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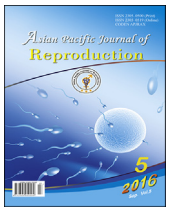

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Ovarian hyperstimulation syndrome followed by ovarian torsion in premenopausal patient using adjuvant tamoxifen treatment for breast cancer

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ABSTRACT

Tamoxifen is a popular medication used in the adjuvant therapy of hormone sensitive breast cancer. In this case report we describe a 39 years old woman presented with ovarian hyperstimulation on the underlying thamoxifen treatment and consecutive ovarian torsion.

1. Introduction

The anti-estrogen tamoxifen has been widely used in the adjuvant treatment of breast cancer in patients with positive estrogen receptors [1]. Tamoxifen is currently the endocrine treatment of choice for all stages of breast cancer in both pre and postmenopausal women [2]. The evidence shows that tamoxifen therapy results in substantially reduced recurrence and mortality rate and produce survival advantage [3]. Despite its anti-estrogen activity in breast cancer, it may exert estrogenic effects in the female genital tract [4]. In this regard, tamoxifen has been used for ovulation induction in patients with anovulatory infertility with similar efficacy to clomiphene citrate [5]. Nevertheless, agonistic effect of drug leading to a spectrum of uterine abnormalities such as endometrial polyp, hyperplasia, cystic enlargement of the ovaries, adenomyosis as well as malignant transformation into endometrial carcinoma and uterine sarcoma [6]. There are several side effects of tamoxifen and ovarian hyperstimulation syndrome (OHSS) is one of the rare complications associated with its use [7]. In the present study, we report an OHSS in a 39-year-old woman induced by tamoxifen as adjuvant treatment for estrogen positive breast cancer with consecutive cyst torsion.

2. Case report

A premenopausal 39-year-old woman was admitted to the Department of Obstetrics and Gynecology, MohebeYas Hospital (Tehran, Iran) for a gynecological consult with lower abdominal discomfort, nausea and bilateral ovarian cysts. One year earlier, the patient had undergone conservative breast surgery for high-grade ductal carcinoma of the left breast. Following surgery, radiotherapy was administered and adjuvant tamoxifen citrate 20 mg/d was started and continued until now. She hadn't menstrual cycles during the last 9 months. The patient had no history of ovarian enlargement before tamoxifen administration but on admission bilateral multicystic mass and ovarian enlargement was observed. The right ovary disclosed a 113 mm × 98 mm × 74 mm multicystic mass and the left ovary disclosed a smaller similar mass (78 mm × 71 mm × 40 mm) (Figure 1). Color duplex sonography showed normal arterial and venous vascularity in both ovaries. There was evidence of mild ascites. Given the patient's history and age serum tumor markers was requested. Her carcino embryonic antigen, CA19-9, CA125, α FP and prolactin stood within the

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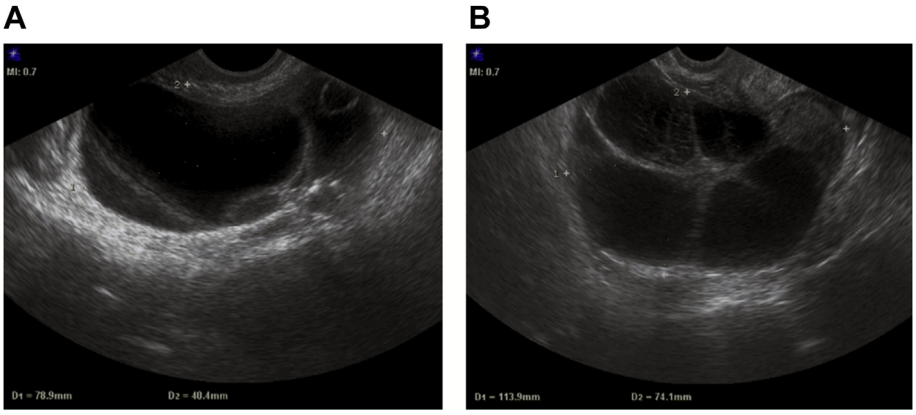

Figure 1. A 39 years old female presented with complaint of lower abdominal discomfort. Her transvaginal sonography at admission showed a multilocular cyst in left ovary (a) and in right side (b).

normal range. Serum estradiol level was elevated (1700 pg/mL). There was no evidence of increased β-hCG titer, liver and thyroid function tests.

Ovarian epithelial neoplasm was still one of the differential diagnose. So for better evaluation of other parts of abdomen and to rule out metastasis the patient had been prepared for performing CT scan of abdomen/pelvis. The patient complained acute right lower quadrant pain. This pattern was suggestive of right ovarian torsion and immediately CT scan of abdomen/pelvis was carried out. No finding in favor of metastatic foci was detected in CT scan of pelvis/abdomen however thickening in the ovarian cysts wall in right adnexa without enhancement was

