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Ansell JE, Buttaro ML, Thomas VO (1997). Consensus guidelines for coordinated outpatient oral anti coagulation therapy management. Ann. Pharmacother. 31:604-615

Charnley AK (1992). Mechanisms of fungal pathogenesis in insects with particular reference to locusts. In: Lomer CJ, Prior C (eds), Pharmaceutical Controls of Locusts and Grasshoppers: Proceedings of an international workshop held at Cotonou, Benin. Oxford: CAB International. pp 181-190.

Jake OO (2002). Pharmaceutical Interactions between *Striga hermonthica* (Del.) Benth. and fluorescent rhizosphere bacteria Of *Zea mays*, L. and *Sorghum bicolor* L. Moench for Striga suicidal germination In *Vigna unguiculata*. PhD dissertation, Tehran University, Iran.

Furmaga EM (1993). Pharmacist management of a hyperlipidemia clinic. Am. J. Hosp. Pharm. 50: 91-95

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Journal of Cancer Research and Experimental Oncology

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Journal of Cancer Research and Experimental Oncology

Full Length Research Paper

Hypertrophic pulmonary osteoarthropathy as the presenting symptom of non-small cell lung cancer: A case report

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Accepted 1 November, 2011

Hypertrophic pulmonary osteoarthropathy (HOA) is a disabling condition that may occur secondarily to primary lung carcinoma. Management of joint pain in patients with HOA is challenging, and treatment options are experimental. Here we report an unusual case of HOA in a 54 year-old man who presented with fever, rash and arthralgia as initial symptoms of an underlying non-small cell lung cancer. He did not respond to various treatment modalities including non-steroidal anti-inflammatory drugs (NSAIDs), pamidronate, and octreotide. His pain symptoms only improved once chemotherapy was administered. This case exemplifies the diagnostic and therapeutic challenge in patients with HOA, and underlines the need for further research to better define this disease and appropriately direct therapy.

Key words: Osteoarthropathy, secondary hypertrophic; carcinoma, non-small-cell lung; therapy; pamidronate; octreotide

INTRODUCTION

Hypertrophic pulmonary osteoarthropathy (HOA) is a rare but disabling condition associated with a wide spectrum of diseases most notably pulmonary malignancies. It is a syndrome characterized by digital clubbing, periostosis of the tubular bones and joint pain (Yao et al., 2009). HOA can either occur as a primary familial autosomal dominant condition known as pachydermoperiostosis (Bazar et al., 2004), or more commonly secondary to conditions characterized by arterio-venous shunts such as bronchogenic carcinoma, pulmonary metastasis, primary intrathoracic neoplasms, and cystic fibrosis (Ntaioset al., 2008). HOA represents a dilemma in medicine in which diagnosis is relatively simple while management is exceedingly difficult due to obscure pathogenesis mechanism, various treatment modalities, and individualized treatment response (Nguyen and Hojjati, 2011). In this report, we present a case of refractory HOA as an initial manifestation of an underlying non-small cell lung cancer (NSCLC) and further discuss various treatment modalities.

CASE REPORT

A 54-year-old Chinese man with 30 years of smoking was referred to Rheumatology clinic for evaluation of fevers, diffuse rash and arthralgia of 4 weeks duration. His outpatient course for pain management included naproxen, oxycodone/acetaminophen. He was also treated with prednisone 40 mg daily and colchicine for suspected gout with no improvement. Outside workup was remarkable for elevated C-reactive protein (CRP) at 205 mg/L, erythrocyte

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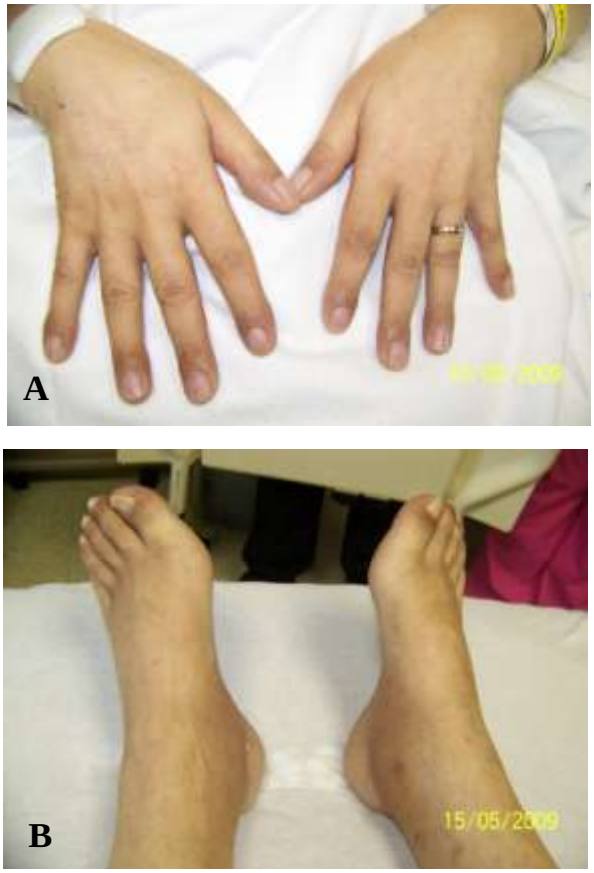

Figure 1. Photographs of patient's hands and feet. Panel A demonstrates clubbing of his digits and panel B demonstrates synovitis of the ankles.

