CEOG Clinical and Experimental Obstetrics & Gynecology

Case Report

Marked improvement of the aromatase induced arthralgia syndrome following treatment with dextroamphetamine sulfate

J.H. Check[1,2], D.L. Check[2], M.P. Dougherty[3]

[1]Cooper Medical School Of Rowan University, Department of Obstetrics and Gynecology, Division of Reproductive Endocrinology & Infertility, Camden, NJ

[2]Cooper Institute For Reproductive Hormonal Disorders, P.C. Marlton, NJ

[3]The Commonwealth Medical College, Scranton, PA (USA)

Summary

Purpose: To evaluate a novel treatment for aromatase induced arteralgia (AIA) syndrome. *Materials and Methods:* A woman already treated with dextroamphetamine sulfate for many years for a form of fibromyalgia developed AIA after 15 months of taking letrozole following mastectomy for breast cancer. Though she had already been taking dextroamphetamine sulfate 30mg extended release capsules for 25 years for other issues, her dosage was increased to 45mg. *Results:* Within a short length of time, the AIA manifesting as severe bilateral shoulder pain markedly improved. *Conclusions:* About 20% of women stop aromatase inhibitor therapy before the ideal 5 year time period because of bone pain and arthralgia. Sympathomimetic therapy should be considered. Hopefully this case will stimulate a larger prospective series. *Content:* Increasing the dosage of dextroamphetamine sulfate improved the pain from aromatase-induced arthralgia manifesting with severe bilateral shoulder pain.

Key words: Aromatase inhibitor, arthralgia, dextroamphetamine sulfate, letrozole, sympathetic nervous system

Introduction

Recent studies have concluded that aromatase inhibitors are the most effective adjuvant anti-hormone therapy for post-menopausal women with estrogen receptor positive breast cancer [1]. Unfortunately about 50% of these women who are treated with aromatase inhibitors complain of significant joint pain which has been termed aromatase inhibitor-induced arthralgia (AIA) syndrome [2-4]. The pain can be so bothersome that 13-22% will stop the aromatase inhibitors before the five-year recommended time [4, 5].

There has not been found an ideal therapy other than stopping the aromatase treatment. Unfortunately stopping treatment may preclude the best outcome for preventing recurrence of breast cancer or new lesions in the other breast. Occasionally switching to another aromatase inhibitor may be helpful [6]. Reported, herein, may be a new treatment option for AIA, treatment with dextroamphetamine sulfate.

Case Report

A 53-year-old woman developed Stage I breast cancer and was treated with a mastectomy. She was subsequently treated with letrozole 2.5 mg daily. After 15 months she developed severe right shoulder pain. Following an evaluation with an orthopedic specialist, no organic cause was determined by testing. She was diagnosed with a frozen shoulder syndrome.

She proceeded with physical therapy, but not only did she not improve, but the pain spread to her left shoulder. The pain was worse at night and would keep her from sleeping most of the night. Non-steroidal anti-inflammatory drugs did not relieve the pain. This woman had been treated for 25 years for unexplained thigh pain and edema which was exacerbated by running. This was completely relieved by treating with dextroamphetamine sulfate which has been very effective for many other pain syndromes and has been called the sympathetic neural hyperalgesia edema syndrome [7-9]. In fact, she had been on 30 mg extended release capsules when the arthralgia began. A decision was made to increase the dosage of dextroamphetamine sulfate to 45 mg per day. Within three weeks the pain diminished to the point that she has been able to sleep during the night. The pain is still present but much better and is reduced sufficiently to allow her to function normally. In fact she does not need to even take aspirin or other non-steroidal inflammatory drugs but sometimes uses a heating pad.

Discussion

Sympathomimetic amine therapy has been successful in treating previously intractable pain syndromes involving the musculoskeletal system [7-11]. The median time of treatment with aromatase inhibitors and the AIA syndrome is 1.6 years, similar to this patient who is reported herein [4]. One cannot state with certainty that the pain was caused

Revised manuscript accepted for publication February 22, 2018

Clin. Exp. Obstet. Gynecol. - ISSN: 0390-6663
XLVI, n. 2, 2019
doi: 10.12891/ceog4707.2019

7847050 Canada Inc.
www.irog.net

Published: 10 April 2019

by the letrozole since it has been suggested that to demonstrate the existence of AIA, one should demonstrate abatement of symptoms after stopping aromatase drugs and return of symptoms when resuming, and this was not done for this patient.

