Original Article

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Investigation of Plasma Metastin Levels in Reproductive-Age Women with Polycystic Ovary Syndrome Diagnosed with Adnexal Masses

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ABSTRACT

Purpose: Metastin has been shown to inhibit metastasis in breast cancer and malignant melanoma and is reported to be elevated in patients with polycystic ovary syndrome (PCOS). We hypothesized that in PCOS patients presenting with an adnexal mass, metastin levels would demonstrate a negative correlation with tumor markers in cases of malignancy. The aim was to evaluate plasma metastin levels and their relationship with tumor markers in PCOS patients in whom adnexal masses were detected.

Methods: This prospective observational case-control study was conducted after obtaining approval from the University of Health Sciences Turkey, Şişli Hamidiye Etfal Training and Research Hospital Ethics Committee (approval no: 742, date: 24.01.2017). Between February and July 2017, women aged 18-49 years who had previously been diagnosed with PCOS and who presented to the gynecology and obstetrics clinic were evaluated. Patients with adnexal masses detected during examination and PCOS patients without adnexal masses were included, while patients who did not meet inclusion criteria or did not wish to participate were excluded. Patients with masses and without masses were included. The number of patients in the groups was determined by power analysis based on previous studies, with 90% power and a 0.05 alpha error. Serum metastin, cancer antigen (CA) 125 (<35 U/mL), CA 19-9 (<37 U/mL), and carcinoembryonic antigen (CEA) (<5.0 ng/mL) levels were measured.

For comparisons between the two groups, Student's t-test was used for normally distributed variables, and the Mann-Whitney U test for non-normally distributed variables. Spearman correlation was used for non-normally distributed variables in correlation analyses. Chi-square test was used for categorical variables. A p value of <0.05 was considered statistically significant, and statistical analyses were performed using SPSS version 25.

Results: A total of 83 patients were included, 40 (48.2%) in the control group and 43 (51.8%) in the case (adnexal mass present) group. The case group had significantly higher mean age and CA-125 values (p<0.05). No significant difference was found between groups in levels of metastin, CA-19.9 and CEA, or age at menarche. No significant correlation was found between metastin and tumor markers in the case group.

Conclusion: Although a significantly higher CA-125 value in the case group compared to the control group was expected, the lack of difference in metastin levels between the groups, despite all patients being diagnosed with PCOS, suggested that even if pelvic masses are detected in long-term PCOS patients with high metastin levels, the likelihood of malignancy may be low.

Keywords: Polycystic ovary syndrome, metastin, kisspeptin, adnexal mass

INTRODUCTION

Polycystic ovary syndrome (PCOS) is the most common reproductive endocrinology-related disorder in women of reproductive age and is known to be associated with long-term health risks. PCOS affects approximately 6-8% of women of reproductive age.[1] PCOS is a pathology characterized by oligomenorrhea, hyperandrogenism, and polycystic ovaries detected by ultrasonography.[2] The impaired feedback of steroid sex hormones leads to elevated luteinizing hormone (LH) levels.[3] However, because elevated LH is not observed

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in half of PCOS patients, especially in obese women with PCOS, elevated LH may not be the main cause of PCOS.[3-5] Antagonists of kisspeptin and neurokinin B may reduce gonadotropin releasing hormone (GnRH) pulsatility, normalize LH concentrations, improve folliculogenesis, and induce ovulation in PCOS patients.[6] The classical neuroendocrine dysfunction leading to the ovarian phenotype in women with PCOS is characterized by increased LH pulsatility, decreased follicle stimulating hormone (FSH) secretion, and impaired GnRH secretion, resulting in an altered LH/FSH ratio.[7] Since kisspeptin/*KISS1R* acts as an upstream regulator of GnRH and LH secretion, serum kisspeptin levels are expected to be elevated in women with PCOS. Reproductive age is the period in which adnexal masses are most frequently encountered, although 80-85% of such masses are benign and often ovarian in origin. Functional ovarian cysts are the most common adnexal pathologies and include follicular cysts, corpus luteum cysts and theca lutein cysts (Table 1). The importance of functional cysts stems from the difficulty in clearly differentiating them from true neoplasms. Kisspeptin is a metastasis-suppressor gene product identified by its ability to block metastasis without affecting primary tumor formation. Reduced kisspeptin expression is clinically associated with poor cancer prognosis. Kisspeptin has been proposed to prevent metastasis by inhibiting tumor cell migration and proliferation.[8,9] In a study investigating the effects of Kisspeptin-10 on endothelial cell migration and proliferation, it was shown that Kisspeptin-10 inhibited cell migration and proliferation at high concentrations, while both processes increased at lower concentrations.[10] The present study investigated whether there was a difference in the correlation between tumor markers and metastin levels in PCOS patients diagnosed with adnexal masses compared with PCOS patients without such masses.