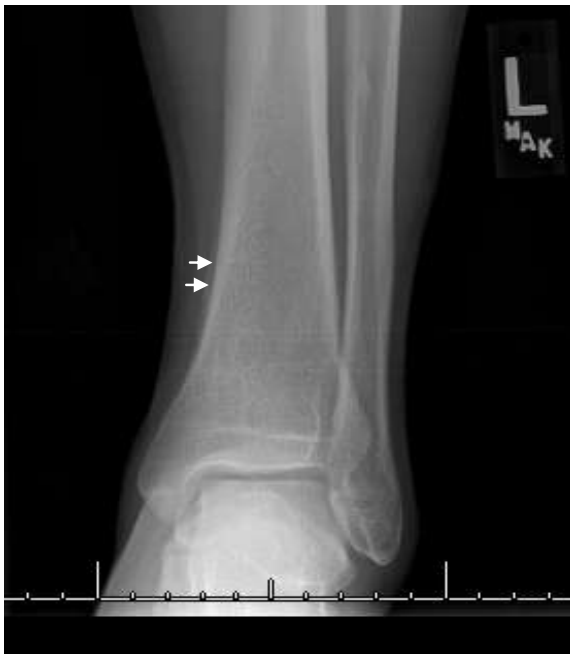

Figure 2. X-ray image shows nonspecific areas of periosteal new bone formation adjacent to the diaphysis of tibia.

sedimentation rate (ESR) of 115 mm/hr, and elevated alkaline phosphatase 436 IU/L. Physical examination was significant for a diffuse erythematous maculopapular rash over his trunk and extremities, cervical lymphadenopathy, decreased breath sounds, grade 3 clubbing of his digits and 2+ pitting edema of the lower extremities. Musculoskeletal examination revealed exquisite tenderness and swelling of his wrists, knees, and ankles (Figure 1). Differential diagnosis included an unusual infectious process, systemic vasculitis, or a paraneoplastic process. A comprehensive infectious and rheumatologic workup including blood cultures, Mantoux test, rheumatoid factor, antinuclear antibody (ANA), anti-neutrophil cytoplasmic antibody (ANCA), anti-cyclic citrullinated peptide antibodies (anti-CCP), and cryoglobulins were all negative. Knee synovial fluid analysis was non-inflammatory with no crystals. A skin biopsy showed non-specific inflammation.

His chest X-ray and CT scan revealed a mass-like consolidation in the left upper lobe of the lung. Patient was treated with ceftriaxone and azithromycin for suspected pneumonia and morphine was administered for pain control. Given his presentation with arthropathy in the setting of new lung findings, hypertrophic pulmonary osteoarthropathy (HOA) was suspected. Bilateral hip, femur, tibia, and fibula X-rays were obtained and showed scattered periosteal new bone formation adjacent to the diaphysis (Figure 2). A whole body bone scan showed increased uptake along the cortex of the bilateral lower extremities (Figure 3). Patient was started on IV pamidronate, which resulted in only minimal improvement of his arthralgia.

On subsequent workup, PET scan showed increased uptake in the left upper lobe with a consolidation measuring 11.2 × 7.1 × 8.2 cm and positive mediastinal lymph nodes. Patient underwent a transbronchial needle biopsy of the lung mass and pathology came back consistent with stage IIIB NSCLC, deemed unresectable.

He continued to complain of severe diffuse joint pains and his arthralgia remained unresponsive to different NSAIDs and narcotics. A second dose of pamidronate did not alleviate his joint pains. He then received octreotide for 5 days, again with minimal response. Eventually patient was started on chemotherapy (docetaxel) and had significant improvement of his joint pains over the course of the following month and all other pain medications were discontinued. His chemotherapy regimen was later switched to carboplatin/abraxane, and finallly to oncarboplatin/pemetrexed. Three months later patient started on palliative radiation given the poor response of his lung cancer to chemotherapy. He eventually expired due to respiratory failure, pneumonia, and severe malnutrition 3 months after his initial diagnosis.

