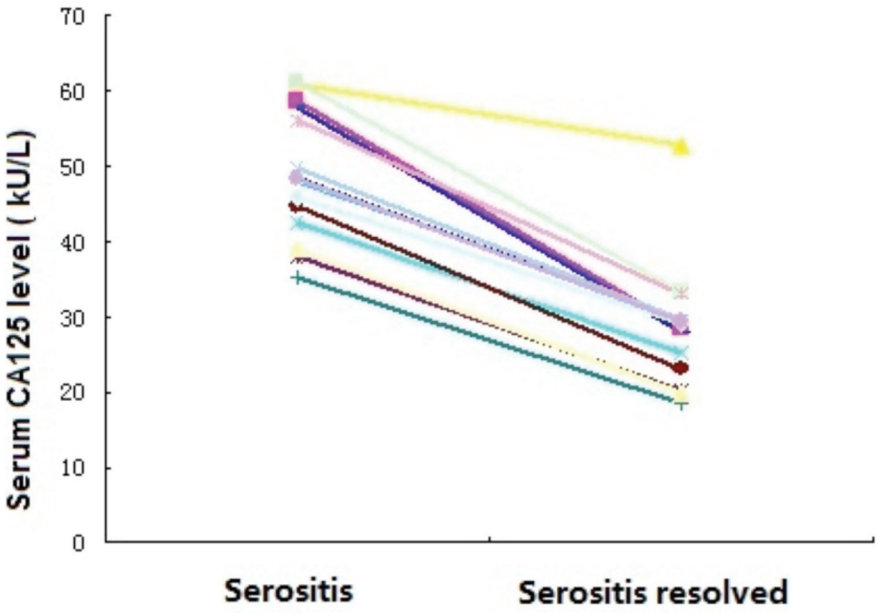

Fig. 2. The change of CA125 concentration with serositis resolved in SLE.

renal involvement (reported by Miret *et al*. (10)), disease activity (reported by Moncayo *et al*. and Szekanecz *et al*. (9, 20)) of SLE.

Serositis is a common manifestation and classification criterion for SLE. In current study, 18 (11.5%) SLE patients had serositis, consistent with the ratio reported by Cervera *et al*. (22). Although independent association of serositis with serum CA125 elevation was found in this study, cause and effect between them can not be addressed based on the retrospective study. On the one hand, CA125 is, as we know, a coelomic epithelial antigen produced by mesothelial cells that line the peritoneum, pleural cavity and pericardium, and the involvement of the serosa including peritonitis, pleuritis and pericarditis, may result in the elevation of CA125 level. On the other hand, CA125 contains carbohydrate motifs and can serve as cellular adhesion molecules, which is involved in tumour cell adherence to endothelium and mesothelium (23-24). Thus, CA125 could be involved in adhesive interactions underlying autoimmune serositis of SLE. Anyway, the causality between serositis and CA125 elevation in SLE remain further to be investigated in a prospective study.

In addition, we also assessed the diagnostic strength of CA125 for serositis in SLE by ROC curve analysis. Of particular interest, the results suggested that serum CA125 displays a good diagnostic significance (AUC: 0.777; 95%CI: 0.685-0.868; p<0.001) for serositis in SLE, and the best cut-off is 38 kU/L with 85% sensitivity and 75% specificity. Furthermore, the serum CA125 concentrations fell into the normal range again with the improvement of serositis in SLE patients. Since serum CA125 concentration can be measured easily in the clinical laboratory and applied in medical practice, it should be used as a routine serum marker for serositis of SLE, especially in the follow-up of well established serositis.

This study is not without limitations. Firstly, we did not assess the precise causality between serositis and serum CA125 elevation as described above. Secondly, because of too few SLE patients with serositis, we did not divide them into pleural, peritoneal and pericardial involvement groups and could not further explore the association of serum CA125 elevation with these three groups, respectively. Actually, in this study, serum CA125 elevation was found in all (100%) of SLE patients with peritoneal (6 cases) and pleural (10 cases) involvement and in 7 (77.8%) of those with pericardial involvement (9 cases). Thirdly, the number of patients included into this study is not still large enough. Therefore, the conclusions drawn from our findings should be cautiously addressed, which needs to be confirmed in another population with a larger size.

In conclusion, our current study suggested that, of various clinical and laboratory features of SLE, serositis is independently associated with serum CA125 elevation, and serum CA125 can serve as a useful serum marker for adjuvant diagnosis and monitoring of serositis in SLE.