METHODS

This prospective observational case-control study was conducted after obtaining approval from the University of Health Sciences Turkey, Şişli Hamidiye Etfal Training and Research Hospital Ethics Committee (approval no: 742, date: 24.01.2017). Women aged 18-49 years who had been previously diagnosed with PCOS and presented to the Obstetrics and Gynecology Clinic between February and July 2017 were evaluated based, on the 2003 Rotterdam ESHRE/ASRM criteria for diagnosis of PCOS:

- oligo- and/or anovulation,
- clinical and/or biochemical signs of hyperandrogenism,
- polycystic ovaries.

Patients who had ≥12 follicles measuring 2-9 mm in a single ovary or ovarian volume ≥10 mL on ultrasound were evaluated, and those with adnexal masses detected during examination were included along with PCOS patients without adnexal masses. After excluding patients who did not meet the inclusion criteria or declined participation, 43 patients with adnexal masses and 40 patients without adnexal masses were included. Sample size was determined using power analysis based on data from previous research (90% power and $\alpha=0.05$).

The age, height, and weight of patients were recorded, and obstetric and medical histories were obtained. For patients in the case group, the size and characteristics of the masses were documented. Patients showing sonographic features suggestive of malignancy[11] (septations, papillary projections, solid nodules, multilocularity, ascites) were referred for oncology consultation, and those who were not taken under oncology follow-up were included. Patients with bilateral masses were excluded.

Venous blood samples for metastin and tumor markers were drawn during the early follicular phase, after overnight fast in the morning, and under the same time conditions for both groups. Samples were centrifuged at +4 °C at 4000 rpm for 10 minutes. Plasma samples were stored at -80 °C until analysis. Plasma metastin, cancer antigen (CA)-125 (normal cut-off <35 U/mL), CA-19.9 (normal cut-off <37 U/mL), and carcinoembryonic antigen (CEA) (normal cut-off <5.0 ng/mL) were measured. Plasma samples were tested using the Human KISS-54 ELISA Kit (Catalog No: E-EL-H5618, www.elabscience.com) and read with a Biotek ELX800 microplate reader using Gen5 software. The detection range was 62.5-4000 pg/mL. All samples were run in duplicate. Tumor markers were analyzed at our hospital laboratory. Exclusion criteria were: hypothalamic hypogonadism; delayed puberty; pregnancy; menopause; known malignancy; congenital adrenal hyperplasia; androgen-secreting tumors; Cushing syndrome; hyperprolactinemia; diabetes; hypertension; oral contraceptive use; and obesity defined as a body mass index >30 kg/m^2.

Statistical Analysis

For statistical analysis, Student's t-test was used for normally distributed data, and the Mann-Whitney U test was used for non-normal data. Spearman correlation was used for evaluating correlations between variables. Categorical variables were analyzed using the chi-square test. Statistical significance was set at $p<0.05$ using SPSS, version 25 (IBM Inc., Armonk, NY, USA).

RESULTS

A total of 83 patients were included in the study. Of these, 40 (48.2%) constituted the control group (PCOS patients without adnexal masses), whereas 43 (51.8%) comprised the case group (PCOS patients with adnexal masses in either ovary). Table 2 shows the age range, tumor marker and metastain results for the whole study cohort.

Table 3 shows the malignancy rate and surgical operation status of the patients in the case group with adnexal mass.

Tables 4-5 shows comparison of the case and control groups for age, age at menarche and the median or mean levels of tumor markers and metastatin.