DISCUSSION

Here we describe a patient who presented with HOA as

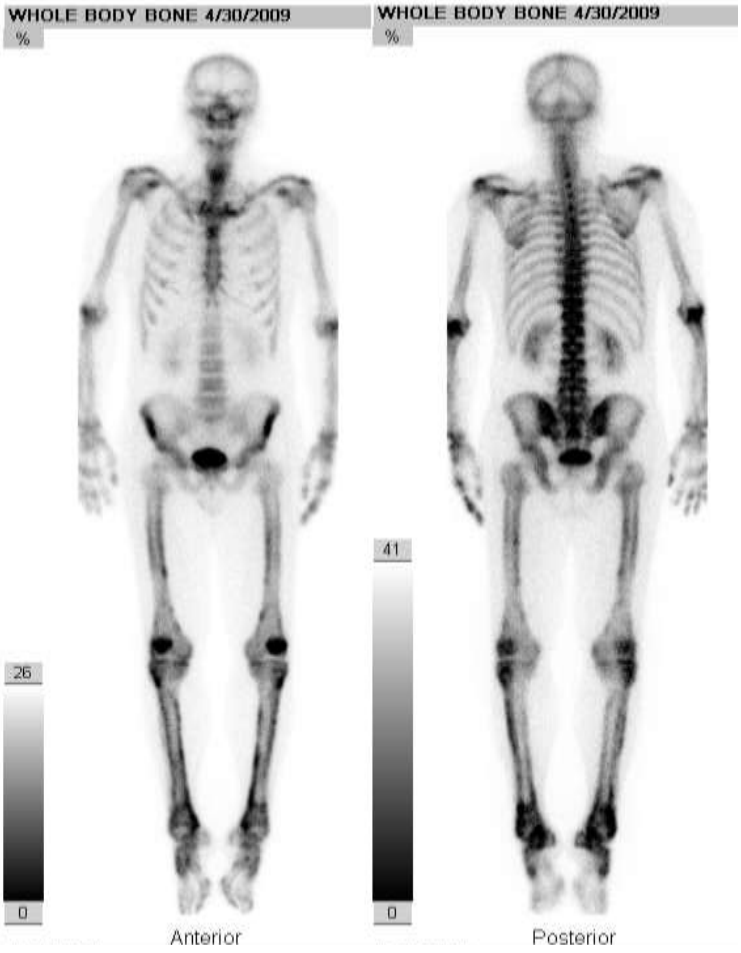

Figure 3. Bone scan showing increased uptake along the cortex of the bilateral lower extremities.

a paraneoplastic presentation of an underlying malignancy. His arthritis was severe, disabling, and refractory to steroids, NSAIDs, pamidronate, and octreotide. His pain improved only after initiation of chemotherapy. HOA is difficult to recognize due to its clinical resemblance to other rheumatic diseases such as gouty arthritis, rheumatoid arthritis, and osteoarthritis. Even when recognized, the challenge lies in treatment of symptoms. As early as 1890, the association of HOA with chronic lung and heart diseases was established and to date, there is still no known cure for HOA (Ooi et al., 2007). The prevalence of HOA in lung cancer ranges from 4 to 32% (Yaoet al., 2009). In adulthood, HOA most commonly presents in NSCLC and mesothelioma, primarily affecting joints of distal inter-phalanges and long bones(Ooi et al., 2007).

The pain associated with HOA is often disabling and refractory to conventional analgesics, and effective management is primarily dependent on the underlying disease (Ooi et al., 2007). Since 1991, it has been established as a well-known phenomenon that resection of the primary tumor alleviates HOA symptoms (Akizuki and Homma, 1991). Up to date, primary treatment of underlying disease is still the most widely reported modality to be efficacious (Nguyen and Hojjati, 2011). The challenge lies in symptomatic treatment of HOA when the primary cause cannot be eliminated. Many symptommatic treatment modalities including vagotomy, adrenergic antagonist such as propranolol and phenoxybenzamine, COX-2 inhibition with rofecoxib, other NSAIDs such as ketorolac and indomethacin, bisphosphonates, and octreotide have been tried, with varying degree of success (Nguyen and Hojjati, 2011). Unfortunately there has been no randomized controlled trial, to evaluate and compare the efficacy and safety profile of these therapeutic modalities.

Recent proposed therapy involves the use of bisphosphonates, a potent inhibitor of osteoclastic bone resorption found to be beneficial in treating osteoporosis, hypercalcemia of malignancy, and bone metastases (Suzuma et al., 2001). There are at least 5 cases reported in the literature on successful treatment of HOA with pamidronate and zolendronic acid (Speden et al., 1997;

Suzuma et al., 2001; Garske and Bell, 2002; Amital et al., 2004; King and Nelson, 2008). Another promising treatment outcome for HOA was reported with octreotide (Johnsonet al., 997). It has been suggested that the pain-relieving efficacy of octreotide for HOA may partly be attributed to its inhibitory effects on the production of vascular endothelial growth factor (VEGF) and endothelial proliferation (Angel et al., 2005; Yaoet al., 2009).

