

Serum CA125 and PSA Concentrations in Patients With Lymphoma

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Abstract: Serum determinations of CA125 and prostate-specific antigen (PSA) have been useful in monitoring the status of ovarian and prostate cancer, respectively. However, these antigens are not specific for these neoplasms and ignorance of that fact may lead to confusion in certain settings. Serum CA125 can be elevated in many benign and malignant conditions in which coelomic epithelium is involved. Although lymphoma cells do not secrete CA125, several investigators have reported serum elevations of CA125 in as many as 40% of patients with non-Hodgkin lymphoma (NHL), particularly when peritoneal, pleural, or pericardial effusions are present. In such patients, CA125 levels appear to correlate with disease activity, whereas levels prior to treatment have correlated with disease-free and overall survival in some, but not all, studies. A number of investigators have suggested including serum CA125 levels in prognostic indices for lymphoma. PSA elevations have been reported in patients with NHL less frequently than CA125 elevations, but the PSA in such cases appears to be secreted by the lymphoma cells themselves. The available data are reviewed here.

CA125 is an antigen expressed on a 220 kDa glycoprotein produced by cells originally derived from coelomic epithelium (ie, peritoneum, pleura, and pericardium), epithelium of the female genital tract, mucosal cells of the stomach and colon, and mesothelial cells of serous membranes.¹⁻³ The antigen was initially defined by the murine monoclonal antibody OC 125, which was raised against the human serous ovarian carcinoma cell line OVCA 433.^{4,5} Human cultured mesothelial monolayers secrete CA125 in vitro and secretion is enhanced by exposure to inflammatory cytokines such as interleukin (IL)-1 β and tumor necrosis factor α .² Initially, elevated serum concentrations of CA125 were thought to be specific for ovarian carcinoma,⁶ however, it is now known that elevated serum levels are found in a large proportion of individuals with a variety of benign and neoplastic conditions, such as cervical and endometrial carcinoma,⁷ benign and malignant ascites,⁸ kidney cancer,⁹ non-small cell lung cancer,¹⁰ breast cancer,¹¹

Keywords

CA125, PSA, non-Hodgkin lymphoma

gastric cancer,¹² pediatric¹³ and adult^{5,14-19} lymphoma, pelvic inflammatory disorder, pregnancy,^{7,20} and others.²¹ This review summarizes the data relevant to lymphoma and attempts to put them into perspective.

Serum CA125 in Non-Hodgkin Lymphoma

A number of single case reports of elevated serum CA125 concentrations in patients with lymphoma have appeared, often involving abdominal organs,²² nodes,²³ ascites,²⁴ or pericardial fluid²⁵ infiltrated with lymphoma cells. These case reports have stimulated investigation into the prognostic value of CA125 serum levels in the diagnosis and management of lymphoma. One of the earliest series, reported by Canney and colleagues,²⁶ found that none of the 15 patients with non-Hodgkin lymphoma (NHL) had a serum CA125 level above the upper limit of normal at diagnosis. Subsequently, however, Liu and coworkers²⁷ reported that among 61 patients with NHL, serum CA125 was elevated in 47.7% of patients with nodal disease and 70.6% with extranodal disease prior to therapy. Elevated CA125 correlated with the presence of peritoneal involvement, but not with histologic type or the presence of B symptoms. Histochemical staining of tumor tissue from 11 patients with elevated serum CA125 revealed no CA125 in the lymphoma cells.

In another early report, Lazzarino and coauthors²⁸ found that 40% of 157 NHL patients had an elevated serum CA125 level at diagnosis, as did 41% of patients with recurrent disease, but CA125 was normal in all patients studied in complete remission. In that study, CA125 elevation was associated with advanced disease, aggressive histology, mediastinal or abdominal involvement, bulky tumor, effusions, and extranodal disease, and correlated directly with both elevated serum lactate dehydrogenase (LDH) and β 2-microglobulin levels.