The mean age of the case group was significantly higher than that of the control group ($p<0.05$) (Figure 1). The median CA-125 value of the case group was also significantly higher than that of the control group ($p<0.05$) (Figure 2). However the median values of CA-125 were within normal limits in both case and control groups. There was no significant difference

Table 1. Causes of adnexal masses in reproductive age[12]	
Ovarian causes	**Other causes**
- Follicular cyst - Corpus luteum - Corpus hemorrhagicum - Theca lutein cyst - Cystadenoma - Endometrioma - Tubo-ovarian complex - Tubo-ovarian abscess - Ectopic pregnancy - OHSS - Hydrosalpinx - Paraovarian cyst - Morgagni cyst	- Pedunculated or intraligamentary myoma - Cecal/sigmoid colon filled with feces or gas - Diverticulitis - Ileitis - Appendicitis - Intra-abdominal hematoma - Pseudocyst (peritoneal inclusion) - Retroperitoneal pathology - Congenital anomalies of the reproductive, gastrointestinal or urinary systems
Neoplastic	
Cystadenoma, cystadenocarcinoma, germ cell tumors	Colorectal tumors, metastases
OHSS: Ovarian hyperstimulation syndrome	

Table 2. Characteristics of the study population						
	Age (years)	**Age at menarche (years)**	**CA 125 U/mL**	**CA 19.9 U/mL**	**CEA ng/mL**	**Metastin pg/mL**
Mean	29.7	12.83	22.74	15.1	3.75	1992.47
Standard deviation	7.84	0.98	25.02	21.5	22.31	944.73
Median	29	13	15.2	8.8	1.1	1862.3
Minimum	18	10	1.5	0.6	0.1	450
Maximum	46	15	176	156.7	204.4	4000
CA: Cancer antigen, CEA: Carcinoembryonic antigen						

Table 3. Distribution of adnexal masses in the case group		
	n	**%**
Benign mass (operated)	20	24.1
Malign mass (operated	1	1.2
Mass but not operated	22	26.5

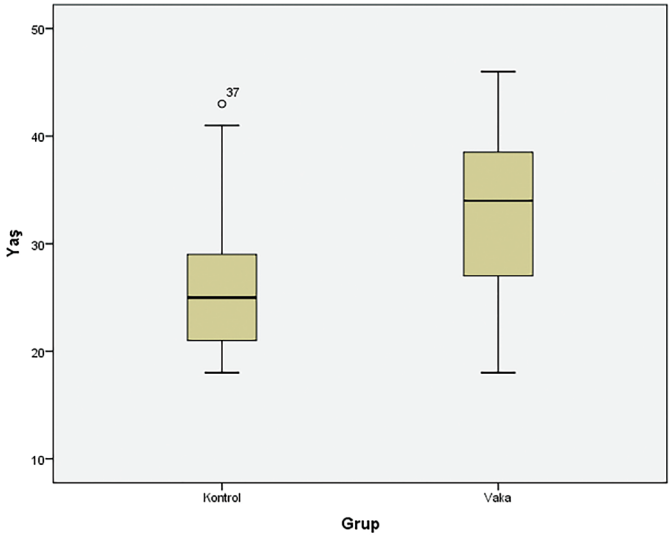

Figure 1. Distribution of case and control groups by age

between the groups in terms of average metastin, (Figure 3), CA 19.9 (Figure 4), CEA levels (Figure 5), or age at menarche. When the relationships between tumor markers in the case group were examined, a moderate positive relationship was found between the three biomarkers CA-19.9, CA-125 and CEA. An increase in one of these tumor markers increases the likelihood of an increase in the other. However, as can be seen in Figures 6 and 7, these relationships are not linear and should be supported by further studies. No significant correlation was found between metastin levels and other tumor markers in the case group. In other words, increases or decreases in metastin levels were independent of CA-19.9, CA-125, and CEA tumor markers. No relationship was found among these markers. In addition, no significant relationship was found between age and metastin levels, CA 19.9, CA 125, and CEA. Although age had a significant effect on adnexal masses, no relationship was observed between age and tumor marker levels. No significant differences were found between the groups with respect to levels of metastin, CA-19.9, CEA levels, or age at menarche. A moderate positive relationship was found between CA-19.9 and CA-125 and CEA in the case group. No significant correlation was observed between metastin levels and other tumor markers in the case group.

