

- levobupivacaine and dexamethasone for infra-clavicular block in surgical treatment of forearm fractures
- Recurrent ovary cancer presenting with scleroderma - a rare case report

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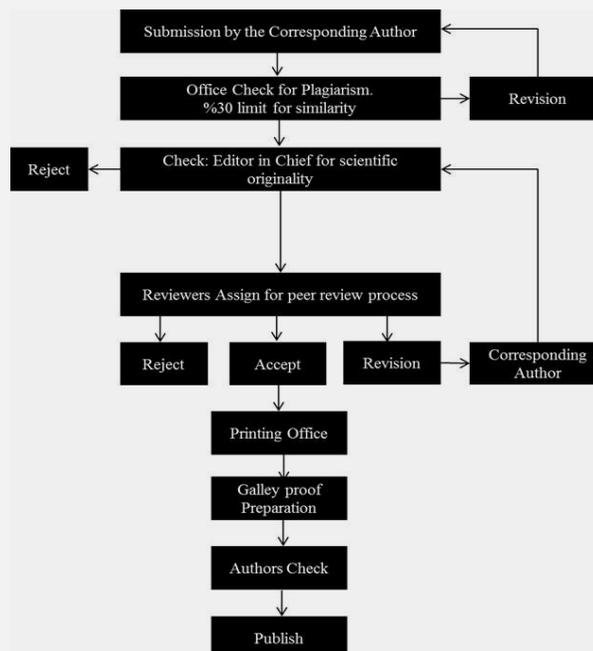
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## The effects of application of 0.5% levobupivacaine together with 5 mg dexamethasone for infra-clavicular block in surgical treatment of forearm fractures

Ertugrul Kilic<sup>1\*</sup>, Burcin Karsli<sup>2</sup>, Mehmet Kursat Evrenos<sup>3</sup>, Murat Erkek<sup>2</sup>, Ayse Mizrak<sup>4</sup>

### Abstract

**Objective:** We aimed to investigate the effects of adding 5mg dexamethasone to 0.5% levobupivacaine on postoperative analgesia after US-guided infra-clavicular block.

**Methods:** This prospective study was performed at Şehitkamil Government Hospital, Gaziantep, Turkey, between september 2012 and february 2013. Ninety patients presented with fracture of forearm bones. Patients were randomly allocated to receive ultrasound guided infraclavicular brachial plexus blockade using levobupivacaine 0.5% in conjunction with or without dexamethasone 5 mg. In Group I (n=45), 0.9% NaCl was added as adjuvant. In Group II (n=45), 5 mg dexamethasone was added to 0.5% levobupivacaine and surgical anesthesia was provided. Postoperative pain control was provided by using morphine with intravenous patient controlled analgesia (IVPCA). one mg bolus dose was administered, continued with limit of 5 mg/hour and 10 min of locking time. Verbal ranting scala (VRS), patient satisfaction score (PSS) and total morphine consumption were controlled for postoperative 48 hours.

**Results:** Sensory block onset time was significantly longer in group I. Sensory block time was longer in group II. PSS was higher in group II, total morphine consumption was found more in group I, VRS was significantly higher in group I.

**Conclusion:** Application of 0.5% levobupivacaine together with 5 mg dexamethasone for infra-clavicular block in surgical treatment of forearm fractures reduces sensory block initiation time, prolongs duration of Sensorial Block and reduces analgesic consumption.

**Keywords:** Forearm fracture, infra-clavicular block, 0.5% levobupivacaine, dexamethasone

### Introduction

Infra-clavicular brachial plexus block (IBPB) is one of the most preferred nerve block techniques among regional anesthesia techniques for particularly hand, wrist, forearm and distal humerus surgery and/or for post-operative pain control in the same regions (1). Axillary and musculo-cutaneous nerve block is a frequently preferred peripheral nerve block technique as it may be done before branching from brachial plexus and distribution fields of both nerves with a single intervention (1-3).

Nerve localization may be observed, needle tip can be visually controlled and the injected local anesthetic (LA) may be observed with introduction of ultrasound (US) technology in peripheral nerve blocks. Block success rate increases and complication rate decreases with US guidance (4).