The marked improvement of pain persisted for 12 months and is enabling her to remain on aromatase therapy hopefully for the five years that is planned. At the 2014 American Association for Cancer Research, Nirwvath *et al.,* presented the theoretical basis for prescribing high dosage vitamin D to help the AIA syndrome. They are approved for a randomized controlled study of 184 women, half of which will receive high dosage vitamin D (50,000 IU vitamin D) three times per week for 12 weeks, followed by 2,000 IU vitamin D for 40 weeks, whereas the controls will receive standard dose vitamin D3 of 800 IU vitamin D3 daily for 52 weeks [12]. High-dosage vitamin D3 has several potential side effects. In contrast dextroamphetamine sulfate is very well tolerated and in the dosages used can be stopped abruptly without withdrawal symptoms and drug dependence does not occur in the usual prescribed dosages [7]. One does not usually develop resistance to this treatment over time. Thus, it is hoped that this case report can stimulate a trial of dextroamphetamine sulfate for AIA especially if the high dose vitamin D trial does not prove very effective [12].

References

[1] Puglisi F., Minisni A.M.: "Adjuvant endocrine therapy in postmenopausal breast cancer patients: Does hormone receptor status influence decision-making?" *Oncol. Hemat.*, 2011, *77*, 87.

[2] Niravath P.: "Aromatase inhibitor-induced arthralgia: a review". *Ann. Oncol.*, 2013, *24*, 1443.

[3] Crew K., Greeniee H., Capodice J., Raptis G., Brafman L., Fuentes D., et al.: "Prevalence of joint symptoms in postmenopausal women taking aromatase inhibitors for early stage breast cancer". *J. Clin. Oncol.*, 2007, *25*, 3677.

[4] Henry N., Giles J., Ang D., Mohan M., Dadabhoy D., Robarge J., *et al.*: "Prospective characterization of musculoskeletal symnptoms in early stage breast cancer patients treated with aromatase inhibitors". *Breast Cancer Res. Treat.*, 2008, *111*, 365.

[5] Dent S., DeValentin T., Vendermeer L., Spaans J., Verma S.: "Long term toxicities in women with early stage breast cancer treated with aromatase inhibitors: data from a tertiary care center". *Breast Cancer Res. Treat*., 2006, *100*, S190.

[6] Briot K., Tubiana-Hullin M., Bastit L., Kloos I., Roux C.: "Effect of a switch of aromatase inhibitors on musculoskeletal symptoms in postmenopausal women with hormone-receptor-positive breast cancer: the ATOLL study". *Breast Cancer Res. Treat.*, 2010, *120*, 127.

[7] Check J.H., Cohen R., Katsoff B., Check D.: "Hypofunction of the sympathetic nervous system is an etiologic factor for a wide variety of chronic treatment-refractory pathologic disorders which all respond to therapy with sympathomimetic amines". *Med. Hypoth.*, 2011, *77*, 717.

[8] Check J.H., Cohen R.: "Marked improvement of headaches and vasomotor symptoms with sympathomimetic amines in a woman with the sympathetic hyperalgesia-edema syndrome". *Clin. Exp. Obstet. Gynecol.*, 2011, *38*, 88.

[9] Boimel P., Check J.H.: "Marked improvement of intractable arthritic pain in a woman with rheumatoid arthritis with sympathomimetic amine treatment despite previous failure with standard therapy and possible implications for last trimester unexplained fetal demise – case report". *Clin. Exp. Obstet. Gynecol.*, 2007, *34*, 254.

[10] Check JH, Cohen R: Marked improvement of pain from long term fibromyalgia with dextroamphetamine sulfate in a woman who failed to improve with conventional pharmacologic treatment. *Clin. Exp. Obstet. Gynecol.*, 2014, *41*, 90.

[11] Check JH, Cohen R: Sympathomimetic amine therapy found effective for treatment of refractory chronic complex regional pain syndrome (reflex sympathetic dystrophy). *Clin. Exp. Obstet. Gynecol.*, 2014, *41*, 478.

[12] Niravath P.A., Hilsenbeck S., Wang T., Rimawi M.: "A randomized, controlled trial of high dose vs. standard dose vitamin D for aromatase inhibitor-induced arthralgia in breast cancer survivors. Proceedings, Part 2: Clinical Trials and Late-Breaking Abstracts from the 105th Annual Meeting of the American Association for Cancer Research, April 5-9, 2014, San Diego, CA. Philadelphia, abstract #CT319. *Cancer Res.*, 2014, *74*, CT319.

Corresponding Author:
J.H. CHECK
7447 Old York Road
Melrose Park, PA 19027 (USA)
e-mail: laurie@ccivf.com