DISCUSSION

In women with PCOS, the classical neuroendocrine dysfunction leading to the ovarian phenotype is characterized

Table 4. Comparison of variables between case and control groups

	Case	Control	Levene test	*p*
Mean age (years)	33.09±7.82	26.05±6.08	0.068	**<0.001***
Mean metastin (pg/mL)	1968.3±884.4	2018.43±1016.29	0.270	0.811*
Median age of menarche (years)	13	12.5	-	0.081**
Median CA-125 (U/mL)	17.7	12.95	-	**0.003****
Median CA-19.9 (U/mL)	12.6	7.25	-	0.061**
Median CEA (U/mL)	1.1	1.05	-	0.837**

*Student's t test **Mann-Whitney U test
CA: Cancer antigen, CEA: Carcinoembryonic antigen

Table 5. Correlation between age, age at menarche and tumor markers in the case group

	Age	Menarche age	Metastin	CA 125	CA 19.9	CEA
Age Spearman rho *p* value		0.284 0.065	0.041 0.795	0.266 0.084	-0.036 0.821	0.250 0.105
Menarche age Spearman rho *p* value	0.284 0.065		0.132 0.398	-0.007 0.963	-0.241 0.119	0.130 0.406
Metastin Spearman rho *p* value	0.041 0.795	0.132 0.398		0.067 0.671	0.113 0.469	0.138 0.378
CA 125 Spearman rho *p* value	0.266 0.084	-0.007 0.963	0.067 0.671		0.307 **0.045**	-0.002 0.998
CA 19.9 Spearman rho *p* value	-0.036 0.821	-0.241 0.119	0.113 0.469	0.307 **0.045**		0.484 **0.001**
CEA Spearman rho *p* value	0.250 0.105	0.130 0.406	0.138 0.378	-0.002 0.998	0.484 **0.001**	

CA: Cancer antigen, CEA: Carcinoembryonic antigen

by increased LH pulsatility, decreased FSH secretion, and impaired GnRH secretion, resulting in disruption of the LH-FSH ratio.[7] Since the kisspeptin/GPR54 system is the upstream central regulator that induces GnRH (and LH) secretion, it can be predicted that kisspeptin levels will be higher in women with PCOS.

The reproductive period is the age range in which most adnexal masses are seen; however, 80-85% of these masses are benign and are often of ovarian origin (Table 5).[12] In our study population, 20 patients (24.1%) underwent surgery and were histopathologically benign; 1 patient (1.2%) underwent surgery and was histopathologically malignant; and 22 patients (26.5%) had adnexal masses but were not operated. Considering the patients who were not operated as benign, and given that only one patient was found to be malignant, we detected benign masses at a rate higher than 85%. Of all patients in the case group, only one patient (2.3%) underwent surgery and was confirmed to be malignant.

We initially expected that metastin levels would be lower in cases where the mass was malignant and would show a negative correlation with tumor markers. However, since we had only one malignant case, the sample size was insufficient to interpret the correlation with malignancy.

CA-125, the most commonly used tumor marker in patients with adnexal masses, is synthesized intracellularly, directed

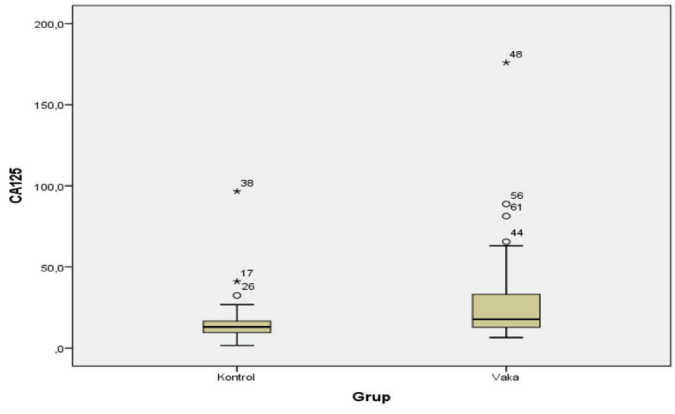

Figure 2. Distribution of case and control groups according to CA-125 levels. Statistically, patient numbers that fall outside the range of values and make a difference

CA: Cancer antigen

toward the luminal surface, and actively secreted into the lumen. Various benign and other causes may also lead to increased levels. The threshold value for CA-125 is 35 U/mL. Since no single screening method is 100% accurate, current screening uses a combination of methods. In our study, the CA-125 value of the case group was significantly higher than that of the control group although only one patient in the case group was proven to have malignant disease.