In addition, US enables a successful nerve block when molecular response to neuro-stimulant stimuli cannot be evaluated. Regional anesthesia with low volume is a frequently preferred method in orthopedics operations (5). Some adjuvant drugs were used for prolonging regional block time. For example, epinephrin reduces systemic absorption of the drug through vasoconstriction and thereby prolongs duration of action. It also shows analgesic effect through alpha-2 adrenergic pathway (6). Similarly, addition of clonidine to LA drugs with moderate duration of action prolongs anesthetic and post-anesthetic analgesia time through pre-synaptic and post-synaptic effect with alpha-1 and alpha-2 agonistic effect (7,8). Dexamethasone, a long-acting glucocorticoid (t<sub>1/2</sub> >36 h) has potent anti-inflammatory and analgesic effects (9).

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Dexamethasone's prolonging duration of action of bupivacaine in nerve block was shown in humans and animals (10-12).

This study was designed to investigate the efficacy of adding of dexamethasone to levobupivacaine for IBPB on block initial time (motor and sensorial), block duration, quality of post-operative analgesia and drug consumption following surgical treatment of forearm fractures.

## Material and method

It was planned to enroll 90 patients aged between 18-70 years, who would undergo forearm bone fracture surgery, in American Society of Anesthesiologists (ASA) I-II. Patients were randomly allocated to receive ultrasound guided infra-clavicular brachial plexus blockade using levobupivacaine 0.5% in conjunction with or without dexamethasone 5 mg. After local ethics committee approval (Gaziantep University Medical Ethical committee Gaziantep, Turkey approval date 04.june.2012 no:231, chairperson Prof. B. Alasehirli) had been obtained. This prospective study was performed at Sehitkamil Government Hospital, Gaziantep, Turkey, between september 2012 and february 2013

Randomization was done by a computer-generated table of random numbers. Patients were randomly divided into two groups of 45 each. The patients were taken to regional anesthesia room in the operating room and monitored for (SaO<sub>2</sub>), non-invasive blood pressure (NBP), heart rate (HR) and heart rhythms (ECG). Intravenous (IV) route was opened using a 22G needle and 0.09% saline solution was started in the dose of 3 ml/kg/hour. Sedation was provided by 2 mg IV midazolam (Dormicum®, Roche, Basel, Switzerland). The patients were taken to supine position and brachial plexus was visualized with US (Mindray ®DC 9, Shenzhen, China) guidance from mid-clavicular line. After skin had been cleaned with an antiseptic solution, 2% lidocaine was applied subcutaneously and local anesthesia was provided.

The study drug was prepared by an anesthesiologist not involved in the study and the anesthesiologist performing the block was blinded about the study drug. Brachial plexus was visualized with US guidance, surgical anesthesia was provided with a total of 20 ml 0.5% levobupivacaine at hour 5,7 and 9 directions with plane approach. Group I (n=45) was administered placebo (2 cc saline) in addition to 0.5% levobupivacaine. Group II (n=45) was administered 5 mg dexamethasone in addition to 0.5% levobupivacaine and surgical anesthesia was provided. The whole IBPB procedure was performed by the same anesthesiologist. Drugs were prepared by another anesthesiologist.

Sensory block and motor block initiation times and durations were recorded in the patients who were applied US-IBPB. Sensory block was assessed every 3

min and motor block was evaluated every 5 min within the first 30 min following completion of drug administration. Ice battery was used for cold test and 23 G needle tip was used for pin-prick test. Sensory block was verified with cold test in all dermatomes of the brachial plexus (C5-T1).

The 25% or more sensory loss in one arm compared to another was accepted as sensory block initiation time in cold test and pin-prick test. Similarly, the time that less than 25% sensory loss occurred in one arm compared to another was determined the end of sensory block. Hand, forearm elevation, wrist flexion and extension powers were measured for determination of motor block initiation time and duration, and results were given as follows: Grade 1: forearm flexion and extension are present, Grade 2: Wrist and finger flexion and extension are present, Grade 3: Only finger flexion or extension is present, Grade 4: No movements in forearm, wrist or fingers. Grade 4 development time was recorded as motor block initiation time. The time to regress to Grade 1 was recorded as motor block termination time and duration was calculated. Operative time was recorded as the time interval between motor block initiation time and the end of skin suturing time.