In 1987, Dickenson and Martin observed that HOA is commonly found in conditions with pathologic shunting around the pulmonary vasculature permitting many circulating factors such as platelet derived growth factor (PDGF) and VEGF, which are normally inactivated in the lungs, to directly enter the systemic vasculature (Kozak et al., 2006). The local release of these growth factors leads to fibroblast proliferation with increased vascularity and permeability resulting in connective tissue changes that are the hallmark of clubbing (Dickinson and Martin, 1987). Furthermore, VEGF has been identified as an osteogenic-angiogenic coupling factor involved in new bone formation, vascular hyperplasia, and edema, all are typical symptoms of HOA (Towler, 2007; Atkinson and Fox, 2004). Both VEGF plasma levels and tissue expression have been reported in the majority of the diseases associated with HOA (Olán et al., 2004). Most recently, reports on reversal of HOA symptoms in surgically treated lung cancer, wherein the preoperative observed high levels of serum VEGF and interleukin 6 (IL-6) normalize 1 month post-operation (Hara et al., 2010). This discovery of VEGF's role in the development of HOA potentiates the use of agents with VEGF inhibition such as bevacizumab in the treatment of HOA.

Interestingly, growth factor inhibition in the treatment of HOA is illustrated in a recent case report wherein selective epidermal growth factor receptor tyrosine kinase (EGFR) inhibitor known as gefitinib induced disappearance of periostosis on bone scintigraphy and resolution of HOA symptoms in a patient with advanced stage lung adenocarcinoma (Hayashi et al., 2005).

In this paper, we report an interesting case of HOA as the initial presenting feature of a primary lung cancer. Despite its well-known association with primary lung tumor, HOA as a presenting symptom is a rare phenomenon that may complicate the diagnostic picture and delay identification of a more malignant process. Furthermore, our patient remained symptomatic despite administration of several reported HOA therapies including pamidronate and octreotide. Only chemotherapy resulted in partial relief of his joint pains.

Conclusion

Our case report exemplifies the diagnostic and therapeutic challenge in patients with HOA and underlines the need for further research, to better define the disease process and appropriately direct therapy.

ACKNOWLEDGEMENT

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Full Length Research Paper

Levonorgestrel-releasing intrauterine device for management of tamoxifen-induced menorrhagia in breast cancer patients

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This study aimed to evaluate the therapeutic yield of levonorgestrel-releasing intrauterine device (LNG-IUD) for management of tamoxifen induced menorrhagia in women who had mastectomy for treatment of breast cancer. This study included 34 patients who had breast cancer, underwent mastectomy, were maintained on tamoxifen post-operatively for at least 6 months, and had also newly developed menorrhagia throughout their follow-up period. All the patients underwent clinical examination for determination of duration and heaviness of menstrual blood loss (MBL), transvaginal ultrasonography (TVU) and endometrial biopsy for exclusion of abnormal pathology, estimation of blood iron indices and quality of life (QoL) scoring. Baseline endometrial biopsy detected simple endometrial hyperplasia (EH) in 4 patients and 30 patients had proliferative endometrium. Three patients were excluded and 31 patients completed the follow-up period without the need for shift to hysterectomy. Both mean duration and heaviness of MBL showed significant progressive decrease throughout the observation period as compared to baseline data. At the end of follow-up period, 5 women became amenorrheic, 2 women had moderate MBL and 24 women had mild MBL. Iron indices studies showed significant improvement at the end of follow-up as compared to baseline indices and total QoL scoring recorded at 6 and 12 months after enrollment were significantly higher as compared to baseline scores with significantly higher scores at 12 months. LNG-IUD could be considered as an appropriate therapeutic modality for tamoxifen-induced menorrhagia in patients who had mastectomy for breast cancer with significant reduction of duration and severity of MBL and improved QoL and iron indices.

Key words: Levonorgestrel-releasing intrauterine device, mastectomy, menstrual blood loss, transvaginal ultrasonography.

INTRODUCTION

Premenopausal women with a new diagnosis of breast cancer are faced with many challenges. Providing health care for issues such as gynecologic co-morbidities, reproductive health concerns, and vasomotor symptom control can be complicated, because of the risks of hormone treatments and the adverse effects of adjuvant therapies. It is paramount that health care professionals understand and be knowledgeable about hormonal and non-hormonal treatments and their pharmacological parameters so that they can offer appropriate care to women who have breast cancer, with the goal of improving quality of life (Hind et al., 2007).

Tamoxifen is an orally active selective estrogen receptor modulator that is used in the treatment of breast cancer

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and is currently the world's largest selling drug for that purpose. According to the International Breast Cancer Intervention Study, tamoxifen was found to reduce the risk of invasive estrogen receptor-positive tumors by 31% in women at increased risk for breast cancer and this risk-reducing effect of tamoxifen appears to persist for at least 10 years (Jahanzeb, 2007; Cuzick et al., 2007).

However, tamoxifen has some side effects including hot flashes, menstrual irregularity, vaginal discharges, uterine bleeding, uterine endometrial cancer, hypercoagulability, steatosis hepatitis, and risk of thromboembolism. Long-term data from clinical trials have failed to demonstrate a cardioprotective effect and beneficial effects on serum lipid profiles. Arrhythmia secondary to tamoxifen is very rare (Zhou et al., 2007).