An elevated CA-125 level in patients with adnexal masses was expected, and in our study, PCOS did not contradict this expectation, and the results were consistent. A moderate positive relationship was found between CA 19.9 and CA 125 and CEA in the case group.[13]

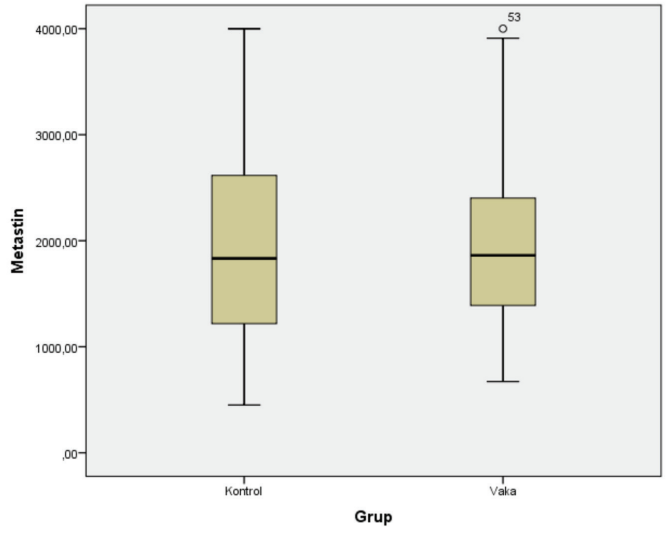

Figure 3. Distribution of case and control groups according to metastin levels

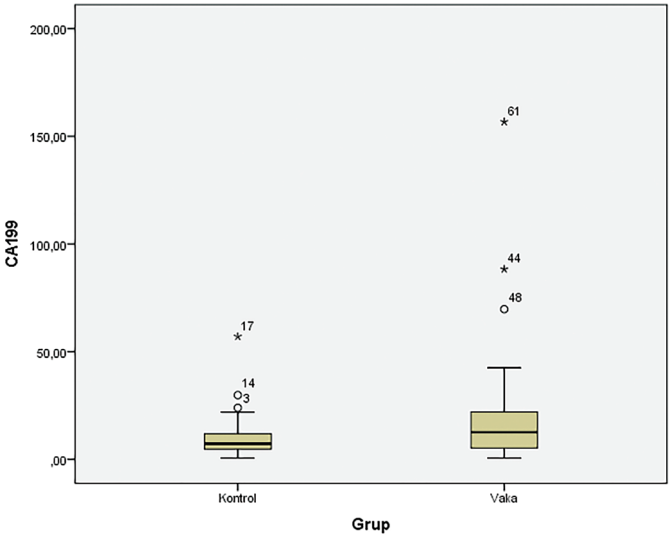

Figure 4. Distribution of case and control groups according to CA-19.9 levels. Statistically, patient numbers that fall outside the range of values and make a difference

CA: Cancer antigen

In studies conducted in 2011 by Redmond et al.[14] and in 2016 by Gottsch et al.[15], *KISS1* directly stimulated LH and FSH secretion in the lateral cerebral ventricle. It is therefore believed to induce puberty via direct action. In our study population, the mean age at menarche was 12.83 (±0.98). Since the age distribution differed between the groups, and because the mean age of the case group was significantly higher than that of the control group, the duration of GPR54 stimulation during the patients' lives varied between the groups and may have influenced our results.

In a study conducted in 2017 by Gorkem et al.[16], serum kisspeptin levels in women with PCOS were found to be significantly higher, and serum kisspeptin levels showed a negative correlation with FSH. Other studies have also

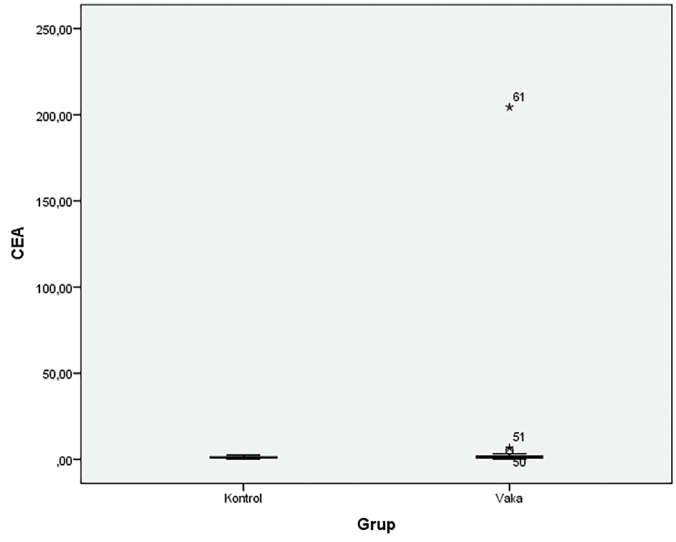

Figure 5. Distribution of case and control groups according to CEA levels (no difference). Statistically, patient numbers that fall outside the range of values and make a difference