VRS was used for monitoring post-operative pain (0=no pain, 10= the most severe pain I have ever felt). VRS was evaluated at post-operative 2, 4, 6, 8, 10, 12, 16, 20, 24, 32, 40 and 48<sup>th</sup> hours. Morphine administration via IV PCA device was allowed for the patients whose post-operative VRS score was 4 or above. PCA device was adjusted each bolus dose was so as to be 1 mg, locking time as 10 min and maximum 5 mg/hour. Morphine consumptions at post-operative total consumption were recorded (mg). Patient satisfaction score (PSS) was used (0=no satisfaction, 1= some satisfaction, 2=satisfied, 3= quite satisfied, 4=satisfied very much). PSS was evaluated at 2, 4, 6, 8, 10, 12, 16, 20, 24, 32, 40 and 48<sup>th</sup>.

At the beginning of the study, power analysis was performed to determine the necessary number of patients for each group based on duration of postoperative analgesia. Power application was determined to be 90% and  $\alpha = 0.05$ . Results were assessed as median, mean ( $\pm$  SD) and the number of patients. The patients who did not agree for participation, who had chronic pain syndrome, diabetes, pregnancy or who were suspected to be pregnant were excluded from the study. Statistical analysis was performed with SPSS for Windows (SPSS Inc., Chicago, IL, USA) version 15. The observations recorded in both groups were tabulated and statistical analysis of demographic data and comparison of groups was carried out using Student's t-test (paired for intragroup and unpaired for intergroup comparison) and Chi-square test.  $P < 0.05$  was taken to be statistically significant.

## Results

Demographic data of the patients and operative times are given in Table 1. A statistically significant difference was not found between demographic data and operative times of the patients.

Sensory and motor block initiation times, durations of sensory and motor block are given in Table 2. Sensory block initiation time was significantly longer in Group I ( $12.6 \pm 0.9$ ,  $11 \pm 0.7$  [ $p < 0.05$ ]). Motor block initiation time was longer in Group I ( $16 \pm 1.2$ ,  $13.9 \pm 0.8$  [ $p > 0.05$ ]). Durations of sensory block was statistically significantly longer in Group II ( $168.9 \pm 3.4$ ,  $201 \pm 10.5$  [ $p < 0.05$ ]). Durations of motor block was longer in Group II ( $137 \pm 14.5$ ,  $156.1 \pm 8.6$  [ $p > 0.05$ ]).

VRS is given in Figure 1. mean VRS at post-operative 4., 6., 8., 20., 24., 32., 40. and 48. hours was significantly lower in Group II. The values were found as 0, 1, 3, 4, 2, 2, 2, 2, 4, 2, 2, and 1.5, respectively in Group I, they were 0, 0, 0, 1, 2, 2, 2, 2, 1, 1, 1, 0 and 0, respectively in Group II.

Total morphine consumption is given in Figure 2. The values were detected significantly lower in Group II ( $17.3 \pm 2.2$ ,  $2.6 \pm 1.9$  [ $p < 0.05$ ]).

When PSS was analyzed, mean values at post-operative 2., 4., 6., 8., 10., 12., 16., 20., 24., 32., 40. and 48. hours were higher in Group II (2.3 (1.0-4.0), 3.8(3.0-4.0)) (Table 2).