A few years later, Benboubker and colleagues¹⁴ examined serum levels of CA125 in 137 patients (69 women, 68 men; median age 57 years) with previously untreated NHL. Histology was low-grade in 63 patients and higher grade in 74. Forty-three percent of patients (47% of the men and 39% of the women) had elevated serum CA125 at diagnosis. In low-grade lymphomas, CA125 was more frequently elevated than was serum LDH. Elevated CA125 was associated with higher stage, bulky disease, a greater number of extranodal sites, B symptoms, marrow involvement, and effusions. Patients with low-grade lymphoma and normal CA125 and LDH at diagnosis had an 87% complete response (CR) rate and a 97% 5-year overall survival (OS) rate. If either CA125 or LDH was elevated, the CR rate was 45% and the 5-year OS rate was 67%, whereas if both markers were elevated at diagnosis, the 5-year OS rate was 22% and no patient

achieved a CR. These differences were highly statistically significant ($P < .00002$). Bairey and associates⁵ reported an identical rate of CA125 elevation in 46 men and 62 women with NHL, most of whom did not have low-grade disease. In that study, elevated serum CA125 correlated with advanced stage, bulky tumor, B symptoms, marrow involvement, extranodal disease, poor performance status, higher International Prognostic Index (IPI) score, and effusion. Patients with elevated CA125 had poorer OS and event-free survival rates than those with normal CA125 levels. Zidan and coworkers²⁹ reported many of the same findings in a small study in which 45% of patients had elevated serum CA125 at diagnosis, as did Dilek and associates¹⁵ (although in that study there was no correlation between elevated CA125 and presence or absence of extranodal disease).

Several larger studies have appeared since 2005. Batlle and colleagues¹⁶ reported on 200 lymphoma patients (114 men, 86 women; median age 56 years, range 18–88) with the following histologies: low-grade ($n=66$), diffuse large B-cell lymphoma (DLBCL; $n=95$), and other ($n=39$). Again, 43% of all patients studied had elevated levels of serum CA125 at diagnosis. Elevated serum LDH was found in 27% of patients and elevated serum β 2-microglobulin was noted in 24%. CA125 was the only elevated marker in 21% of patients. Elevated CA125 levels positively correlated with advanced clinical stage, poor performance status, pleural involvement, and, in DLBCL, gastrointestinal tract involvement. A CR was achieved in 61% of patients with normal CA125 and in 45% of patients with elevated levels ($P=.033$). Furthermore, elevated serum CA125 at diagnosis was associated with shorter OS.

Wei and associates¹⁷ reported on 355 NHL patients from China. Although the study concerned adults primarily, some children were included. The median age of the patients was 48 years (range, 2–84). The diagnosis was indolent lymphoma in 87 patients, aggressive lymphoma in 216, and undetermined histology in 32 patients. Women accounted for 127 of the patients and 208 were male. A B-cell immunophenotype was demonstrated in 220 patients, whereas 77 had a T-cell immunophenotype, and 58 patients were not immunophenotyped. The rate of elevated serum CA125 for all patients was 59.1%—the highest reported in any series. Elevated CA125 positively correlated with many of the factors noted by others, such as advanced clinical stage, effusion, B symptoms, bulky tumor, and high IPI score, but not with marrow involvement. However, consistent with other reports, the estimated 5.5-year OS was 65% for patients with a normal CA125 level and 25% for those with an elevated serum level. The investigators also immunohistochemically demonstrated that lymphoma cells do not produce CA125.

Most recently, Bonnet and colleagues¹⁹ reported on 78 NHL patients, including 27 with indolent lymphoma and 51 with DLBCL. An elevated CA125 level was found at diagnosis in 45% of the former and 19% of the latter, for an overall rate of approximately 28%—much lower than in most other series. They found that elevated CA125 positively correlated with B symptoms, advanced clinical stage, marrow involvement, mediastinal involvement, effusions, high IPI score, and other factors, but did not correlate with OS or progression-free survival. Because of the latter finding they suggested that CA125 levels are of little use in managing patients with lymphoma.