CEA: Carcinoembryonic antigen

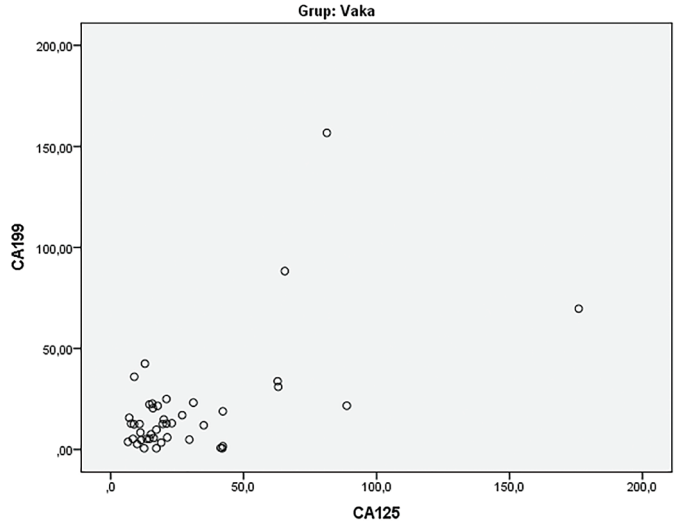

Figure 6. Correlation between CA-19.9 and CA-125 in the case group

CA: Cancer antigen

shown that serum kisspeptin levels are elevated in women with PCOS.[17,18] Since increased LH secretion occurs in PCOS patients, kisspeptin levels were suggested to be higher than in normo-ovulatory women in another study.[19]

Although there was no difference in metastin levels between the control group consisting only of PCOS patients and the case group of women with PCOS and adnexal masses detected, and the detected masses were predominantly benign. When we evaluated the metastin value in the only malignant case, the level was unexpectedly close to the mean and median levels. Since previous studies have shown an association between malignancy and low metastin levels[20,21], this was an unexpected finding.

Cortes et al.[6] showed in 2015, that kisspeptin and neurokinin B antagonists reduced GnRH pulsatility, regulated high LH levels, improved folliculogenesis, and induced ovulation in women with PCOS, and thus metastin levels in PCOS patients are expected to be high. The mean metastin level was 1992.47 (±944.73) in the present study with no significant difference between the groups.

In our study, since both groups consisted of patients with PCOS, the lack of difference in metastin levels between the groups and the proximity of metastin values to the upper limit of the kit used are consistent with findings of previous studies. Including a completely healthy non-PCOS group in future studies would provide more informative results. Studies conducted in 2010 and 2013 showed that kisspeptin exerts anti-metastatic effects in many human cancers, such as melanoma, thyroid, ovarian, bladder, gastroesophageal, pancreatic, lung, and pituitary cancers.[8,22] Clinically, decreased kisspeptin expression is associated with poor prognosis in cancer patients. It has been proposed that kisspeptin prevents metastasis by suppressing cancer cell migration and dissemination.[8]

Although the number of malignant cases was limited, the absence of a significant difference in metastin levels between patients with and without adnexal masses may suggest that high metastin levels in PCOS patients could indicate a lower probability of malignancy even when adnexal masses are detected. The significantly higher CA-125 levels in the case group were expected and align with current diagnostic approaches. In a 2016 study by Cao et al.[20], a prospective analysis of 40 cases with epithelial ovarian cancer showed that the overall survival rate and mean survival time were 28.9% and 38.35±2.84 months, respectively. Furthermore, both residual tumor size and preoperative kisspeptin-1 messenger RNA (mRNA) were significantly associated with prognosis. The same study demonstrated that metastasis and residual tumor size were negatively associated with *KISS1* mRNA, suggesting that patients with low kisspeptin-1 expression were more likely to develop metastasis or residual tumors.[20] Furthermore, kisspeptin-1 was shown to have a significant negative correlation with tumor metastasis and invasion, providing more evidence that it may be a metastasis suppressor molecule in human colorectal cancer.[21]