**Table 1.** Comparison of the Demographic Data of the Groups.

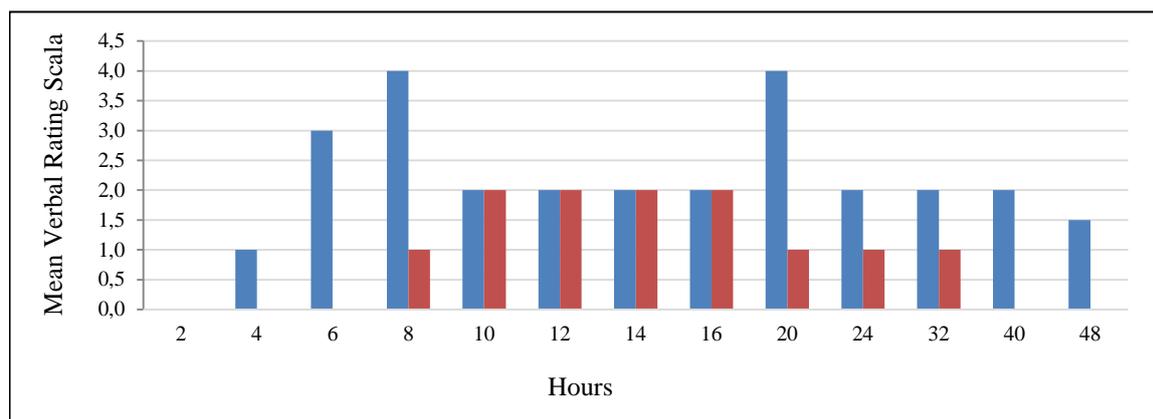
	Group I	Group II	p
Age (Years)	$34.4 \pm 16.3$	$34 \pm 12.5$	0.8
Male /Female	29/16	29/16	0.6
BMI (Body Mass Index)	$29.3 \pm 5.2$	$30.1 \pm 4.4$	0.6
ASA I/II	30/15	30/15	0.8
Duration of Operation (Minutes)	$67.1 \pm 3.4$	$67.3 \pm 2.8$	0.7

$P > 0.05$  when compared the groups. n=45

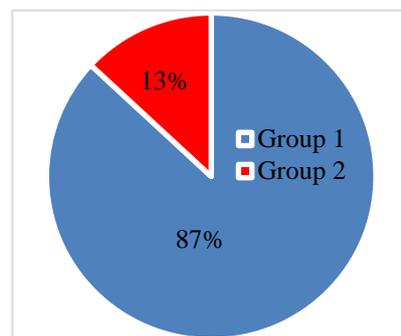
**Table 2.** Comparison of the Data of the Groups.

	Group I	Group II	p
The Initial Time of Sensorial Block (Minutes)	$12.6 \pm 0.9$	$11 \pm 0.7$	0.01*
The Duration of Sensorial Block (Minutes)	$168.9 \pm 3.4$	$201 \pm 10.5$	0.00*
The Initial Time of Motor Block (Minutes)	$16 \pm 1.2$	$13.9 \pm 0.8$	0.07
The Duration of Motor Block (Minutes)	$137 \pm 14.5$	$156.1 \pm 8.6$	0.09
Total Analgesic Consumption in Postoperative (Morphine mg)	$17.3 \pm 2.2$	$2.6 \pm 1.9$	0.00*
The Satisfaction Score of the Groups	2.3 (1.0-4.0)	3.8(3.0-4.0)	

\* $P < 0.05$  when compared the group I and II, n=45



**Figure 1.** The Comparison of the postoperative VRS of the Groups. \* $P < 0.05$  when compared the group I and Group II, n=45



**Figure 2.** Total consumption of morphine,  $P < 0.05$  when compared the groups.  $n = 45$

## Discussion

Our study revealed that use of 0.5% levobupivacaine and 5 mg dexamethasone mixture shortened sensory and motor block initial times, prolonged duration of both blocks and also prolonged post-operative analgesia time in infra-clavicular block procedure done under US guidance in anesthesia in forearm fracture operations.

In meta-analysis of Huynh et al., they reported that dexamethasone use prolonged motor and sensory block times in upper and lower peripheral nerve blocks, and block initiation time shortened in the blocks done using 10 mg dexamethasone. Woo JH et al. (14) detected that sensory and motor block time prolonged as dose increased with 12 ml 0.5% ropivacaine and 2.5, 5 or 7.5 mg dexamethasone use in inter-scalene block done for shoulder arthroscopy. Peter A et al. (15) detected that use of 8 mg dexamethasone together with 20 ml 0.5% bupivacaine, 1:20000 ephedrine and 75 µg clonidine mixture prolonged sensory and motor block time. Dexamethasone is suggested to prolong post-operative sensory and motor block time through prolonging absorption time of local anesthetic drugs by causing vasoconstriction (16,17,18). Levitan et al. (19) showed that dexamethasone prolonged duration of action of local anesthetics by affecting glucocorticoid receptors which increase inhibitor potassium channels in C-fibers. They observed that peri-neural dexamethasone use minimally prolonged sensory and motor block initiation time in 8 out of 14 studies about the influences of peri-neural dexamethasone use in brachial plexus blocks and in 435 out of 1022 patients (20). However we consider that dexamethasone dose and surgical methods used in these studies varied and dexamethasone applied in various doses is effective. Dexamethasone is suggested to prolong post-operative analgesia time due to increasing duration of action of local anesthetic drugs (8,21,22). Sensory block, motor block and analgesia times may be different in the studies.