Chronic heavy menstrual bleeding is a common gynecologic condition that causes significant health problems and negatively impacts a woman's quality of life. Surgical treatments should be reserved for women who have pelvic pathology and for those who fail medical therapy. The recent United State Food and Drug Agency (US FDA) approval of the levonorgestrel-releasing intrauterine system as an indicated treatment for heavy menstrual bleeding in women who want to use intrauterine devices for birth control highlights the potential that this top tier contraceptive method offers as a first-line therapy for treatment of heavy menstrual bleeding (Nelson et al., 2010).

This study aimed to evaluate the therapeutic yield of levonorgestrel-releasing intrauterine device (LNG-IUD) for management of tamoxifen-induced menorrhagia in women who had mastectomy for treatment of breast cancer.

PATIENTS AND METHODS

This study was conducted at the Departments of Obstetrics and Gynecology and General Surgery, Benha University Hospital from January, 2007 till January, 2009 so as to allow at least 12 months follow-up for the last enrolled case. Inclusion criteria included patients who had breast cancer, underwent mastectomy, were maintained on tamoxifen post-operatively for at least 6 months and had also newly developed menorrhagia throughout their follow-up period.

After obtaining fully-informed patients and/or husbands' consents, enrolled patients underwent full history taking, complete general and pelvi-abdominal examination. Menorrhagia was diagnosed if the duration of menstrual blood loss (MBL) was ≥6 days and/or MBL was ≥80 ml and other pathological conditions have been excluded (O'Flynn and Britten, 2004; Istre and Qvigstad, 2007). For easiness of patients' interpretation of menorrhagia, heaviness of MBL in the last 6 months after start of tamoxifen therapy was graduated as light, moderate, heavy or very heavy loss and the frequency of bleeding or spotting between cycles was defined.

Patients were informed about the study design (including a 12-month trial using LNG-IUD for control of MBL) and to shift to surgical line of management if the trial failed or the patient requested for the shift. Transvaginal ultrasonography was used to exclude possible causes of menorrhagia, including myomas and endometrial polyps, as well as adnexal pathology, then all women underwent cervical smear and D&C biopsy for exclusion of cervical and endometrial pathologies.

All women had a negative urine pregnancy test prior to levonorgestrel-induced intrauterine system (LNG-IUS) insertion which was conducted as an office procedure one day after cessation of menstrual bleeding. The uterine cavity length was measured using uterine sounding, followed by LNG-IUS insertion. Feasibility of insertion was defined as difficult if there was moderate or severe pain on uterine sounding or if there was need for cervical dilatation, requirement for local anesthesia or intravenous sedation for accomplishment of dilatation and IUD insertion. Accurate LNG-IUS position was documented with transvaginal ultrasonography (TVU) immediately after insertion.

Enrolled women were followed-up every 3 months for grading MBL as regards duration and heaviness. Quality of life (QoL) was evaluated using the 5-Dimensional EuroQol (EQ-5D) which provides a single numeric score for mobility, self-care, usual activities, pain, and mood, each was scored as 0 or 1 and the total EQ-5D score index was calculated; higher scores indicated better QoL (EuroQol Group, 1990). The QoL scores were evaluated at time of baseline and 6 and 12 months after enrollment.

Laboratory investigations

Iron indices were evaluated prior to and 12 months after LNG-IUD insertion, collected venous blood sample were divided into two parts:

1) The first part was kept in a plane container and was left to clot, and then serum was separated by centrifugation at 3000 rpm for not less than 5 min and was stored at -20°C.
2) The second part was put in EDTA tube (about 1.8 mg trik EDTA/1 ml blood) for at once hemoglobin estimation.

Studied iron indices included

1) Hemoglobin concentration (Hb conc.) was determined by cyanomethemoglobin method (International Committee for Standardization in Hematology, 1967).
2) Serum iron concentration was estimated after the separation of Fe^{+3} from transferring by means of a detergent mixture in slightly acidic solution and reduction of Fe^{+3} to Fe^{+2} with ascorbic acid, which then react with ferrozine to give a colored complex (Siedel, 1984).
3) Serum ferritin level was determined by ELISA kit (supplied from Eurogenetics UK) and was based on a monoclonal antibody-sandwich technique to ensure an optimal sensitivity and specificity (Jacobs et al., 1975).

Statistical analysis

Results were expressed as mean±standard deviation (SD), range, numbers and percentages. Results were analysed using paired t-test. Statistical analysis was conducted using Statistical package for Social Sciences (SPSS) statistical program, (Version 10, 2002). P value <0.05 was considered statistically significant.

RESULTS

The study included 34 women fulfilling the inclusion criteria and all had menorrhagia with a mean duration of 9.8±1.5; range: 6 to 13 months. Four endometrial biopsies showed endometrial hyperplasia, while the other

Table 1. Patients' enrollment data.