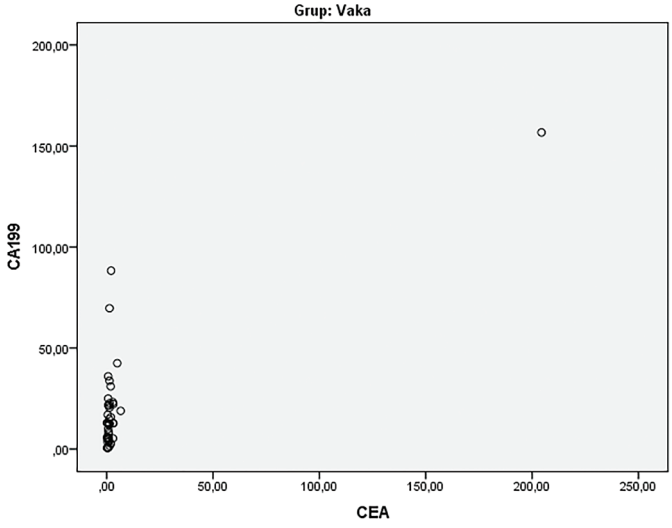

Figure 7. Correlation between CA 19.9 and CEA in the case group
CA: Cancer antigen, CEA: Carcinoembryonic antigen

Study Limitations

Our sample size for evaluating malignancy was too small. Increasing the number of cases and controls and including healthy individuals without a diagnosis of PCOS would strengthen the study.

Hormone levels were not taken on standardized menstrual cycle days and that smokers were not excluded are also limitations. Follow-up of the non-operated patients was incomplete. This may have led to misinterpretation of tumor risk and metastin levels in the group with masses.

The significant age difference between the two groups suggests that the risk of adnexal masses increases with age. Although this difference cannot be eliminated, more homogeneous groups may be formed in future studies.

Blood samples taken on different menstrual days may have altered our values; standardizing the timing of sampling may yield more accurate future results.

CONCLUSION

Measuring metastin levels in completely healthy individuals using the same exclusion criteria may explain the high metastin levels observed in PCOS patients and may provide insight into future research on the etiology of PCOS. Long-term follow-up of PCOS patients may show that, despite high metastin levels, the probability of malignancy may be low even if pelvic masses are detected. Evaluating metastin together with tumor markers in larger future studies and analyzing pathology results may validate the use of metastin as a tumor marker but a great deal of additional data is required. If future studies demonstrate that low metastin levels are associated with malignancy, this relationship may no longer apply in PCOS patients with increased ovarian volume and may be accepted as an exclusion criterion.

Ethics

Ethics Committee Approval: This prospective observational case-control study was conducted after obtaining approval from the University of Health Sciences Turkey, Şişli Hamidiye

Etfal Training and Research Hospital Ethics Committee (approval no: 742, date: 24.01.2017).

Informed Consent: Written informed consent was obtained from all participants.

Authorship Contributions

Surgical and Medical Practices: N.M.E., A.E.Y., Concept: N.M.E., A.E.Y., Design: N.M.E., A.E.Y., Data Collection or Processing: N.M.E., A.E.Y., Analysis or Interpretation: N.M.E., A.E.Y., Literature Search: N.M.E., A.E.Y., Writing: N.M.E., A.E.Y.

Footnotes

Conflict of Interest: No conflict of interest was declared by the authors.