Type of surgery, the nerve that block is applied, block level and chemical structure of the local anesthetics that dexamethasone is added to could influence these times.

In our study, we observed that VRS was significantly lower in dexamethasone group in all of follow ups and in mean of follow up scores. In post-operative follow up, VRS reached maximum values at 8 and 10 hours in both groups. Even in this period, mean VRS score had a less than a half of control group in dexamethasone group.

Kim YJ et al. (22) used 5 mg dexamethasone or 1:400,000 ephedrine as adjuvant in inter-scalene block procedure done using 10 ml 0.5% levobupivacaine in patients who underwent shoulder laparoscopy under general anesthesia. They observed that post-operative VRS was statistically significantly lower in dexamethasone group, similarly to ours. Dexamethasone use as adjuvant was observed to prolong post-operative analgesia time in many studies (15,16,24,25,26). However mechanism of analgesic effect of dexamethasone could not be fully revealed (24). Its prolonging sensory and motor block time or affecting the activity of inhibitor potassium channels in C-fibers is emphasized (16,25,27).

In our study, when we analyzed post-operative analgesic consumption, we observed that total consumption was significantly lower in dexamethasone group and maximum consumption was observed at 8 hours for both groups, analgesic consumption is much more in control group.

Persec et al. (28) observed that adding 4 mg dexamethasone to 25 ml 0.5% levobupivacaine in various upper extremity surgeries significantly reduced post-operative analgesic consumption. Many studies showed that dexamethasone used together with various local anesthetics reduced post-operative analgesic consumption (15,29,30,31). We consider that it would be beneficial to investigate the influences of dexamethasone on local anesthetics in various regional anesthesia methods.

## Conclusion

In our study, mean patient satisfaction scores were observed to be significantly higher in dexamethasone group.

PSS's being high in patients whose post-operative VRS and analgesic consumption are lower is an expected outcome and similar results were observed in many studies (15,23,29,30). A satisfactory pain control is known to be an important factor for patient satisfaction (32,33). We consider that PSS is higher in dexamethasone group due to sufficient pain control also in our study.

In conclusion, adding 5 mg dexamethasone as adjuvant to 20 ml of 0.5% levobupivacaine shortens sensory and motor block initiation time and prolongs duration of both blocks in US-IBPB for forearm fractures. It also prolongs post-operative analgesia time, decreases VRS, increases PSS and reduces analgesic consumption. We consider that these findings should be supported by studies done with different surgery types and different peripheral block procedures in order to reveal the influences of dexamethasone in regional anesthesia.

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## Recurrent ovary cancer presenting with scleroderma - a rare case report

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### Abstract

Scleroderma is a chronic autoimmune multisystem disorder which is characterized by progressive fibrosis of the skin and internal organs. Ovary cancers with scleroderma have been reported in the literature. But recurrent ovary cancer with scleroderma has not been reported before. Here, we report a 65 -year old female patient presenting with recurrent ovary cancer and subsequently diagnosed with scleroderma. To the authors' knowledge, this is the first case of presenting with recurrent ovary cancer and scleroderma.