Finally, Birgen and coauthors¹³ studied 42 children (median age 7 years) with Burkitt (n=11) or non-Burkitt (n=31) lymphoma. Serum CA125 was elevated at diagnosis in 57% of the children and was highest in patients with Burkitt lymphoma. Elevated CA125 levels positively correlated with serous membrane involvement. Patients with stage I or II disease had a 41% rate of CA125 elevation, as did 68% of patients with stage III and IV disease; the rate of CA125 elevation was 80% for patients with effusions and 36% for those without effusions.

Serum CA125 in Hodgkin Lymphoma

There are many fewer reports of CA125 in Hodgkin lymphoma than in NHL, and most have included data on only a few patients. Dilek and associates¹⁵ reported that 28% of 25 patients had an elevated serum CA125 level at diagnosis and that elevation of the marker did not correlate with age, sex, stage, B symptoms, mediastinal involvement, histologic subtype, or extranodal disease. Subgroups of patients were very small. Therefore, an accurate analysis of correlations is essentially impossible. Bonnet and colleagues¹⁹ reported that 29% of 21 patients with Hodgkin lymphoma had elevated pretreatment serum CA125 levels, but gave little additional information, and Birgen and coworkers¹³ reported that only 2 of 17 (11.8%) children with Hodgkin lymphoma had an elevated CA125 level.

More recently, Russo and coauthors¹⁸ published data on a large group of patients that was examined in some detail. They found elevated levels of CA125 at diagnosis in 90 of 221 patients (41%)—a frequency similar to that found in most reports of NHL. Seventy-nine of the 90 patients with elevated CA125 had advanced-stage disease. Patients with elevated CA125 had a significantly lower CR rate (76% vs 98% for those with normal CA125 levels; $P<.0001$). Patients with normal CA125 had event-free survival and OS rates of 92% and 94%, respectively, compared with 60% and 70%, respectively, for those with elevated serum CA125 (statistically significant). The authors demonstrated that no CA125 was

detectable in paraffin-embedded tumor specimens from 15 patients and none could be found in the supernatants from 4 different Hodgkin-derived cell lines. Therefore, it is unlikely that in patients with Hodgkin lymphoma and elevated serum CA125, the source of the CA125 is the lymphoma itself.

Serum CA125 in Other Hematologic Malignancies

For the sake of completeness, the few available data on other hematologic neoplasms are reviewed here. Acin and associates³⁰ reported a patient with chronic lymphocytic leukemia (CLL) and pleural effusion who had an elevated CA125 level. Subsequently, Dilek and coworkers¹⁵ reported elevated CA125 in 1 of 14 patients with CLL tested; that patient also had a pleural effusion. Bairey and Shaklai³¹ reported the largest series of CLL patients, and found elevated CA125 in only 2 of 74 (2.7%) consecutive patients.

In a report of elevated serum CA125 levels in 2 patients with plasma cell dyscrasia, Iwasaki and colleagues³² suggested, based on in vitro analysis, that the neoplastic plasma cells were producing CA125; however, Dilek and coworkers¹⁵ found no CA125 elevations among 9 myeloma patients. With respect to acute leukemia, Birgen and colleagues¹³ noted CA125 elevations in 7 of 30 (23.3%) children with acute lymphocytic leukemia. The child with the highest level had both pleural and pericardial effusions. They also reported that 7 of 14 children with acute myeloid leukemia (AML) had elevated CA125 levels at diagnosis, but Dilek and associates¹⁵ found no elevations among 20 patients with AML and 12 with chronic myelocytic leukemia.