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REFERENCES

1. Goodarzi MO, Quiñones MJ, Azziz R, Rotter JI, Hsueh WA, Yang H. Polycystic ovary syndrome in Mexican-Americans: prevalence and association with the severity of insulin resistance. Fertil Steril. 2005;84(3):766-769.
2. Rotterdam ESHRE/ASRM-sponsored PCOS consensus workshop group. Revised 2003 consensus on diagnostic criteria and long-term health risks related to polycystic ovary syndrome (PCOS). Hum Reprod. 2004;19(1):41-47.
3. Rosenfield RL, Bordini B. Evidence that obesity and androgens have independent and opposing effects on gonadotropin production from puberty to maturity. Brain Res. 2010;1364:186-197.
4. Rosenfield RL. Ovarian and adrenal function in polycystic ovary syndrome. Endocrinol Metab Clin North Am. 1999;28(2):265-293.
5. Rosenfield RL, Mortensen M, Wroblewski K, Littlejohn E, Ehrmann DA. Determination of the source of androgen excess in functionally atypical polycystic ovary syndrome by a short dexamethasone androgen-suppression test and a low-dose ACTH test. Hum Reprod. 2011;26(11):3138-3146.
6. Cortés ME, Carrera B, Rioseco H, Pablo del Río J, Vigil P. The role of kisspeptin in the onset of puberty and in the ovulatory mechanism: a mini-review. J Pediatr Adolesc Gynecol. 2015;28(5):286-291.
7. Norman RJ, Dewailly D, Legro RS, Hickey TE. Polycystic ovary syndrome. Lancet. 2007;370(9588):685-697.
8. Cvetković D, Babwah AV, Bhattacharya M. Kisspeptin/KISS1R system in breast cancer. J Cancer. 2013;4(8):653-661.
9. Smith SC, Theodorescu D. Learning therapeutic lessons from metastasis suppressor proteins. Nat Rev Cancer. 2009;9(4):253-264.
10. Golzar F, Javanmard SH. The effects of kisspeptin-10 on migration and proliferation of endothelial cell. Adv Biomed Res. 2015;4:41.
11. DePriest PD, Gallion HH, Pavlik EJ, Kryscio RJ, van Nagell JR Jr. Transvaginal sonography as a screening method for the detection of early ovarian cancer. Gynecol Oncol. 1997;65(3):408-414.
12. Fleischer, A. C., J. A. Cullinan, and D. M. Kepple. "Color Doppler sonography of pelvic masses." Sonography in Obstetrics and Gynecology. Principles and Practice, 5th edition, AC Fleischer, FA Manning, P. Jeanty, R. Romero, editors, Stamford, CT, Appleton & Lange. (1996):791-813.
13. Dede M, Ercan C.M. Tümör Markerları. In: Ayhan A (Eds). Jinekolojik Onkoloji. 1.Baskı. Ankara, Güneş Kitabevi, 2013; 9: 81-89.
14. Redmond JS, Macedo GG, Velez IC, Caraty A, Williams GL, Amstalden M. Kisspeptin activates the hypothalamic-adenohypophyseal-gonadal axis in prepubertal ewe lambs. Reproduction. 2011;141(4):541-548.
15. Gottsch ML, Cunningham MJ, Smith JT, et al. A role for kisspeptins in the regulation of gonadotropin secretion in the mouse. Endocrinology. 2004;145(9):4073-4077.
16. Gorkem U, Togrul C, Arslan E, Sargin Oruc A, Buyukkayaci Duman N. Is there a role for kisspeptin in pathogenesis of polycystic ovary syndrome? Gynecol Endocrinol. 2017;34(2):1-4.
17. Chen X, Mo Y, Li L, Chen Y, Li Y, Yang D. Increased plasma metastin levels in adolescent women with polycystic ovary syndrome. Eur J Obstet Gynecol Reprod Biol. 2010;149(1):72-76.
18. Jeon YE, Lee KE, Jung JA, et al. Kisspeptin, leptin, and retinol-binding protein 4 in women with polycystic ovary syndrome. Gynecol Obstet Invest. 2013;75(4):268-274.
19. Witchel SF, Tena-Sempere M. The Kiss1 system and polycystic ovary syndrome: lessons from physiology and putative pathophysiologic implications. Fertil Steril. 2013;100(1):12-22.
20. Cao F, Chen L, Liu M, et al. Expression of preoperative KISS1 gene in tumor tissue with epithelial ovarian cancer and its prognostic value. Medicine (Baltimore). 2016;95(46):e5296.
21. Ji K, Ye L, Ruge F, Hargest R, Mason MD, Jiang WG. Implication of metastasis suppressor gene, Kiss-1 and its receptor Kiss-1R in colorectal cancer. BMC Cancer. 2014;14:723.
22. Beck BH, Welch DR. The KISS1 metastasis suppressor: a good night kiss for disseminated cancer cells. Eur J Cancer. 2010;46(7):1283-1289.