**Keywords:** recurrent, ovary cancer, scleroderma

### Introduction

Scleroderma is a chronic autoimmune multisystem disorder which is characterized by progressive fibrosis of the skin and internal organs (1). This disorder develops in the 30–50s and occurs with the average incidence up to 0.002% (2). There are 3 subclasses of systemic scleroderma: limited cutaneous, diffuse cutaneous and sine scleroderma. Prognosis depends on the extent of organ involvement (3). Cutaneous associations of ovarian carcinoma are rare manifestations. These include acanthosis nigricans, Raynaud's phenomenon, scleroderma, dermatomyositis and palmar fasciitis with polyarthrits (4), disseminated superficial porokeratosis (5), multicentric reticulohistiocytosis (MR) (6) and leukocytoclastic vasculitis (7). Here, we report a 65 -year old female patient presenting with recurrent ovary cancer and subsequently diagnosed with scleroderma. In scanning literature, it was seen that recurrent ovary cancer and scleroderma has not been reported yet.

### Case

A 65-year old female patient presented with complaints of diffuse cutaneous sclerosis and thickening along with oedema in right lower limb since four months (Figure 1). She had a history of a serous papillary adenocarcinoma of the ovary. This was diagnosed 4 years prior to her presentation to our clinic and she had been treated adjuvant chemotherapy; paclitaxel and carboplatin. She underwent total abdominal hysterectomy (TAH) with bilateral salpingo-oophorectomy (BSO) and pelvic lymph node dissection.

She had responded well to her treatment. On further questioning, she had noticed thickening and oedema in right lower limb. She did not have medical history about Raynaud's phenomenon, sclerodactylia, pitting scars before. She had no history of smoke or alcohol consumption. The general condition was moderate, oriented and cooperated. Locomotor system examination revealed there was skin thickening in right lower limb. The patient's laboratory findings are presented in Table 1. Doppler ultrasonography was normal. A skin biopsy was taken and the histology showed dermal sclerosis pathology was consistent with scleroderma (Figure 2). Due to the presence of dermal biopsy, acute-phase proteins including erythrocyte sedimentation rate, C-reactive protein and immunological tests including antinuclear antibody were investigated. These tests showed positive antinuclear antibody (ANA) (1 : >100 granular and nuclear membrane), anti-Scl 70 antibody (2+). She was subsequently found to have an elevated carcinoma antigen 125 level of 190 units/ml and the patient was diagnosed as recurrent ovary cancer and scleroderma. Computed tomography (CT) of the chest, abdominal cavity and pelvis were normal with no metastases. She was started on prednisolone (32 mg) and hydroxychloroquine (200 mg) while her subsequent examinations took place. She was later started on paclitaxel chemotherapy for recurrent ovary cancer and until now has received two cycles. Following prednisolone and hydroxychloroquine treatment, her complaints of skin thickening and oedema in right lower limb were improved.

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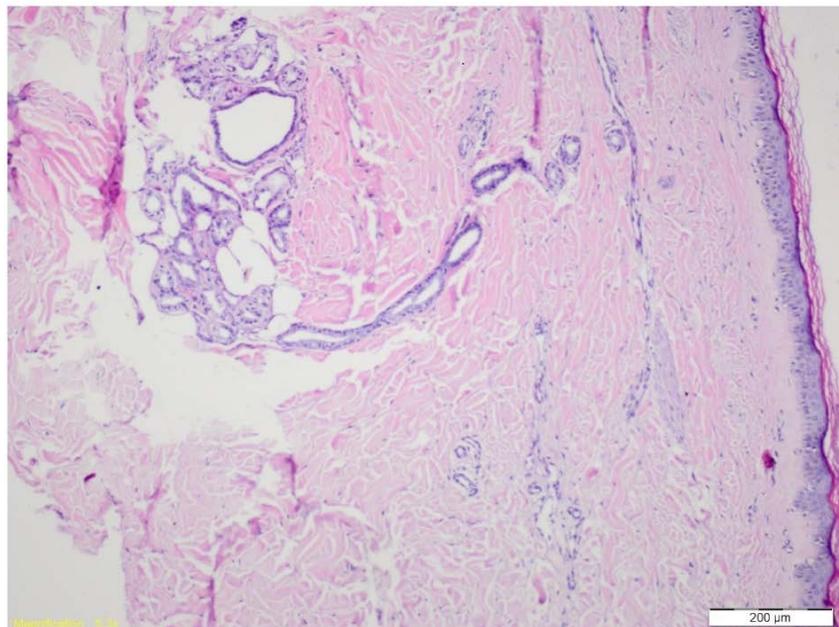
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**Table 1.** Laboratory findings of the patient