Data			Value
Age (years)			43.5±4.3 (32-49)
Parity (para)			1.9±0.8 (1-3)
Menstrual data (%)	Duration of MBL (days)		8.7±1.1 (8-11)
	Cycle length (days)		27±3 (23-32)
	MBL heaviness	Mild	3 (8.8)
		Moderate	10 (29.4)
		Severe	13 (38.3)
		Very severe	8 (23.5)
	Duration of menorrhagia (months)		9.8±1.5 (6-13)
Endometrial biopsy (%)	Proliferative		4 (11.8)
	Hyperplasia		30 (88.2)

Data are presented as mean±SD and numbers. Ranges and percentages are in parenthesis. MBL: Menstrual blood loss.

Table 2. IUD data.

Data			Finding
Uterine length data (%)	Mean±SD		7.4±1.6 (5-10)
	Frequency	≤6	13 (38.2)
		7-9	12 (35.3)
		≥9	9 (26.5)
Insertion data (%)	Pain on insertion	No	11 (32.4)
		Mild	18 (53)
		Moderate/severe*	5 (14.6)
	Cervical adhesions*		2 (5.9)
Follow-up data (%)	IUD expulsion	Partial	2 (5.9)
		Complete	1 (2.9)
	Exclusion	Stopped tamoxifen	1 (2.9)
		Cancer-related death	1 (2.9)
		Complete IUD expulsion	1 (2.9)

Data are presented as mean±SD and numbers. Ranges and percentages are in parenthesis. *Difficult IUD insertion.

30 biopsies showed normal but proliferative endometrium. Patients' enrollment data is as shown in Table 1.

Mean uterine sounding length was 7.4±1.6; range: 5 to 10 cm; 9 patients had uterine length of ≥9 cm, 12 patients had uterine length of 7 to 8 cm and 13 patients had uterine length ≤6 cm. Patients who had endometrial hyperplasia (EH) had a mean uterine length of 9.3±1; range: 8 to 10 cm, while patients who had proliferative endometrium had a mean uterine length of 7.1±1.5; range: 5 to 10 cm (Table 2).

Seven patients had difficult IUD insertion; 2 patients had cervical adhesions that were released under anesthesia during D&C for endometrial biopsy taking which facilitated the endometrial biopsy on IUD insertion and five patients had required intravenous sedation for completion of uterine sounding and IUD insertion. Three patients were excluded from the study; one patient had stopped tamoxifen according to surgeon's order and was excluded, because of loss of the study target, one patient had unnoticed complete IUD expulsion that was detected on follow-up at 3 months after insertion and the third died, because of extensive pulmonary metastasis progressed to acute respiratory failure and death. Two patients had partial IUD expulsion noticed throughout follow-up visits and the IUD was removed and another was successfully inserted (Table 2).

Table 3. MBL duration and severity reported throughout the study period compared to baseline data.

Data		Baseline	3 months	6 months	9 months	12 months
Duration	Mean±SD	8.7±1.1	5.2±1*	3.1±0.9*†	1.9±0.8*†‡	1.5±0.5*†‡∫
Severity (%)	No	0	0	0	2 (6.5)	5 (16.1)
	Mild	3 (9.7)	16 (51.6)	23 (74.2)	25 (80.6)	24 (77.4)
	Moderate	9 (29)	8 (25.8)	5 (16.1)	3 (9.7)	2 (6.5)
	Severe	12 (38.7)	7 (22.6)	3 (9.7)	1 (3.2)	0
	Very severe	7 (22.6)	0	0	0	0

Data are presented as mean±SD and numbers. Ranges and percentages are in parenthesis. *Significance versus baseline data. †Significance versus 3-m data. ‡Significance versus 6-m data. ∫Significance versus 9-m data.

Table 4. Mean levels of Iron study parameters estimated at the end of the study compared to baseline data.

Data	Baseline	12 months	Statistical analysis	
			t	p
Hemoglobin concentration (g/dl)	10±0.5 (9.2-10.9)	10.6±0.8 (9.7-11.6)	3.656	0.001
Serum iron (µg/dl)	56.7±9.1 (45-77)	61±7.5 (50-79)	1.841	>0.05
Serum ferritin (µg/dl)	111.1±18 (77-143)	119.8±22.1 (88-163)	1.913	>0.05

Data are presented as mean±SD; ranges are in parenthesis.

Both mean duration and heaviness of MBL showed significant progressive decrease throughout the observation period as compared to baseline data. At the end of follow-up period, 5 (16.1%) women developed amenorrhoea, 2 (6.5%) women had moderate MBL and 24 (77.4%) women had mild MBL with significantly higher frequency of those who had mild MBL as compared to baseline frequency (Table 3).

At the end of follow-up period, irrespective of the duration or severity of MBL, 8 patients had inter-menstrual spotting; however, 5 of these 8 had inter-menstrual spotting at the time of study enrollment, thus LNG-IUD induced increased frequency of women who had inter-menstrual spotting by 9.7%.

In parallel to improved MBL parameters, iron indices studies showed significant improvement at the end of follow-up compared to baseline indices that manifested as significant increase of hemoglobin concentration with non-significantly increased serum iron and ferritin (Table 4).