Serum PSA in NHL

Prostate-specific antigen (PSA) is a glycoprotein produced by the epithelial cells of the prostate, and serum elevations are found in patients with benign and malignant prostate disease. However, other organs can also produce PSA. In one study, 29% of breast tumor extracts contained detectable levels of PSA and its detectability correlated with estrogen and/or progesterone receptor positivity ($P<.002$).³³ The same laboratory reported detectable free PSA in the sera of some normal women, some women with benign breast disease, and some women with breast cancer.³⁴ Furthermore, Rae and coauthors³⁵ reported a PSA-like protein elevated in the serum of women with renal cell carcinoma.³⁶

Djavan and colleagues³⁷ reported on a patient with biopsy-proven renal lymphoma, IgM paraprotein in his blood, and elevated serum PSA. Multiple prostate

transurethral ultrasound-guided biopsies were normal and the patient's serum PSA returned to normal after a complete remission of the lymphoma was achieved with standard lymphoma chemotherapy. Although the source of the PSA was not demonstrated, it was presumed to be the low-grade lymphoma of the kidney. The authors postulated that a biologically active substance may have been secreted by the tumor and induced PSA production by the prostate. Interestingly, Kato and associates³⁸ have demonstrated that malignant B cells often produce IL-6 and Lin and colleagues³⁹ showed that in the absence of androgen IL-6 increases PSA mRNA levels.

Johnson and coworkers⁴⁰ reported on a patient with T-cell lymphoma involving the prostate who had an elevated serum PSA level and no evidence of other prostate disease. This case is interesting because there seems to be a well-established, but little known, association between low-grade lymphoma and prostate cancer. Of 4,319 patients undergoing radical retropubic prostatectomy at Johns Hopkins University Hospital, 10 patients (0.2%) were incidentally discovered to have concurrent low-grade lymphoma.⁴¹ Others have reported this finding in as many as 0.82% of patients and in most such cases the prostate itself is not involved with lymphoma.⁴² Drinis and coauthors⁴³ reported a patient with a high PSA level, prostate adenocarcinoma, and low-grade lymphoma in the lymphadenectomy specimen. The patient remained free of both malignancies for at least 5 years after prostatectomy alone, without radiation therapy or chemotherapy. The significance of the relationship between low-grade lymphoma and prostate cancer is unknown, but it should be noted that lymphoma has been reported to occur with increased frequency in patients with other adenocarcinomas such as renal,⁴⁴ gastric,⁴⁵ and breast.⁴⁶

In an effort to identify genes that are associated with progression of malignant lymphoma, Nishiu and associates⁴⁷ analyzed the expression profiles of 18,432 genes from DLBCL tissue with microarrays. Forty-eight genes with increased expression were found, including PSA. Increased expression of PSA in advanced lymphoma was confirmed by reverse transcriptase polymerase chain reaction. The 48 genes with increased expression, including PSA, encode proteins that promote cell proliferation.

Ballario and colleagues⁴⁸ reported a patient with adenocarcinoma of the prostate and infiltration of the prostate with CLL who had an elevated PSA level; a patient with prostate cancer, lymphoma, and Klinefelter syndrome with high PSA has also been documented.⁴⁹

The most instructive case on the relationship between PSA and lymphoma was published recently by Oosterheert and coworkers.⁵⁰ Their patient was an elderly man with voiding problems and a PSA level of 62 µg/mL. Multiple prostate biopsies and a digital rectal examina-

tion were normal. However, a computed tomography scan showed a pelvic mass with bladder wall infiltration suggestive of metastatic prostate cancer. He had an axillary node biopsy, as well as biopsy of the pelvic mass, and both demonstrated follicular low-grade lymphoma. In both biopsies the lymphoma cells were CD20- and PSA-positive. After chemotherapy for his lymphoma, he experienced a complete remission and his serum PSA level returned to normal. The mechanism of PSA serum elevation in such a patient is unclear, but the work of Kato et al³⁸ and Lin et al³⁹, mentioned above, may be relevant.

Discussion

Elevated serum levels of CA125, once thought to be specific for ovarian cancer, have been shown by multiple investigators to be present in patients with a variety of benign and malignant conditions involving coelomic epithelium. This should not be surprising in view of the fact that coelomic epithelial cells secrete CA125. The association of serum CA125 levels with various characteristics of NHL is potentially clinically useful. Although it is clear that CA125 is not a product of lymphoma cells, elevated serum levels in approximately 40% of NHL patients at diagnosis, and the fact that in most series levels directly correlate with certain features of the disease, such as stage, response to therapy, and survival, suggests that initial and serial measurements of the antigen may provide prognostic information of value. This may be particularly true when malignant effusions are present. However, it must be noted that there are no reports indicating a direct correlation of CA125 level with magnitude of effusion in such patients. The value of serum CA125 measurements in patients with NHL clearly deserves further evaluation.