	<i>Values</i>	<i>Normal Range</i>
<b>Hemoglobin</b>	13,3 gr/dl	11,7-15,5 gr/dl
<b>Hematocrit</b>	40,4 %	37-44
<b>Leukocyte count</b>	6,63 mkrl	3,800-11,000 mkrl
<b>Platelet</b>	216,000 mkrl	150,000-350,000 mkrl
<b>Erythrocyte sedimentation rate</b>	48 mm/h	0-20 mm/h
<b>C-reactive protein</b>	14,81 mg/l	0-6 mg/l
<b>Urea</b>	27 gr/dl	13-43 gr/dl
<b>Creatinine</b>	0,80 mg/dl	0,7-1,3 mg/dl
<b>ANA</b>	1 : >100 granular and nuclear membrane pattern	Negative
<b>Anti- -Scl 70</b>	++ Positive	Negative

**Figure 1:** Right limb oedeme**Figure 2:** Dermal edema , perivascular lymphocyte infiltration and collagen fibriler hyperplasia

## Discussion

To the knowledge, this is the first case of recurrent ovary cancer presenting with scleroderma. Jedlickova et al. indicated 4 patients with paraneoplastic scleroderma who were diagnosed with cholangiogenic carcinoma, endometrial carcinoma, prostatic adenocarcinoma and adenoma of the suprarenal gland (8). Marek et al. noticed a case with scleroderma-like syndrome in the course of colorectal cancer (2). Several studies have suggested an increased risk of cancer in patients with systemic sclerosis, but the potential risk factors for these cancers remain unknown. Kyndt et al. announced among 123 patients with systemic sclerosis, 14 cases of cancer (11.3%) were found (lung n = 3, breast n = 2, ovarian n = 2, skin n = 1, thyroid n = 1, rectum n = 1, uterine cervix n = 1, larynx n = 1, pancreas n = 1, myelodysplasia n = 1) (9). Bielefeld et al. reported 21 cases of the association systemic scleroderma and cancer. (lung n= 5 , breast n = 2, oesophagus n =1, stomach n = 1 , colon n = 1 , uterus n = 4 , ovarian n= 1 , prostatic n =1, renal n =1 and malignant hemopathies n =6 ) . Bielefeld et al. stated that since 1886, more than three hundred cases of such an association have been reported; essentially lung cancers (more than 100) and epidemiological studies concluded a higher frequency of lung and breast cancers (10). In the literature, we found 27 case-reports exposing the co-existence systemic scleroderma and cancer after this review. Case reports about association of scleroderma and ovary cancer are available in literature (11-16). Su et al. presented a 53-year-old woman with systemic sclerosis and Meigs' syndrome (pleural effusion, ascites and an ovarian tumour) (17). In scanning literature, co- existence of scleroderma and ovary cancers were presented, although recurrent ovary cancer that were presented with scleroderma has not been reported. Also, case reports developing cancer after scleroderma diagnoses were informed. But, recurrent cancer development presenting with scleroderma as in our case is not common. Reynolds et al. announced a 44-year-old woman with a history of recurrent metastatic breast cancer presenting with paraneoplastic scleroderma (18). Findings of our patient didn't supported paraneoplastic scleroderma. Because, a serous papillary adenocarcinoma started for 4 years ago, her laboratory analysis showed anti-Scl 70 antibody positive and she responded good to standard treatment. In the literature, our patient is second case recurrent cancer presenting with scleroderma. Moreover, our patient is first case recurrent ovary cancer presenting with scleroderma.

## Conclusion

We suggest that cutaneous associations of ovarian cancer or other other malignities should be carefully followed until a final diagnosis can be clearly made. When cutaneous lesion develops in patients who have cancer history, the possibility of recurrent cancer should be kept in mind and the patients should be examined in this respect.

**Acknowledgments:** This prospective study was performed at Sehitkamil Government Hospital, Gaziantep, Turkey

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**Ethical issues:** All Authors declare that Originality of research/article etc... and ethical approval of research, and responsibilities of research against local ethics commission are under the Authors responsibilities. The study was conducted due to defined rules by the Local Ethics Commission guidelines and audits.

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