References

1. BAST RC JR, FEENEY M, LAZARUS H *et al*.: Reactivity of a monoclonal antibody with human ovarian carcinoma. *J Clin Invest* 1981; 68: 1331-7.
2. MOORE RG, MACLAUGHLAN S: Current clinical use of biomarkers for epithelial ovarian cancer. *Curr Opin Oncol* 2010; 22: 492-7.
3. BASARAN A, TUNCER SZ: Ascites is the primary cause of cancer antigen-125 (CA-125) elevation in systemic lupus erythematosus (SLE) patients with nephritic syndrome. *Medical Hypotheses* 2007; 68: 197-201.
4. MIRALLES C, OREA M, ESPANA P *et al*.: Cancer antigen-125 associated with multiple benign and malignant pathologies. *Ann Surg Oncol* 2003; 10: 150-4.
5. ZUCKERMAN E, LANIR A, SABO E *et al*.: Cancer antigen-125: a sensitive marker of ascites in patients with liver cirrhosis. *Am J Gastroenterol* 1999; 94: 1613-8.
6. ALAGOZ T, BULLER RE, BERMAN M *et al*.: What is a normal CA125 level? *Gynecol Oncol* 1994; 53: 93-7.
7. BON GG, KENEMANS P, VERSTRAETEN R *et al*.: Serum tumor marker immunoassays in gynecologic oncology: establishment of reference values. *Am J Obstet Gynecol* 1996; 174: 107-14.
8. FAIRHURST AM, WANDSTRAT AE, WAKELAND EK: Systemic lupus erythematosus: multiple immunologic phenotypes in a complex genetic disease. *Adv Immunol* 2006; 92: 1-69.
9. SZEKANECZ E, SZUCS G, SZEKANECZ Z *et al*.: Tumor-associated antigens in systemic sclerosis and systemic lupus erythematosus: Associations with organ manifestations, immunolaboratory markers and disease activity indices. *J Autoimmun* 2008; 31: 372-6.
10. MIRET C, FONT J, MOLINA R *et al*.: Lack of correlation between tumor markers (CA-125 and SCC) and systemic lupus erythematosus activity. *Anticancer Res* 1998; 18: 1341-4.
11. HOCHBERG MC: Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus [letter]. *Arthritis Rheum* 1997; 40: 1725.
12. PAN HF, YE DQ, WANG Q *et al*.: Clinical and laboratory profiles of systemic lupus erythematosus associated with Sjögren syndrome in China: a study of 542 patients. *Clin Rheumatol* 2008; 27: 339-43.
13. CLARKE A: Proposed modifications to 1982 ACR classification criteria for systemic lupus erythematosus: serositis criterion. *Lupus* 2004; 13: 855-6.
14. BOMBARDIER C, GLADMAN DD, UROWITZ MB, CARON D, CHANG DH, AND THE COMMITTEE ON PROGNOSIS STUDIES IN SLE: Derivation of the SLEDAI: a disease activity index for lupus patients. *Arthritis Rheum* 1992; 35: 630-40.
15. TJALMA WA: Ascites, pleural effusion, and CA 125 elevation in an SLE patient, either a Tjalma syndrome or, due to the migrated Filshie clips, a pseudo-Meigs syndrome. *Gynecol Oncol* 2005; 97: 288-91.
16. KOH MS, SUNIL K, HOWE HS: Late onset systemic lupus erythematosus with elevated CA 125 and gastrointestinal ischaemia. *Intern Med J* 2002; 32: 117-8.
17. TAKEDA N, IHN H, TERAMOTO S: Markedly increased levels of IL-6 and CA125 in pleural fluid of an elderly person with overlap syndrome of systemic sclerosis and systemic lupus erythematosus. *Age Ageing* 2001; 30: 171.
18. YUCEL AE, CALGUNERI M, RUACAN S: False positive pleural biopsy and high CA125 levels in serum and pleural effusion in systemic lupus erythematosus. *Clin Rheumatol* 1996; 15: 197-9.
19. SZEKANECZ E, SANDOR Z, ANTAL-SZALMAS P *et al*.: Increased production of the soluble tumor-associated antigens CA19-9, CA125 and CA15-3 in rheumatoid arthritis: potential adhesion molecules in synovial inflammation? *Ann N Y Acad Sci* 2007; 1108: 359-71.
20. MONCAYO R, MONCAYO H: Serum levels of CA-125 are elevated in patients with active systemic lupus erythematosus. *Obstet Gynecol* 1991; 77: 932-4.
21. KIMURA K, EZOE K, YOKOZEKI H, KATAYAMA I, NISHIOKA K: Elevated serum CA-125 in progressive systemic sclerosis with pleural effusion. *J Dermatol* 1995; 22: 28-31.
22. CERVERA R, KHAMASHTA MA, FONT J *et al*.: Morbidity and mortality in systemic lupus erythematosus during a five year period. A multicenter prospective study of 1,000 patients. European working party on systemic lupus erythematosus. *Medicine* (Baltimore). 1999; 78: 167-75.
23. RUMP A, MORIKAWA Y, TANAKA M *et al*.: Binding of ovarian cancer antigen CA125/MUC16 to mesothelin mediates cell adhesion. *J Biol Chem* 2004; 279: 9190-8.
24. SEELENMEYER C, WEGEHINGEL S, LECHNER J, NICKEL W: The cancer antigen CA125 represents a novel counter receptor for galectin-1. *J Cell Sci* 2003; 116: 1305-18.