Unlike CA125, PSA is secreted by the lymphoma cells of some patients, although the paucity of reports in the literature suggests that this occurrence may be rare. The frequency of this phenomenon needs to be established and, if more common than currently appreciated, it will be important to determine whether or not serum PSA levels correlate with clinical features of the disease. At present, there are no data available that speak to that issue.

References

1. Kenemans P, Bast R, Yedima C, Price M, Hilgers J. CA125 and polymorphic epithelial mucin as serum tumor markers. *Cancer Rev*. 1988;11:119-144.
2. Zeillemaker AM, Verbrugh HA, Hoyneck van Papendrecht AAGM, Leguit P. CA125 secretion by peritoneal mesothelial cells. *J Clin Pathol*. 1994;47:263-265.
3. Bischof P. What do we know about the origin of CA125? *Eur J Obstet Gynecol Reprod Biol*. 1993;49:93-98.
4. Bast RC Jr, Feeney M, Lazarus H, Nadler LM, Clovin RB, Knapp BC. Reactivity of a monoclonal antibody with human ovarian carcinoma. *J Clin Invest*. 1981;68:1331-1337.

5. Bairey O, Blickstein D, Stark P, et al. Serum CA125 as a prognostic factor in non-Hodgkins lymphoma. *Leuk Lymphoma*. 2003;44:1733-1738.
6. Bast RC Jr, King TL, St John E, et al. A radioimmunoassay using a monoclonal antibody to monitor the course of epithelial ovarian cancer. *N Engl J Med*. 1983;309: 883-887.
7. Halila H, Stenman UH, Seppala M. Ovarian cancer antigen CA125 levels in pelvic inflammatory disease and pregnancy. *Cancer*. 1986;57:1327-1329.
8. Bergmann JF, Bidart JM, George M, Beaugrand M, Levy VG, Bohuon C. Elevation of CA125 in patients with benign and malignant ascites. *Cancer*. 1987;59:213-217.
9. Grankvist K, Ljungberg B, Rasmuson T. Evaluation of five glycoprotein tumor markers (CEA, CA-50, CA-19-9, CA-125, CA-15-3) for prognosis of renal-cell carcinoma. *Int J Cancer*. 1997;74:233-236.
10. Salgia R, Harpole D, Herndon JE, Pisick E, Elias A, Skarin AT. Role of serum tumor markers CA125 and CEA in non-small cell lung cancer. *Anticancer Res*. 2001;21:1241-1246.
11. Norum LF, Erikstein B, Nustad K. Elevated CA125 in breast cancer—a sign of advanced disease. *Tumour Biol*. 2001;22:223-228.
12. Nakata B, Hirakawa S, Chung K, et al. Serum CA125 level as a predictor of peritoneal dissemination in patients with gastric carcinoma. *Cancer*. 1998; 83:2488-2492.
13. Birgen D, Ertem U, Duru F, et al. Serum CA125 levels in children with acute leukemia and lymphoma. *Leuk Lymphoma*. 2005;46:1177-1181.
14. Benboubker L, Valat C, Linossier C, et al. A new serologic index for low-grade non-Hodgkin's lymphoma based on initial CA125 and LDH serum levels. *Ann Oncol*. 2000;11:1485-1491.
15. Dilek L, Ayakta H, Demir C, Meral C, Ozturk M. CA125 levels in patients with non-Hodgkin lymphoma and other hematologic malignancies. *Clin Lab Haematol*. 2005;27:51-55.
16. Batlle M, Ribera J-M, Oriol A, et al. Usefulness of tumor markers CA125 and CA 15.3 at diagnosis and during follow-up in non-Hodgkin's lymphoma: a study of 200 patients. *Leuk Lymphoma*. 2005;46:1471-1476.
17. Wei G, Yuping Z, Jun W, Bing Y, Qiaohua Z. CA125 expression in patients with non-Hodgkin's lymphoma. *Leuk Lymphoma*. 2006;47:1322-1326.