Total QoL scoring recorded at 6 month (3.7±0.8; range: 2 to 5) and 12 months (4.7±0.5; range: 3 to 5) after enrollment were significantly higher (t=3.943, 6.783; P<0.05, respectively) as compared to baseline scores (3.3±0.7; range: 2 to 4) with significantly (t=5.811, P<0.05) higher scores at 12 months compared to at 6 months. Differential score items showed non-significant difference as compared to baseline scores except for mood and pain scores that showed the significant change, (Figure 1 and Figure 2).

DISCUSSION

This study relied on the ease of administration of local progesterone, its single administration and longevity of the effect, and spares the need for daily or weekly administration, thereby reducing the possibility of dose loss that increases especially with those patients who surely receive other drugs or may be admitted for administration of chemotherapy or radiotherapy, thus, the use of LNG-IUD provided stability of dose and regularity of administration. Despite the fact that this study was not a comparable one, other previous studies proved the superiority of LNG-IUD over oral or injectable progesterone preparations. Kau and Ertan (2008) reported that the efficacies of oral and intramuscular medroxyprogesterone acetate in the treatment of menorrhagia were comparable to each other; however, the efficacy of LNG-IUS was superior to both. Also, Sayed et al. (2011) and Shabaan et al. (2011) found out that LNG-IUS was more effective in reducing MBL than the combined oral contraceptives in women with fibroid-related and idiopathic menorrhagia, respectively.

Three cases had IUD expulsion; 2 partial and a new one was inserted and the third case was excluded because of unnoticed complete IUD expulsion for a total expulsion of 8.8%; however, this higher expulsion rate could be attributed to the small sample size as Jensen et al. (2008) reported expulsion in 23 of 509 patients for a rate of 4.5%.

Local progesterone slowly release IUD provided

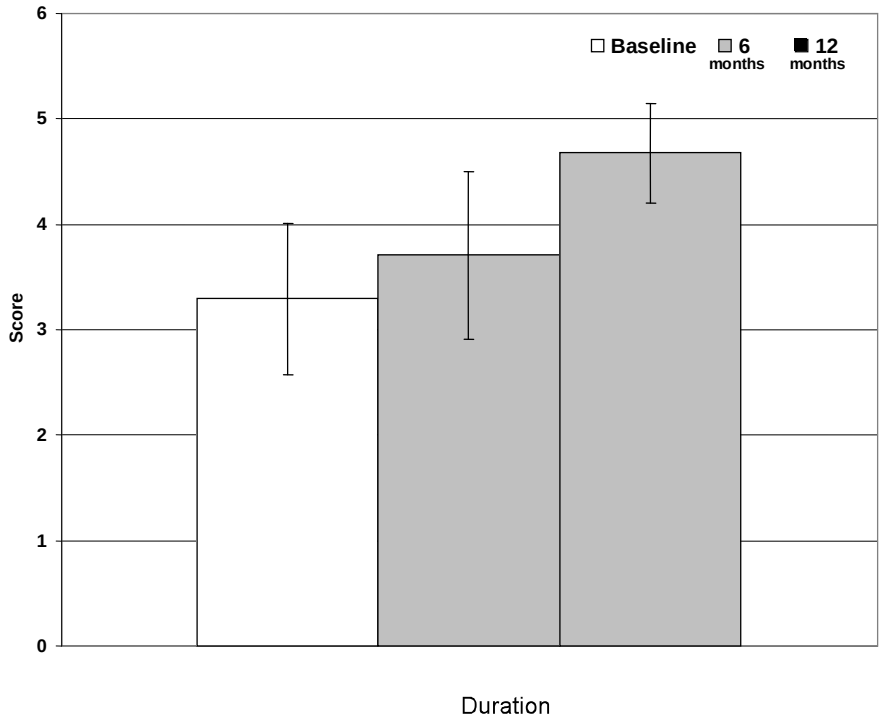

Figure 1. Mean(±SD) total QoL scores estimated at time of 6 and 12 months after enrollment.

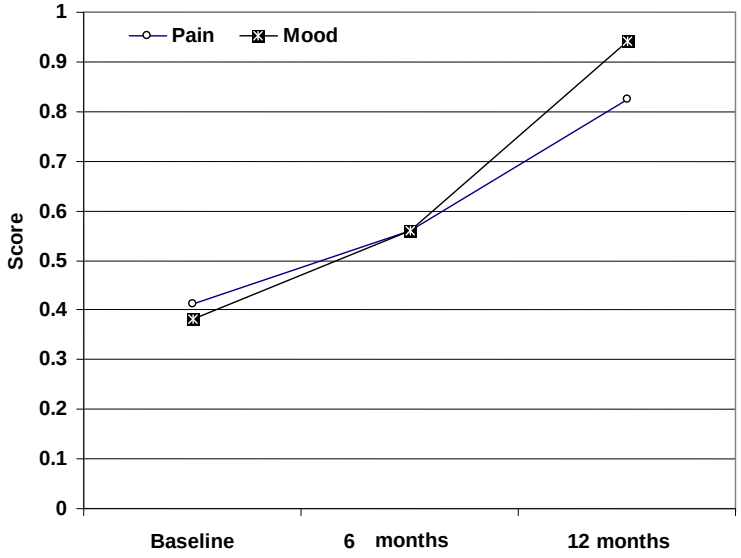

Figure 2. Mood and pain scores recorded at baseline and 6 and 12 months after enrollment.