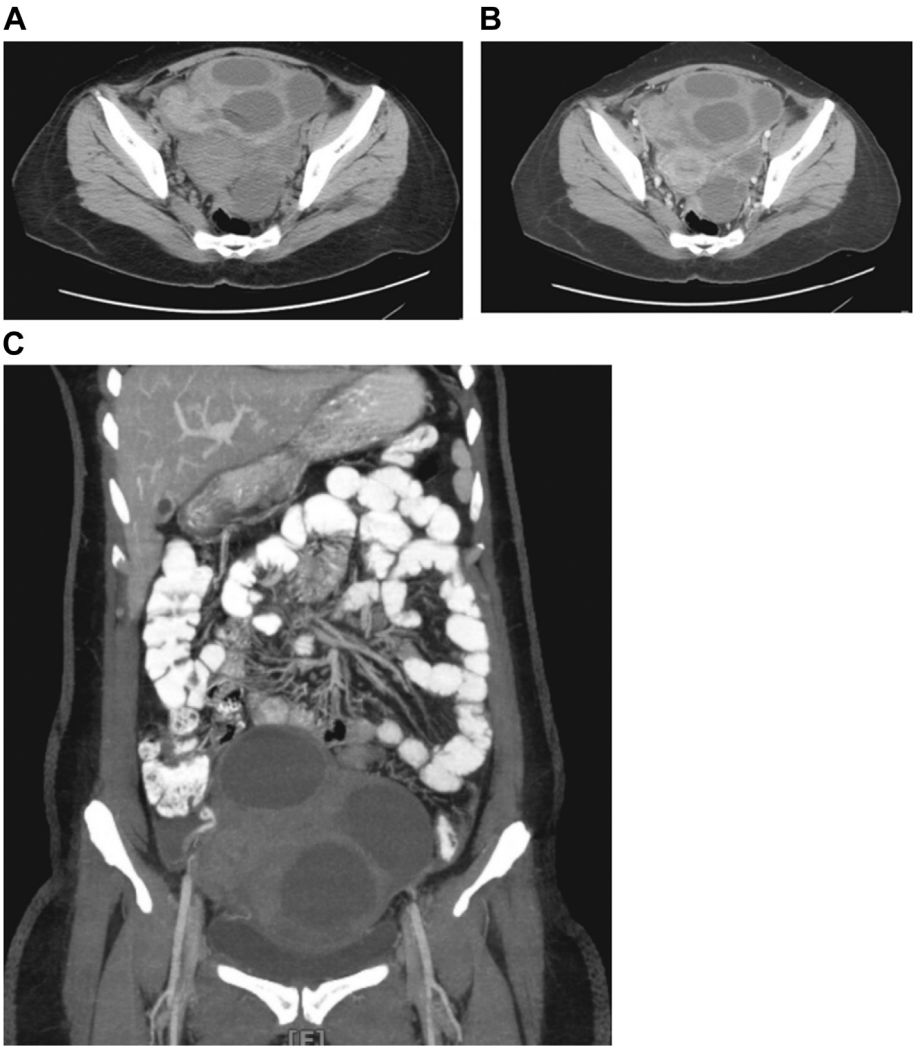

Figure 2. Abdomen and pelvic CT scan of the patient revealed bilateral multilocular cysts. Right side cyst showed wall thickening without wall enhancement. A thick non enhancing torsed pedicle was attached to the right aspect of the ovary. a: before contrast administration; b: with contrast; and c: coronal reconstruction.

detected (Figure 2). Also there was evidence of 53 mm × 40 mm non enhancing mass attached to right ovary. Findings were more likely due to right ovarian torsion on its pedicle which confirmed intra-operatively. Emergent laparoscopy consisting of right side oophorectomy and left side cystectomy was performed. On histopathological examination no neoplastic lesions were found and tamoxifen induced ovarian hyperstimulation was confirmed. Addition of a luteinizing hormone releasing hormone (LHRH) analog to tamoxifen therapy was offered to the patient and was accepted. After surgery the patient discharged without any complications.

3. Discussion

It is well known that tamoxifen induced ovarian cyst in both pre and postmenopausal women treated for breast cancer. On the other hand ovarian cancer can occur in the setting of hereditary syndromes and because patient's age should be ruled out. So the patient's tumor markers were checked out and all of them were in normal range. The abdominal CT scan revealed no evidence of metastasis.

In the interval between 3 and 11 months after treatment initiation the highest incidence of tamoxifen induced ovarian cysts occur [8]. This patient had been on tamoxifen for about one year without any gynecological symptoms.

There is a paucity of data regarding the impact of tamoxifen on OHSS development in breast cancer patients. Madeddu *et al*. reported 2 cases of ovarian hyperstimulation in premenopausal patients during the administration of tamoxifen [9]. Turan *et al*. [10] described ovarian enlargement resembling unilateral OHSS in a 28 years old female and Baigent *et al*. [7] described a 50 year old premenopausal woman with OHSS as a result of tamoxifen treatment. It was suggested that this tamoxifen effect is mainly related to increased estradiol levels by interfering with negative pituitary feedback control and usually leads to cyst formation [9] like as our case. Tamoxifen direct effect on granulosa cells is an additional mechanism that leads to steroid hormone production [2]. It is worth mentioning that recently Yamazaki *et al*. proposed dual mechanisms of adverse effects of tamoxifen on the ovarian function. They explained inhibition of both negative and positive feedback to the hypothalamic-pituitary-axis as a phenomenon induced by tamoxifen on ovarian function [11]. But OHSS or any side effects as a consequence of tamoxifen that need surgical intervention are rare. In OHSS, ascites formation is related to the increased capillary permeability and accumulation of fluid [7].

The patient we describe had moderate OHSS based on the Rizk and Aboulghar classification [12] as evidenced by a presentation of abdominal pain, discomfort, ultrasonic evidence of ascites and bilateral large ovarian cyst masses. There was no evidence of plural effusion and hematological tests were in normal range.

In this setting clinical data favor the use of LHRH agonist plus tamoxifen as a combined approach or LHRH agonist as a single intervention [13,14]. A review of the literature revealed only one case report of a 35 years old female of bilateral ovarian cyst development with consecutive unilateral cyst torsion treated with tamoxifen [8]. This case highlights the occurrence of ovarian cyst formation and OHSS that can secondarily lead to cyst torsion in tamoxifen treated patients.

Therefore, to decrease morbidity it is important to incorporate ultrasound monitoring of ovarian cysts in patients with breast cancer.

Conflict of interest statement

The authors declare that they have no competing interest.

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