18. Russo F, Latoria S, Svanera G, et al. Long-term follow-up study on the role of serum CA-125 as a prognostic factor in 221 newly diagnosed patients with Hodgkin's lymphoma. *Leuk Lymphoma*. 2007;48:723-730.
19. Bonnet C, Beguin Y, Fassotte M-F, Seidel L, Luyckx F, Fillet G. Limited usefulness of CA125 measurement in the management of Hodgkin's and non-Hodgkin's lymphoma. *Eur J Haematol*. 2007;78:399, 404.
20. Spitzer M, Kaushal N, Benjamin F. Maternal CA125 levels in pregnancy and the puerperium. *J Reprod Med*. 1998;43:387-392.
21. Sevinc A, Buyukberber S, Sari R, Kiroglu Y, Turk HM, Ates M. Elevated serum CA-125 levels in hemodialysis patients with peritoneal or pericardial fluids. *Gynecol Oncol*. 2000;77:254-257.
22. Koksali Y, Caliskan U, Ucar C, Reisli I. A case of primary ovarian lymphoma in a child with high levels of CA125 and CA19-9. *Pediatr Hematol Oncol*. 2005; 27:594-595.
23. Kuroda H, Kida M, Watanabe H, Shirao S, Konda K. Serum CA125 level associated with disease activity in a patient with follicular lymphoma. *Rinsho Ketsueki*. 2005;46:281-283.
24. Antonarakis ES, Fradin JM, Petronis JD, Couzi RJ. Not what it seems. *Am J Med*. 2007;120:408-411.
25. Watanabe M, Kanda T, Takatama M, et al. An autopsy case of malignant lymphoma with high serum CA125 level occurring only in the brain and pericardium. *J Med*. 1996;27:221-227.
26. Canney PA, Moore M, Wilkinson PM, James RD. Ovarian cancer antigen CA125: a prospective clinical assessment of its role as a tumour marker. *Br J Cancer*. 1984;50:765-769.
27. Liu CJ, Tzeng CH, Liu JH, et al. CA125 in non-Hodgkin's lymphoma. *Zhonghua Yi Xue Za Zhi*. 1991;48:382-387.
28. Lazzarino M, Oriandi E, Klersy C, et al. Serum CA125 is of clinical value in the staging and follow-up of patients with non-Hodgkin's lymphoma: correlation with tumor parameters and disease activity. *Cancer*. 1998;82:576-582.
29. Zidan J, Hussein O, Basher W, Zohar S. Serum CA125: a tumor marker for monitoring response to treatment and follow-up in patients with non-Hodgkin's lymphoma. *Oncologist*. 2004;9:417-421.
30. Acin P, Besses C, Centelles M, Machengs I, Sans-Sabrafen J. Elevated serum CA125 tumor marker in chronic lymphocytic leukemia with mesothelial involvement. *Am J Hematol*. 1996;53:281.
31. Bairey O, Shaklai M. Serum CA125 levels in patients with chronic lymphocytic leukemia. *Clin Lab Haematol*. 2005;27:57-60.
32. Iwasaki T, Hamano T, Aizawa K, Kobayashi K, Kakishita E. Increased serum CA125 levels in plasma cell dyscrasias. *Acta Haematol*. 1997;98:104-108.
33. Diamandis EP, Yu H, Sutherland DJ. Detection of prostate-specific antigen immunoreactivity in breast tumors. *Breast Cancer Res Treat*. 1994;32:301-310.
34. Borchert GH, Melegos DN, Tomlinson G, et al. Molecular forms of prostate-specific antigen in the serum of woman with benign and malignant breast diseases. *Br J Cancer*. 1997;76:1087-1094.
35. Rae F, Bulmer B, Nicol D, Clements J. The human tissue kallikreins (KLKs 1-3) and a novel KLK1 mRNA transcript are expressed in a renal cell carcinoma cDNA library. *Immunopharmacology*. 1999;45:63-68.