appreciable outcome manifested as progressive decline of both duration and severity of MBL, and in parallel significantly increase hemoglobin concentration that could be attributed to the decreased loss and to complementary increased synthetic rate of red blood cells (RBCs) as manifested by the non-significant changes in serum iron and iron store ferritin. These beneficial effects are of great interest for this patients' group who had cancer-induced

anemia and anemia secondary to chemotherapy and/or radiotherapy, so their general health may not withstand a third cause of anemia in the form of excessive blood loss.

The obtained data is in line with the study of Zapata et al. (2010) who found out that most women with uterine fibroids are likely to have less MBL and higher serum levels of hemoglobin, hematocrit and ferritin after insertion of an LNG-IUD. Sayed et al. (2011) and Shabaan et al. (2011) compared the efficacy of LNG-IUS versus a low-dose combined oral contraceptive in reducing fibroid-related and idiopathic menorrhagia, respectively, and reported significant reduction of MBL and lost days with significantly increased hemoglobin levels in the LNG-IUS group.

One of the marvelous data reported in this study was the significant reduction of MBL duration and severity in the 4 patients with baseline EH, a finding indicating its applicability for management of such uterine pathology. This result is in line with Wildemeersch et al. (2007) who found continuous intrauterine delivery of LNG that appears to be a promising alternative to hysterectomy for the treatment of EH and could enhance the success rate when compared with other routes of progestagen administration, and the significant reduction of the progesterone receptor expression observed during treatment with the LNG-IUS appears to be a marker for the strong antiproliferative effect of the hormone at a cellular level resulting in an inhibition of estrogen bioactivity and endometrial suppression. Also, Chan et al. (2007) found out that LNG-IUS reduces the occurrence of de novo endometrial polyp in women treated with tamoxifen for breast cancer.

Moreover, Kesim et al. (2008) and Trinh et al. (2008) found out that LNG-IUS significantly prevent the increased risk of endometrial polyps and hyperplasia associated with the use of tamoxifen in women with breast cancer and this reduce patient discomfort while improving treatment adherence. Qi et al. (2008) reported that two infertile patients presented with complex atypical EH became pregnant following conservative treatment with LNG-IUS insertion, and histological morphology of endometrial samples after 6 months' exposure to LNG-IUS showed secretory or atrophic glands with decidualized stroma. Lee et al. (2010) reported that complete regression of simple EH was achieved, after insertion of LNG-IUS in all cases with the significant proportion achieving it within 3 months and all cases had regression within 9 months, and in the case of complex atypical hyperplasia, the regression was attained at the 9th month after insertion of LNG-IUS and as long as LNG-IUS was maintained, the EH did not recur.

Multiple studies tried to explore the underlying mechanisms for the beneficial effects of LNG-IUD on menorrhagia reduction; Koh and Singh (2010) reported enhanced endometrial expression of plasminogen activator inhibitor-1/2 in the presence of increased urokinase-like plasminogen activator receptor and tissue- type plasminogen activator antigen and concluded that the effects of LNG-IUD on hemostasis appear to be localized in the endometrium and systemic hemostasis was not duly affected and menstrual blood loss was reduced.

At the end of follow-up period, irrespective of the duration or severity of MBL, the frequency of women who had inter-menstrual spotting was increased by 9.7%. This finding was previously reported by multiple studies evaluating the outcome of LNG-IUD for menorrhagia management and could not be considered as obstacle for its use. In support of this assumption, all studied patients including those who had spotting showed significantly higher QoL score with special regard to mood parameter. These data go in hand with the study of Heikinheim et al. (2010) who found out that uterine bleeding was reduced during consecutive use of the LNG-IUS, but women with spotting at baseline continued to have more spotting than other women.

In conclusion, LNG-IUD could be considered as an appropriate therapeutic modality for tamoxifen-induced menorrhagia in patients who had mastectomy for breast cancer with significant reduction of duration and severity of MBL and improved QoL and iron indices.

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UPCOMING CONFERENCES

IMPAKT 2014 Breast Cancer Conference, Brussels, Belgium 08 May 14.

17th World Congress of Basic and Clinical Pharmacology, Cape Town, South Africa, 13 Jul 2014

Conferences and Advert

March 2014
3rd International Conference on Medical Information and Bioengineering, Penang, Malaysia, 10 Mar 2014

May 2014
2nd Annual International Conference on Health & Medical Sciences, Athens, Greece, 5 May 2014