36. Pummer K, Wirnsberger G, Purstner P, Stettner H, Wandschneider G. False positive prostate specific antigen values in the sera of women with renal cell carcinoma. *J Urol*. 1992;148:21-23.
37. Djavan B, Keffer JH, Molberg K, Roehrborn CG. False-positive serum prostate-specific antigen values in a patient with non-Hodgkin lymphoma of the kidney. *Urology*. 1995;45:875-878.
38. Kato H, Kinoshita T, Suzuki S, et al. Elevated serum interleukin-6 (IL-6) is derived from neoplastic lymphoid cells in patients with B-cell non-Hodgkin's lymphoma: correlation with extent of IL-6 expression and serum concentration. *Br J Haematol*. 1996;92:1014-1021.
39. Lin DL, Whitney MC, Yao Z, Keller ET. Interleukin-6 induces androgen responsiveness in prostate cancer cells through up-regulation of androgen receptor expression. *Clin Cancer Res*. 2001;7:1773-1781.
40. Johnson TR, Barber DB, Teichman JM, Able AC. T-cell lymphocytic lymphoma involving the prostate presenting as elevated PSA in paraplegia: case report. *J Spinal Cord Med*. 1996;19:258-260.
41. Eisenberger CF, Walsh PC, Eisenberger MA, et al. Incidental non-Hodgkin's lymphoma in patients with localized prostate cancer. *Urology*. 1999;53:175-179.
42. Terris MK, Hausdorff J, Freiha FS. Hematolymphoid malignancies diagnosed at the time of radical prostatectomy. *J Urol*. 1997;158:1457-1459.
43. Drinis S, Finkelstein MP, Tortorello DG, Konno S, Choudhury MS. Five-year prognosis after radical prostatectomy in a patient with localized prostate cancer and incidental non-Hodgkin's lymphoma. *Urol Int*. 2001;66:105-107.
44. Kunthur A, Wiernik PH, Dutcher JP. Renal parenchymal tumors and lymphoma in the same patient: a case series and review of the literature. *Am J Hematol*. 2006;81:271-280.
45. Hamaloglu E, Topaloglu S, Ozdemir A, Ozenc A. Synchronous and metachronous occurrence of gastric adenocarcinoma and gastric lymphoma: a review of the literature. *World J Gastroenterol*. 2006;12:3564-3574.
46. Wiernik PH, Hu X, Ratch H, Fineberg S, Etkind P, Walewski JA. Non-Hodgkin's lymphoma in women with breast cancer. *Cancer J*. 2000;6:336-342.
47. Nishiu M, Yanagawa R, Nakatsuka S, et al. Microarray analysis of gene-expression profiles in diffuse large B-cell lymphoma: identification of genes related to disease progression. *Jpn J Cancer Res*. 2002;93:894-901.
48. Ballario R, Beltrami P, Cavalleri S, Ruggera L, Zorzi MG, Artibani W. An unusual pathological finding of chronic lymphocytic leukemia and adenocarcinoma of the prostate after transurethral resection for complete urinary retention: case report. *BMC Cancer*. 2004;4:95.
49. Mattos dos Santos R, Aparecida Rainho C, Carlos Souza Trindade J, Carlos Souza Trindade Filho J, Lauro Viana de Camargo J, Regina Rogatto S. Genotyping of AR and PSA polymorphisms in a patient with Klinefelter syndrome, non-Hodgkin lymphoma, and adenocarcinoma of the prostate. *Cancer Genet Cytogenet*. 2004;153:165-169.
50. Oosterheert JJ, Budel LM, Vos P, Wittebol S. High levels of serum prostate-specific antigen due to PSA producing follicular non-Hodgkin's lymphoma. *Eur J Haematol*. 2007;79:155-158.